



US 20250257408A1

(19) United States

(12) Patent Application Publication

BILLIA et al.

(10) Pub. No.: US 2025/0257408 A1

(43) Pub. Date: Aug. 14, 2025

## (54) CLONAL HEMATOPOIESIS AS A BIOMARKER

(71) Applicant: UNIVERSITY HEALTH NETWORK, Toronto (CA)

(72) Inventors: Filio BILLIA, Toronto (CA); John DICK, Toronto (CA); Robert VANNER, Toronto (CA); Jessie MEDEIROS, Brampton (CA); Fernando SCOLARI, Rio Grande do Sul (BR); Sagi ABELSON, Toronto (CA)

(21) Appl. No.: 18/859,154

(22) PCT Filed: Apr. 24, 2023

(86) PCT No.: PCT/CA2023/050553

§ 371 (c)(1),

(2) Date: Oct. 22, 2024

## Related U.S. Application Data

(60) Provisional application No. 63/333,628, filed on Apr. 22, 2022.

## Publication Classification

## (51) Int. Cl.

C12Q 1/6886 (2018.01)

C12Q 1/6869 (2018.01)

G16B 20/20 (2019.01)

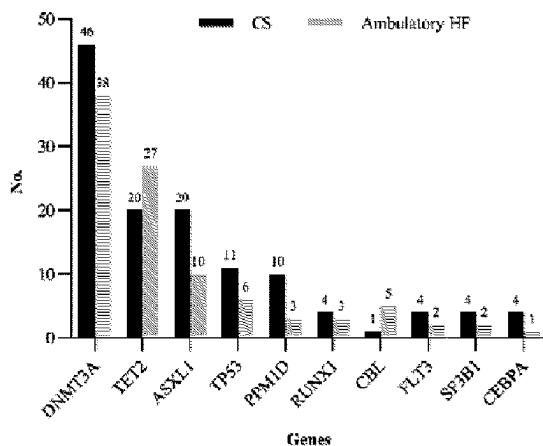
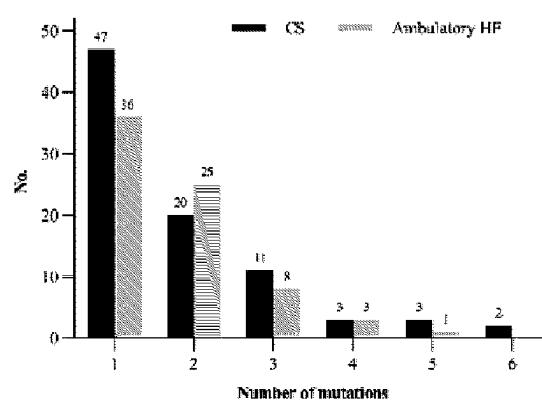
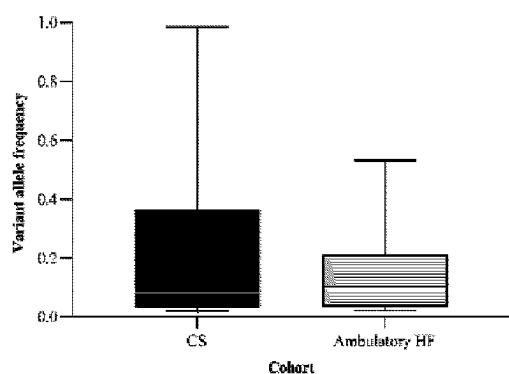
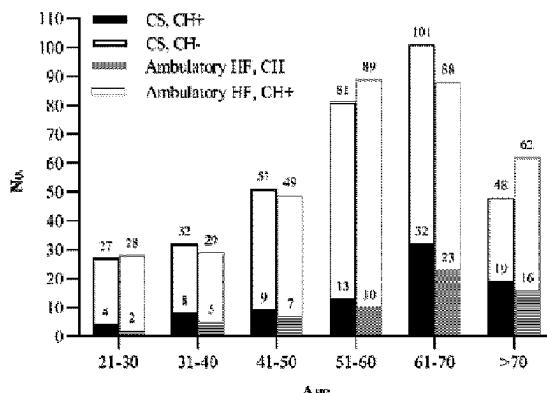
G16H 50/30 (2018.01)

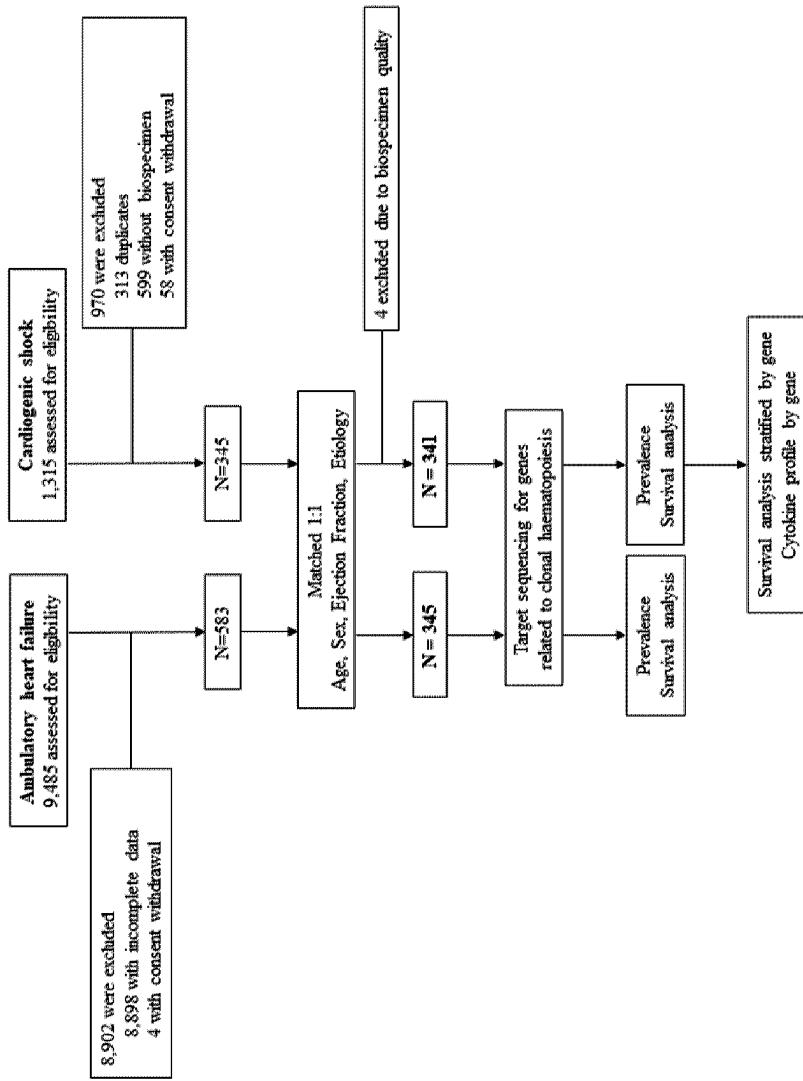
## (52) U.S. Cl.

CPC ..... C12Q 1/6886 (2013.01); C12Q 1/6869 (2013.01); G16B 20/20 (2019.02); G16H 50/30 (2018.01); C12Q 2600/106 (2013.01); C12Q 2600/118 (2013.01); C12Q 2600/156 (2013.01)

## (57) ABSTRACT

There is described herein methods predicting the risk of various disease condition by measuring clonal hematopoiesis in a patient, probes used to make such measurement and methods for treatment or preventive treatment of the disease condition.

**A****B****C****D**



**Figure 1**

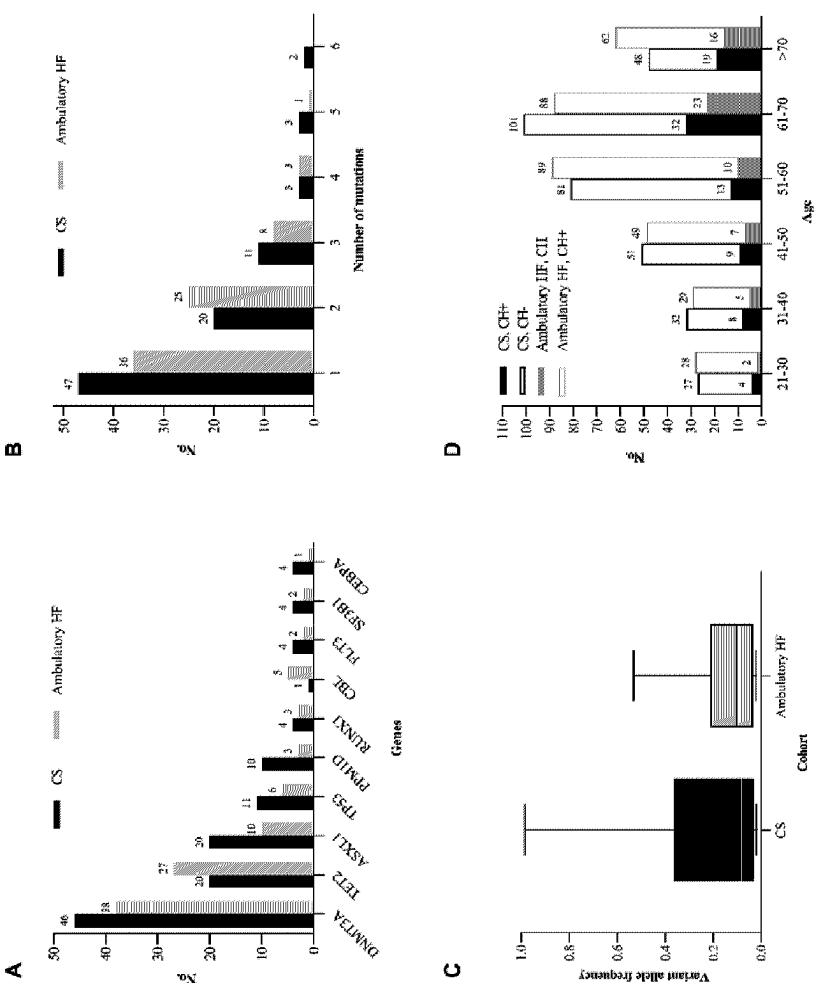


Figure 2

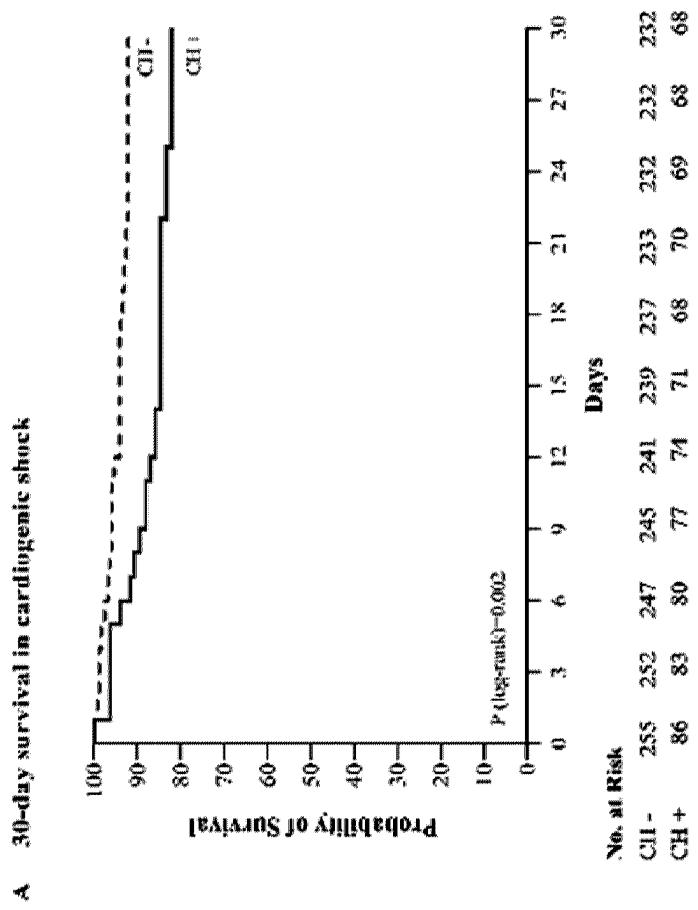


Figure 3

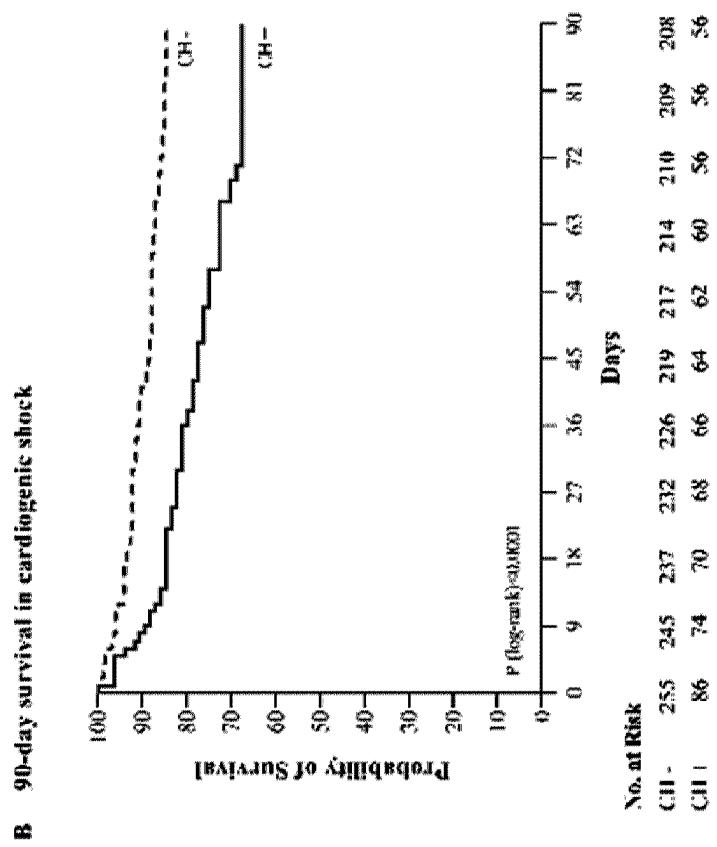


Figure 3

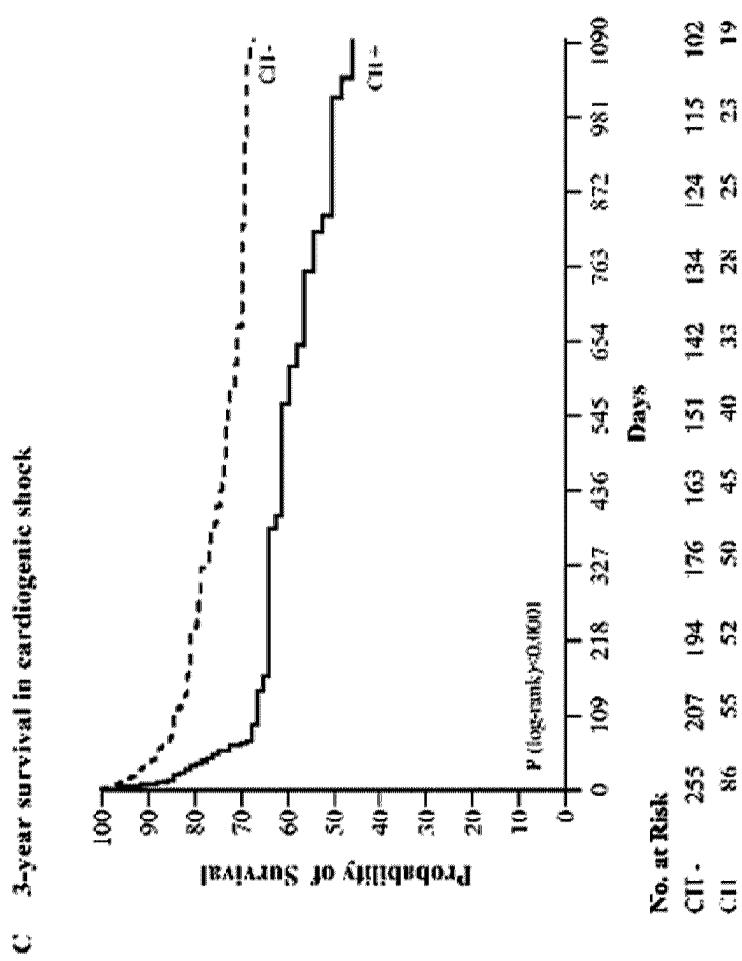


Figure 3

D 30-day survival according to specific genes mutations

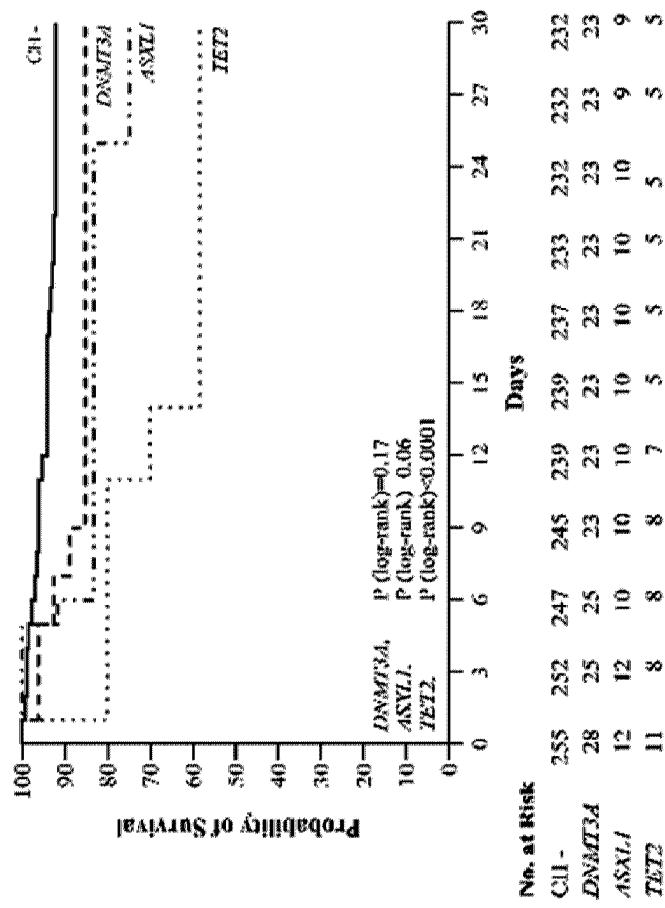


Figure 3

E 90-day survival according to specific genes mutations

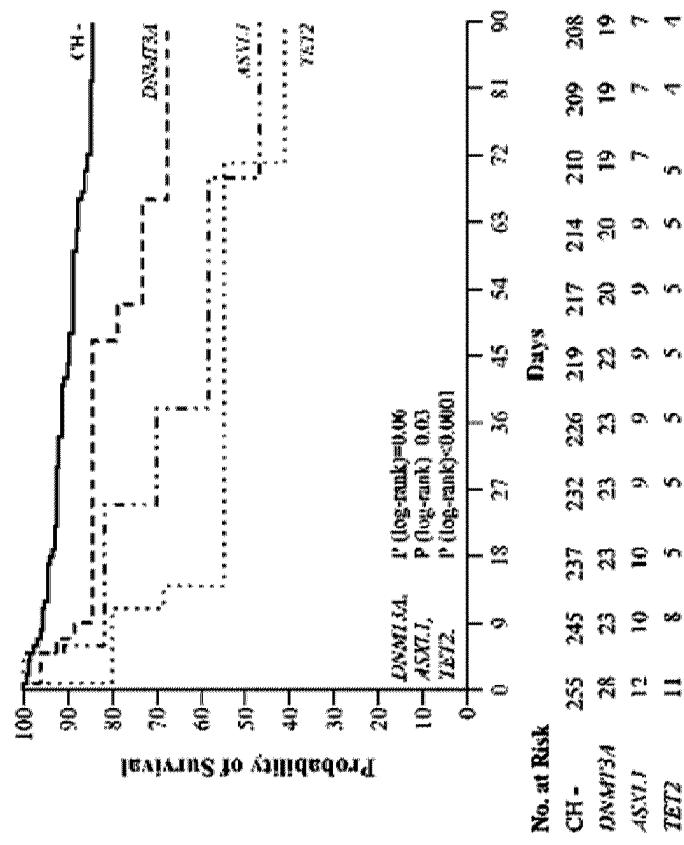
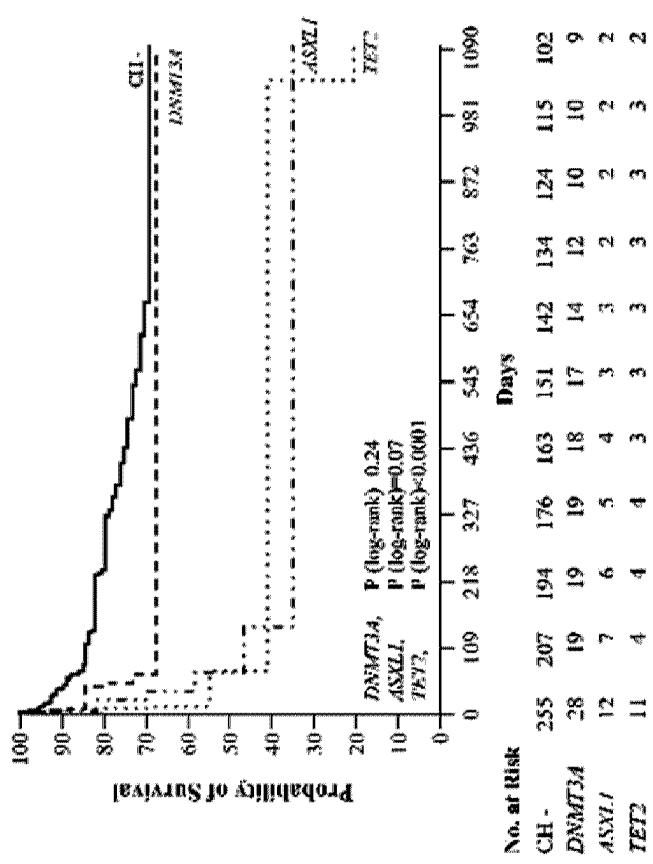
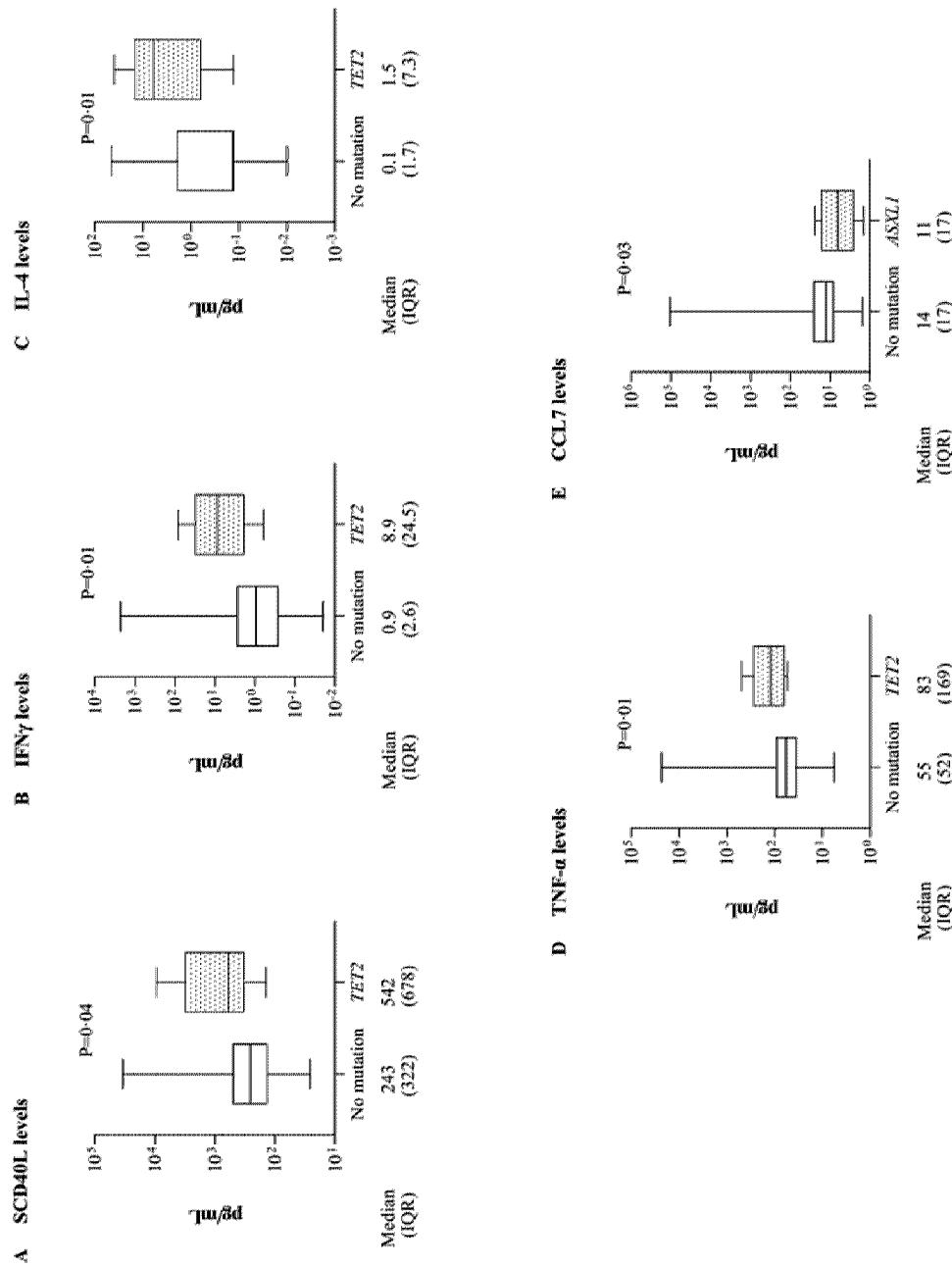


Figure 3

F: 3-year survival according to specific genes mutations



**Figure 3**



**Figure 4**

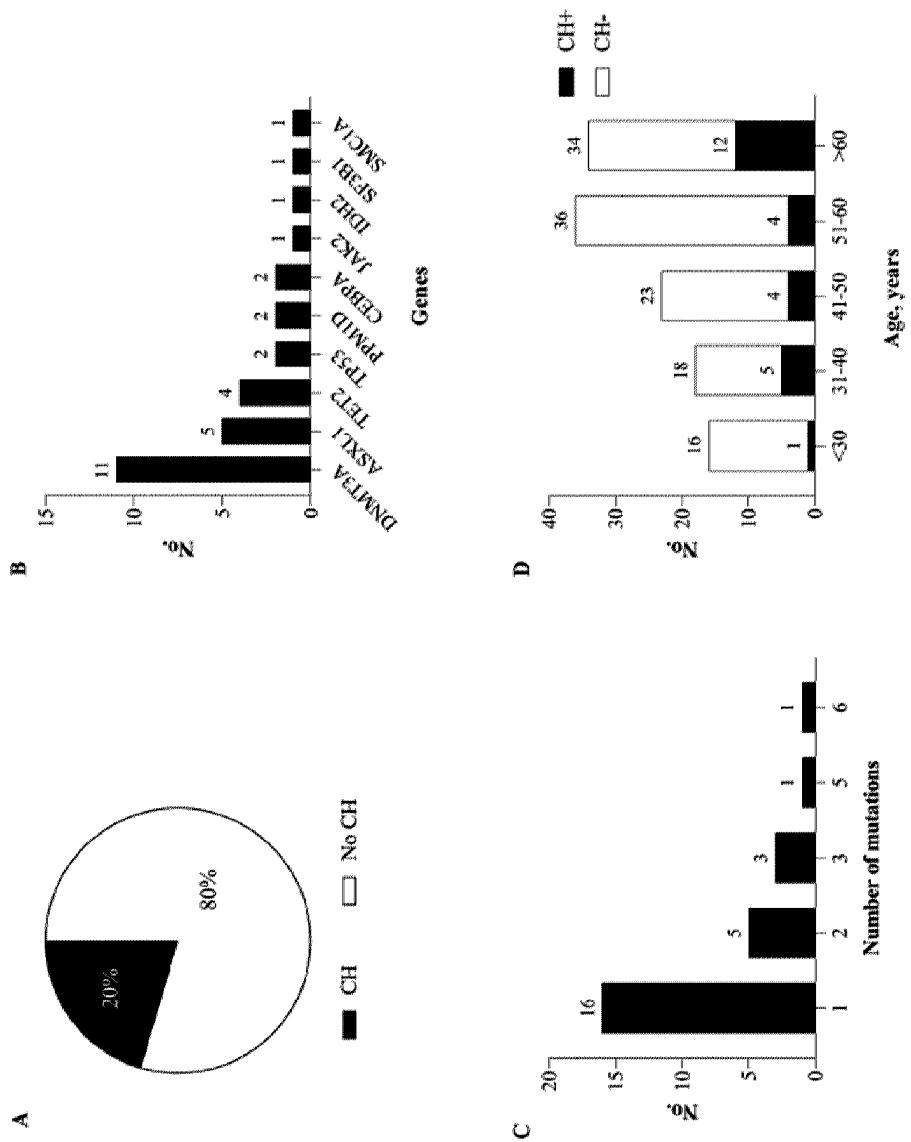


Figure 5

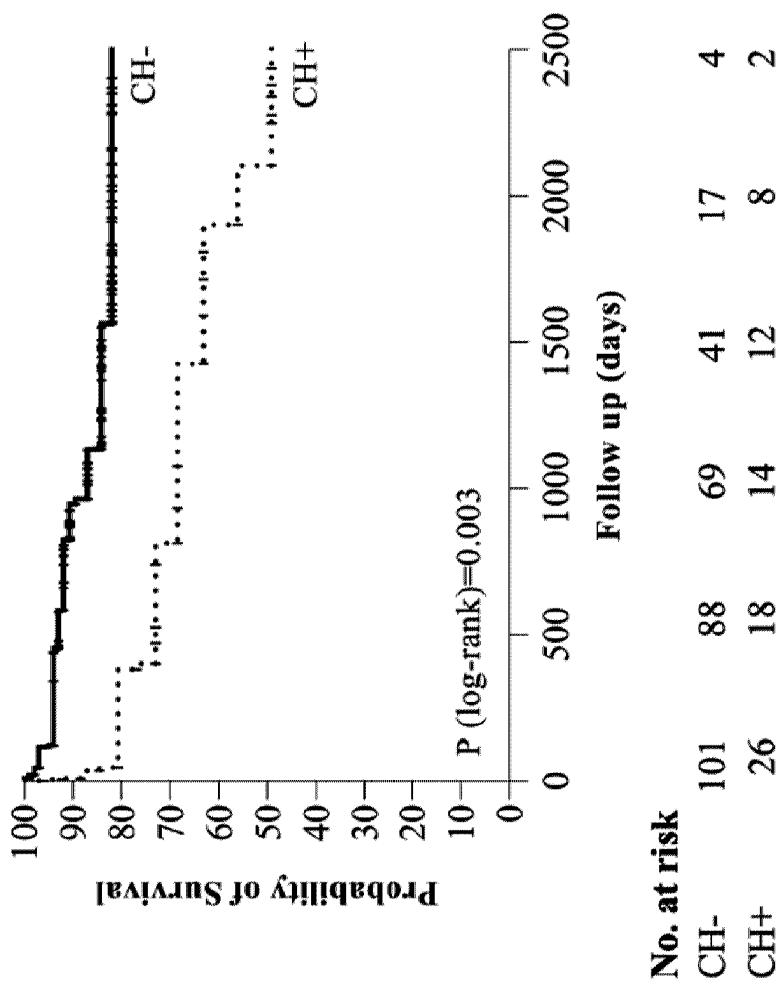


Figure 6

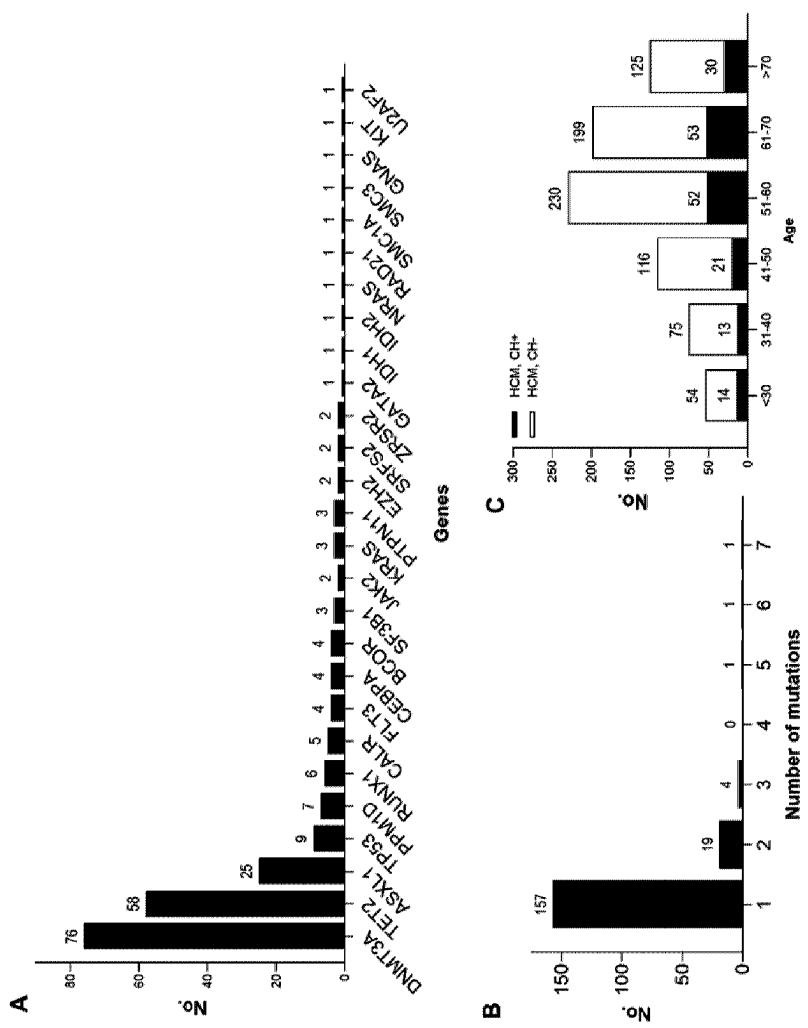
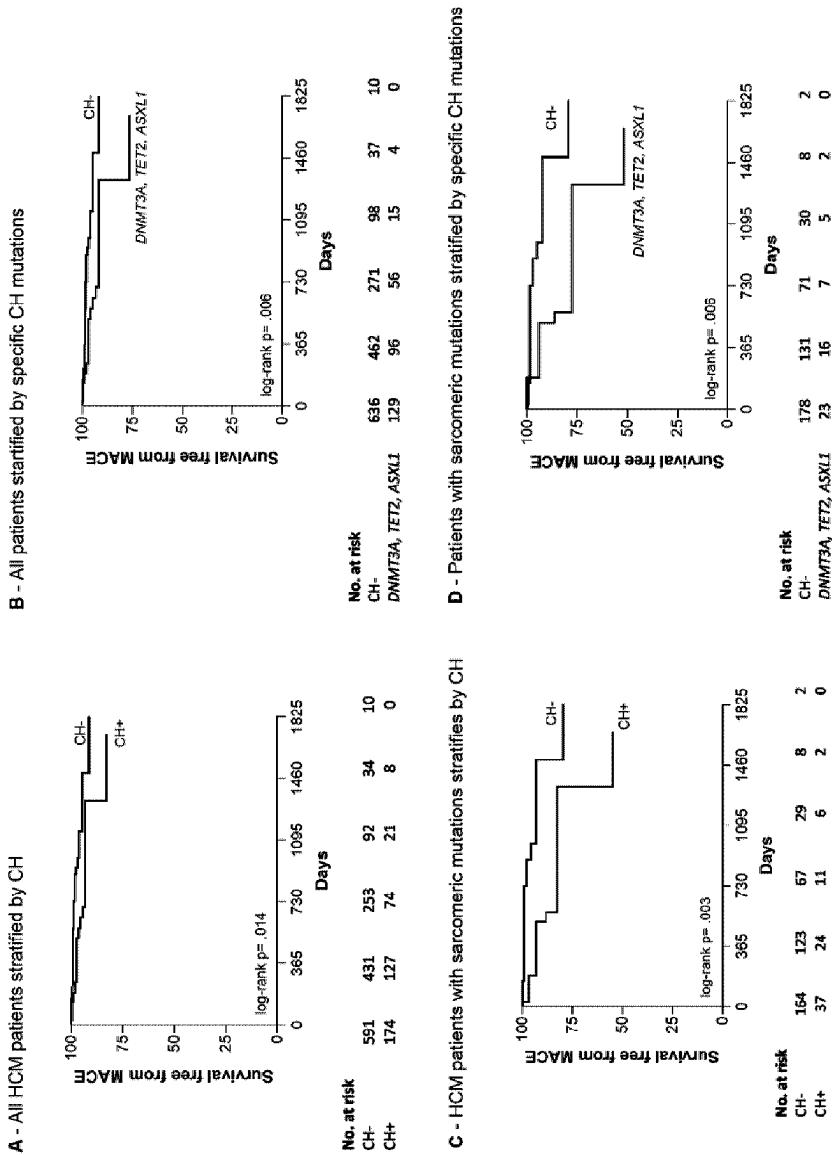
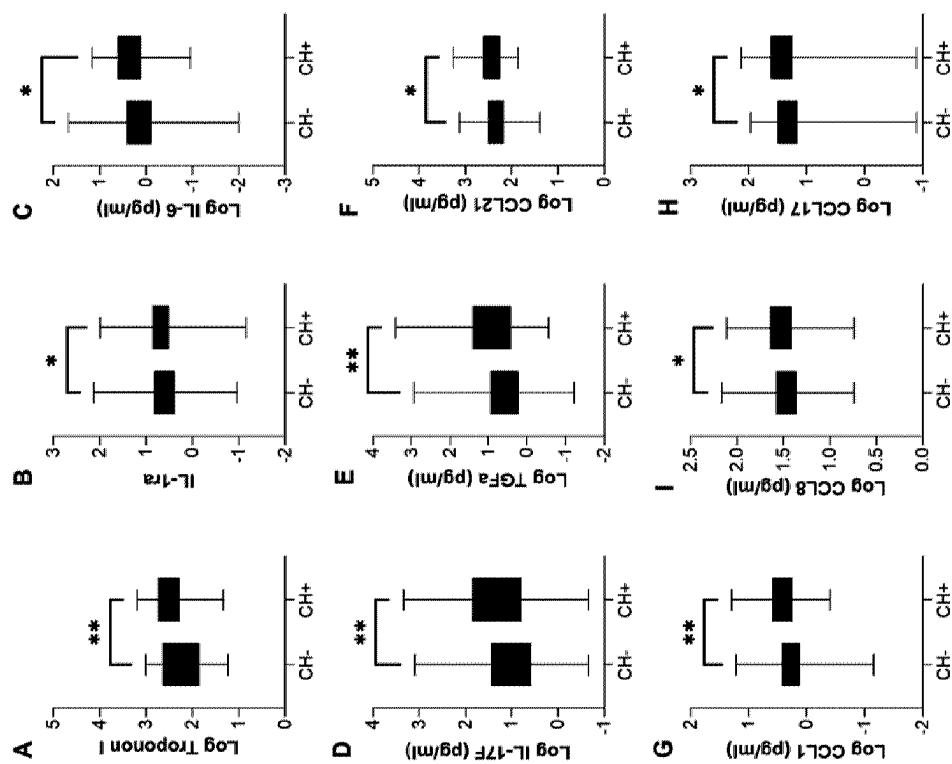


Figure 7



**Figure 8**



**Figure 9**

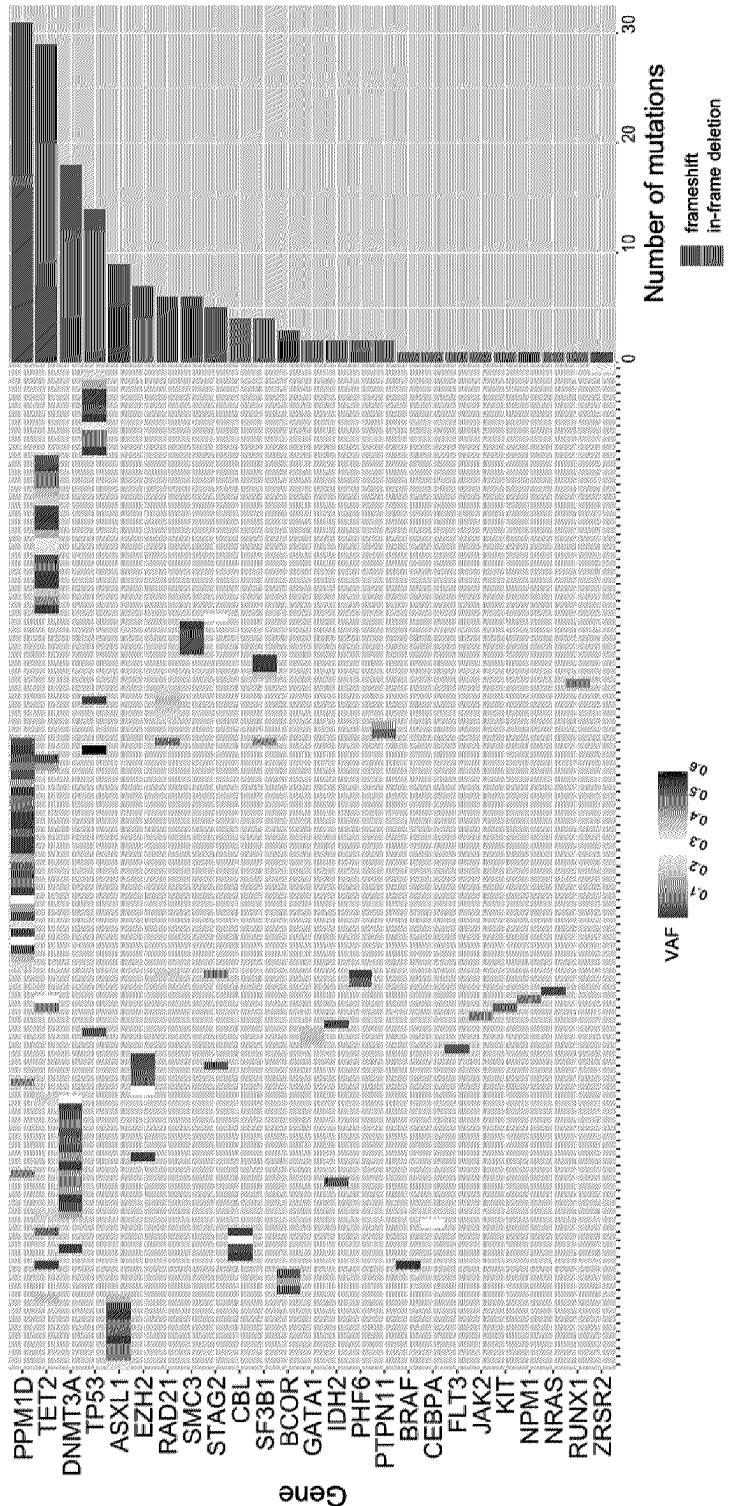


Figure 10A

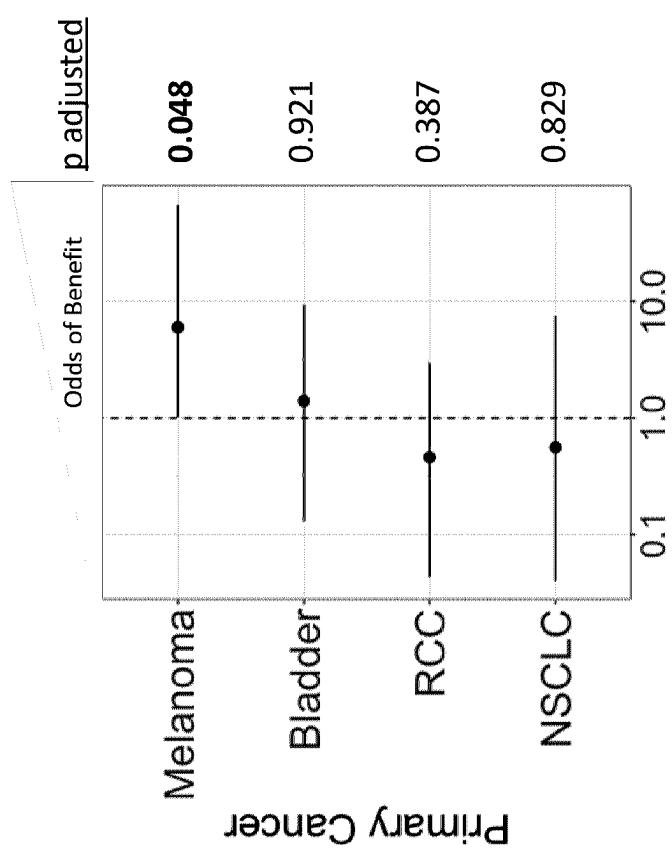


Figure 10B

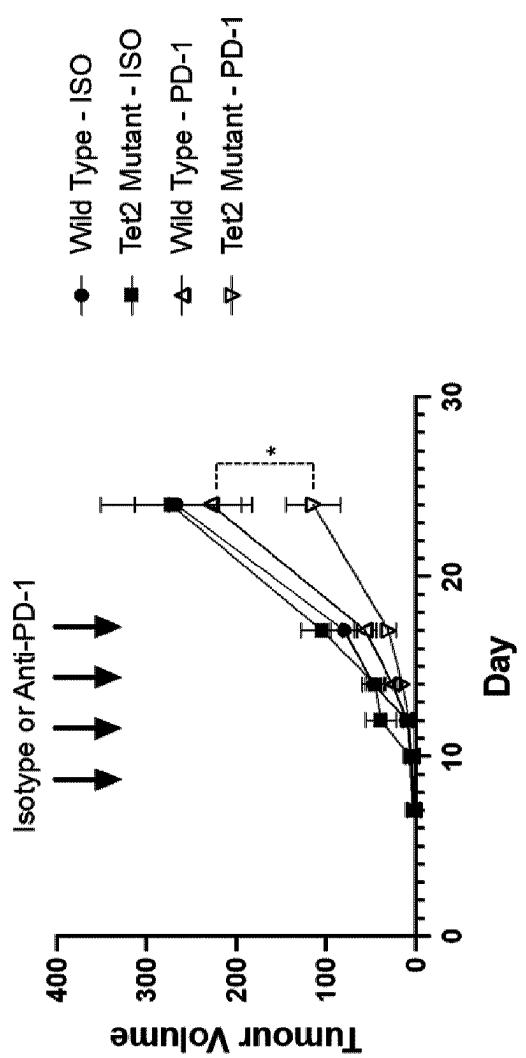


Figure 10C

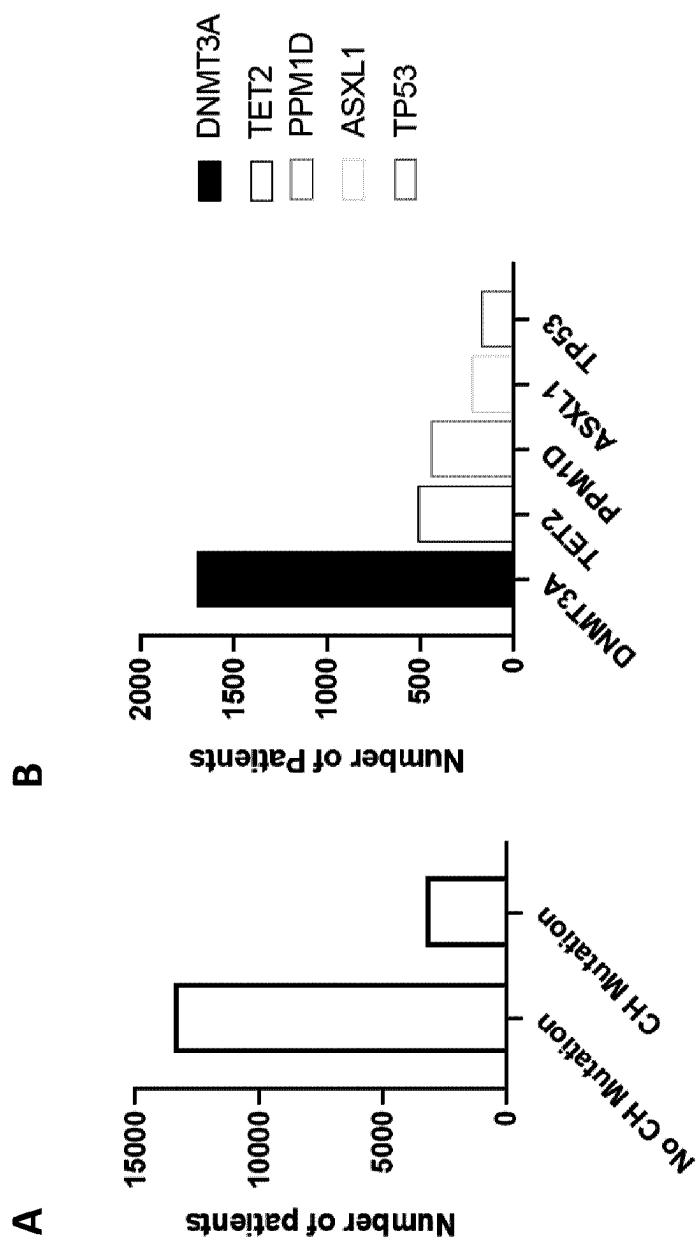
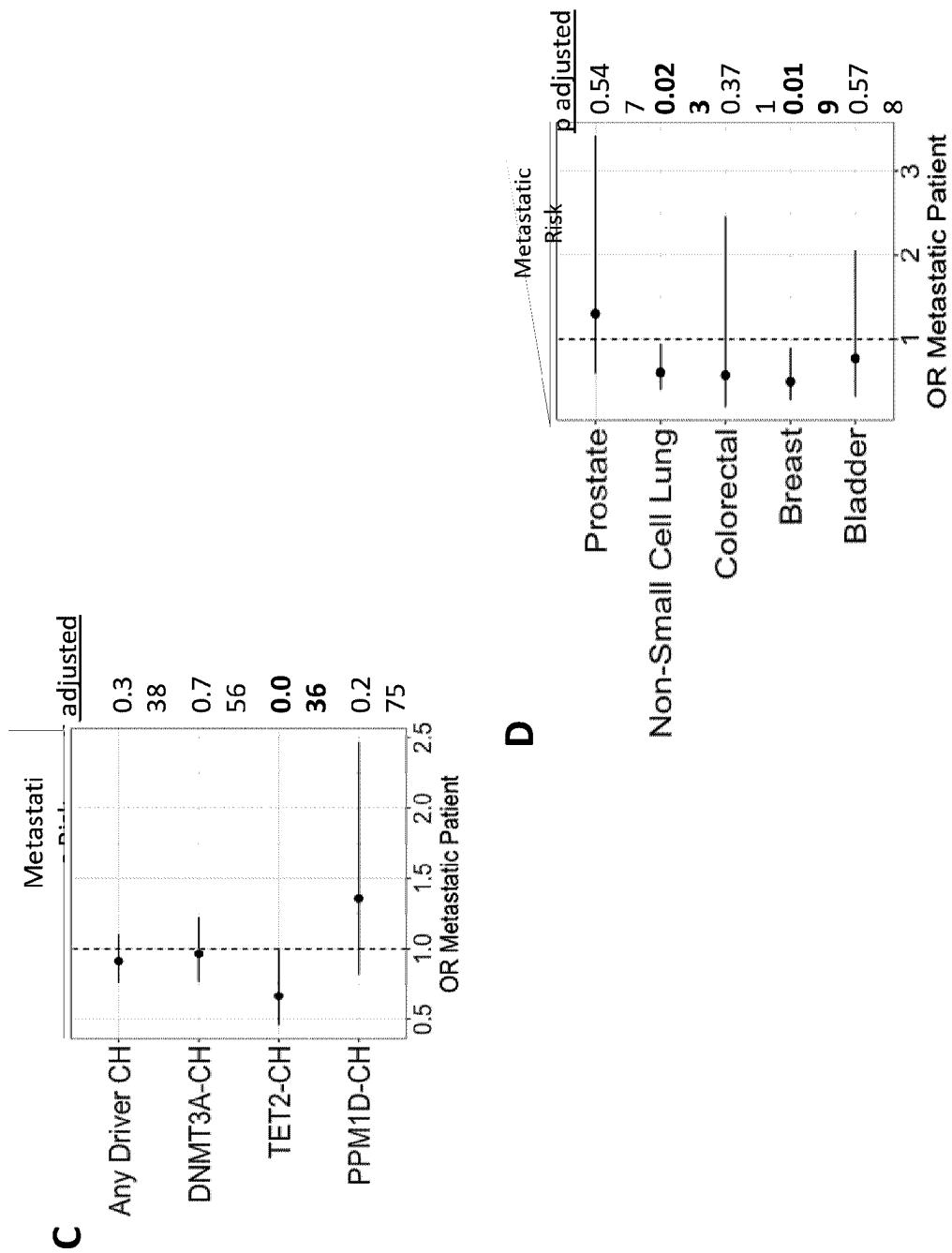
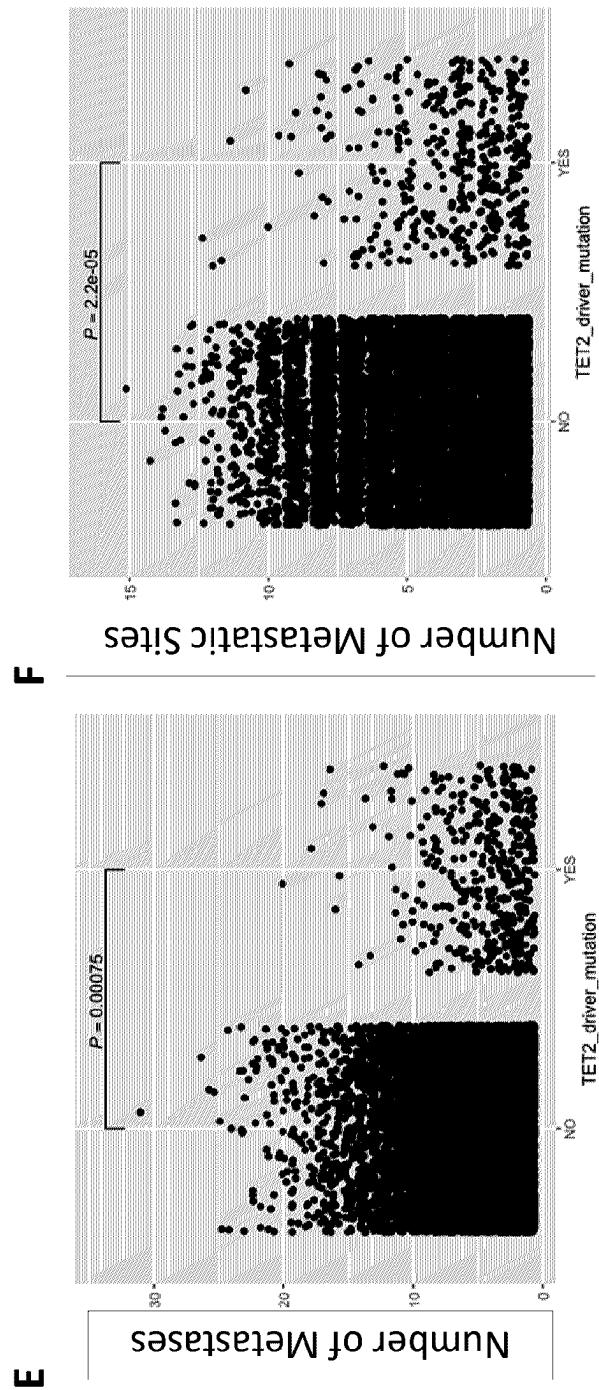


Figure 11



**Figure 11**



**Figure 11**

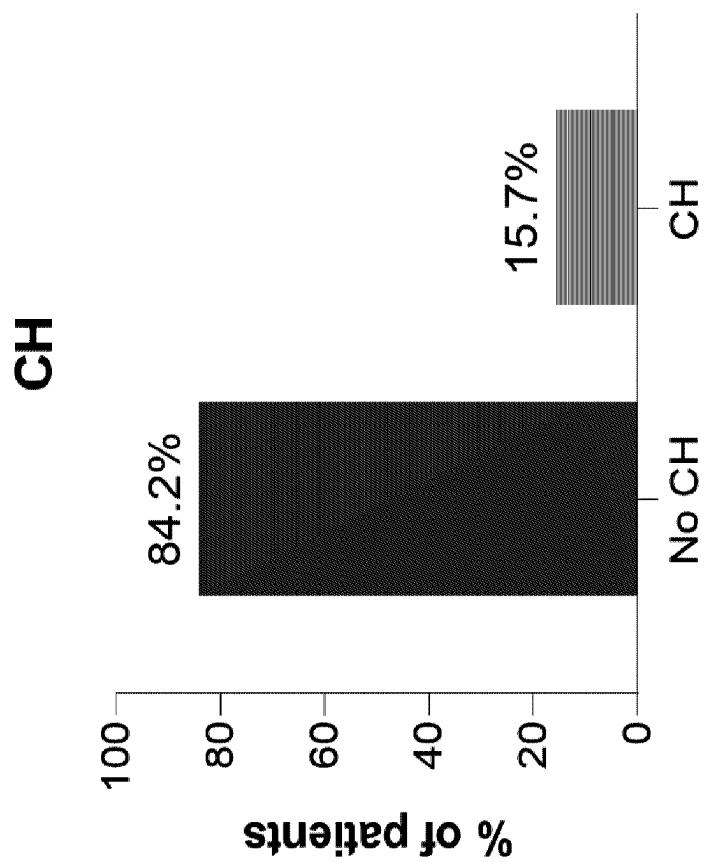


Figure 12

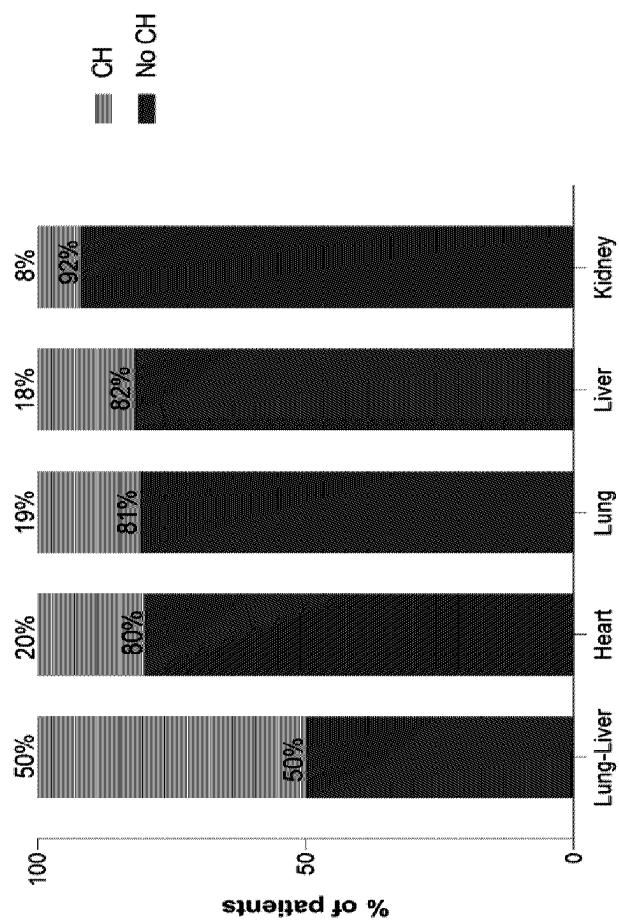


Figure 13

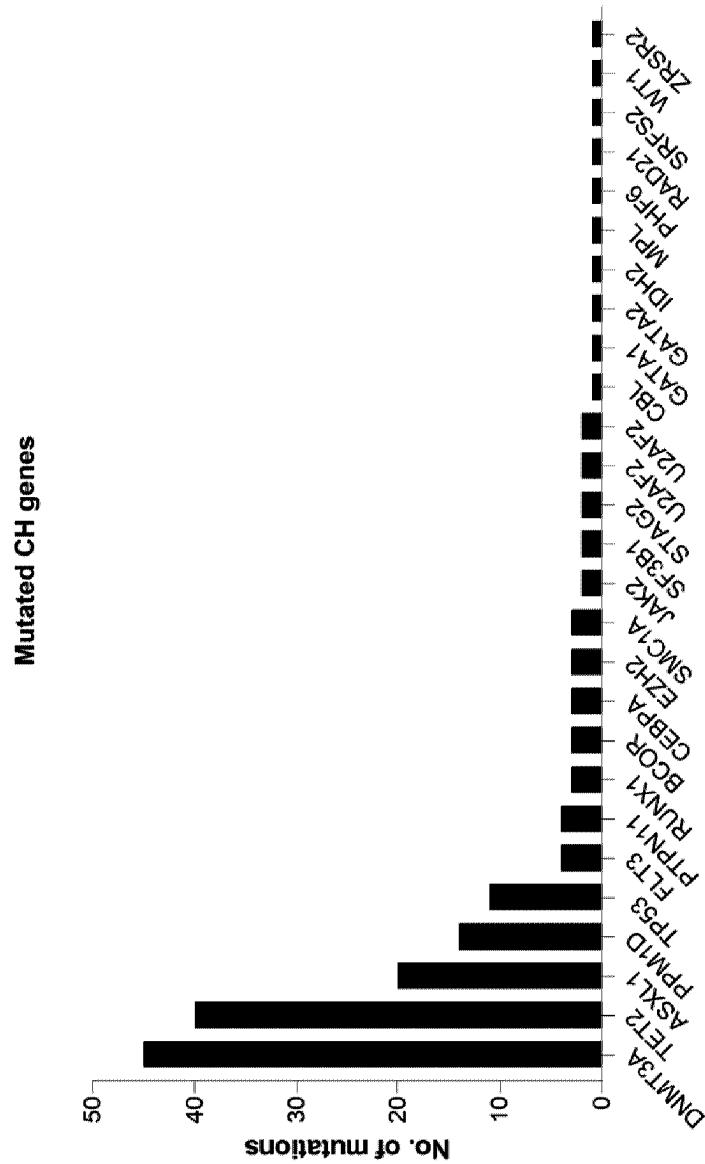


Figure 14

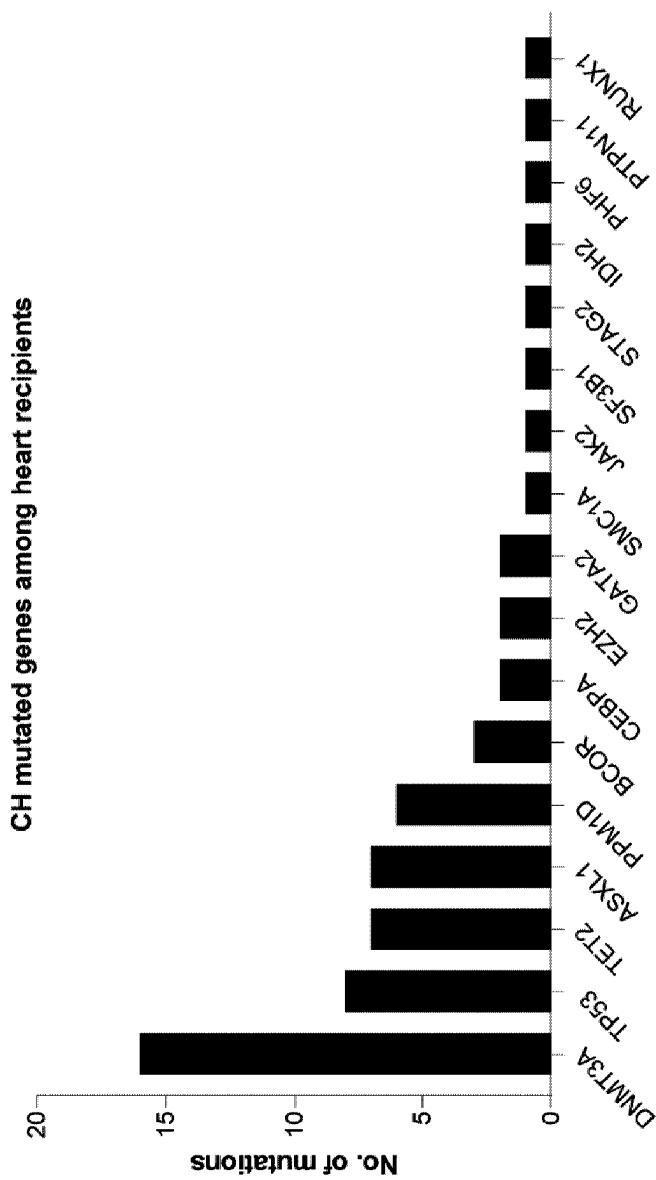


Figure 15

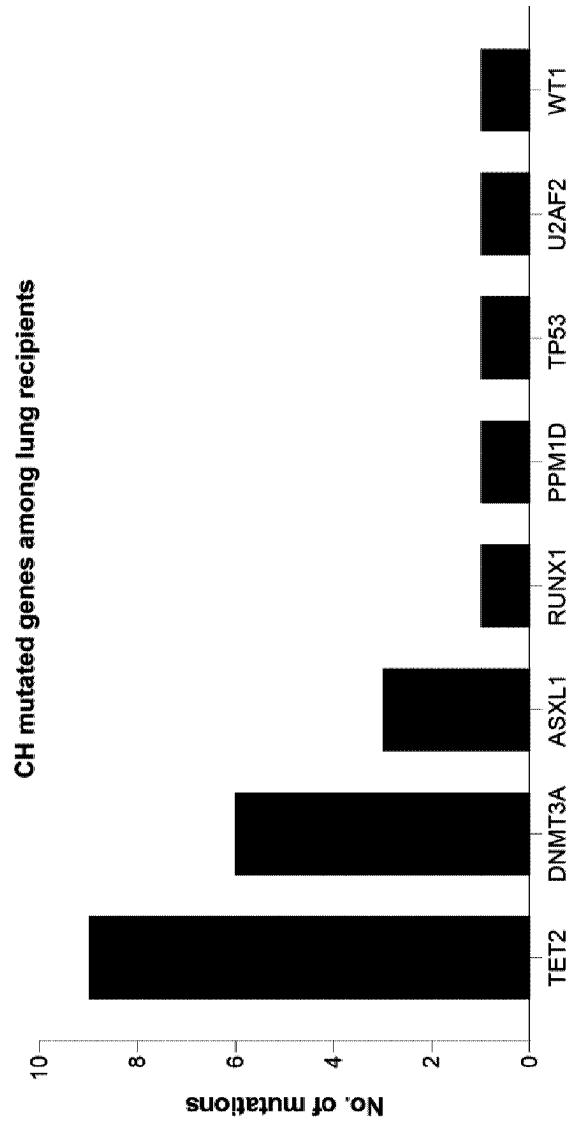


Figure 16

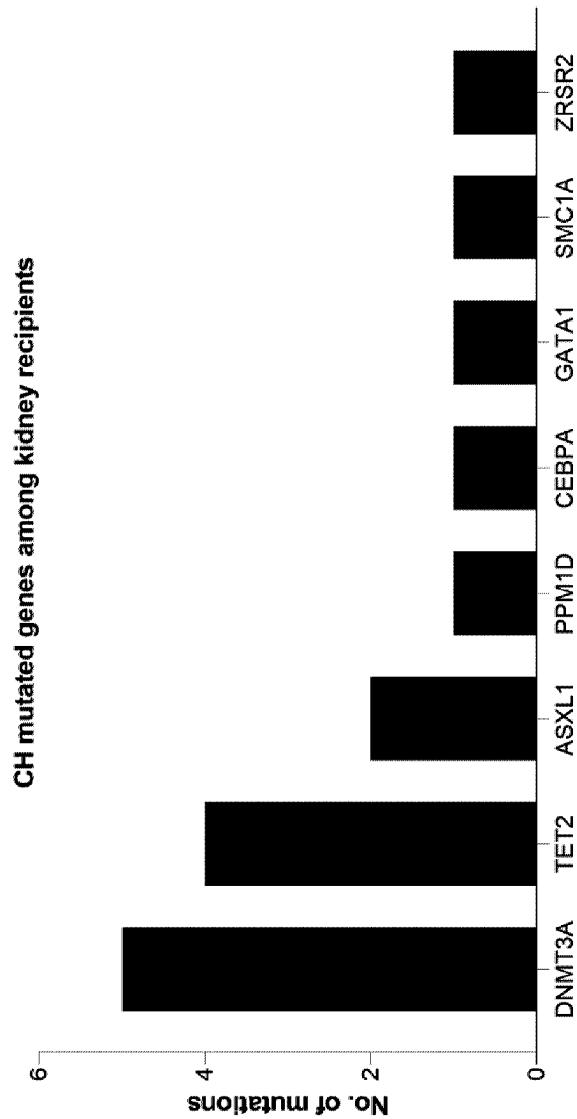


Figure 17

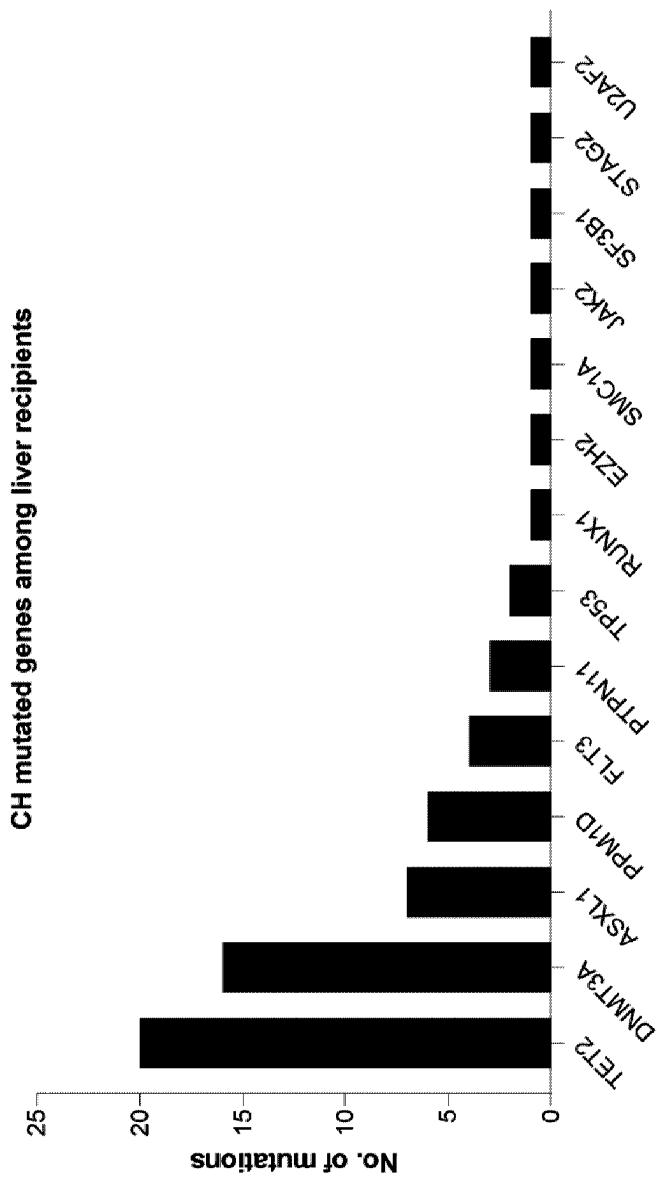
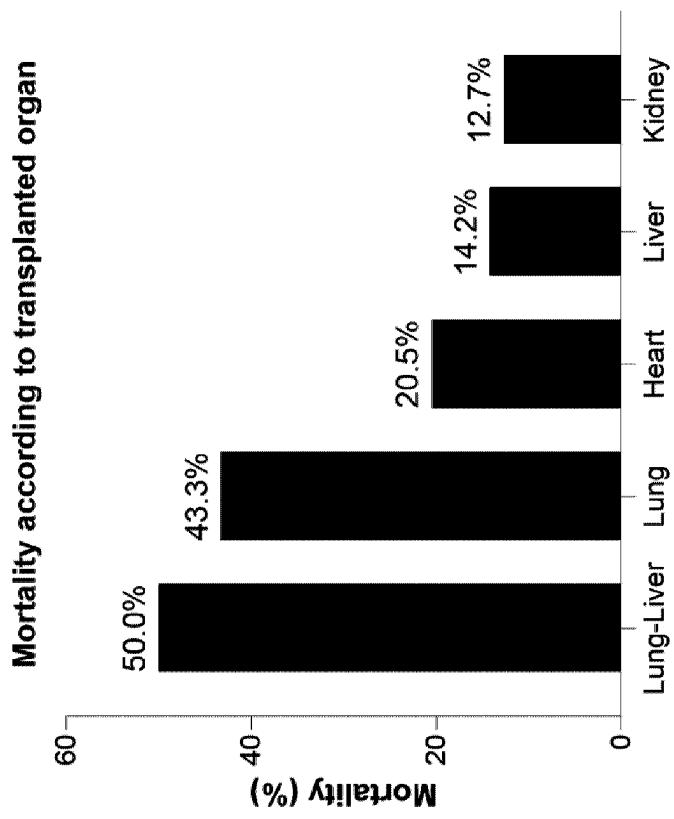


Figure 18



**Figure 19**

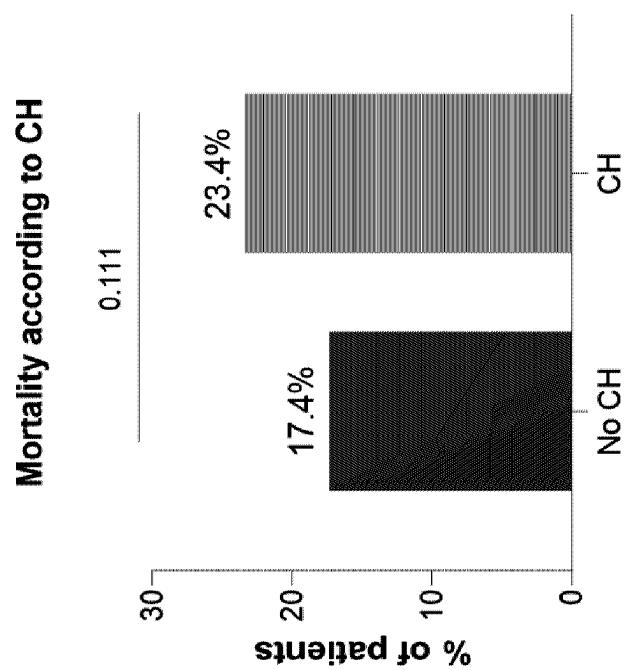


Figure 20

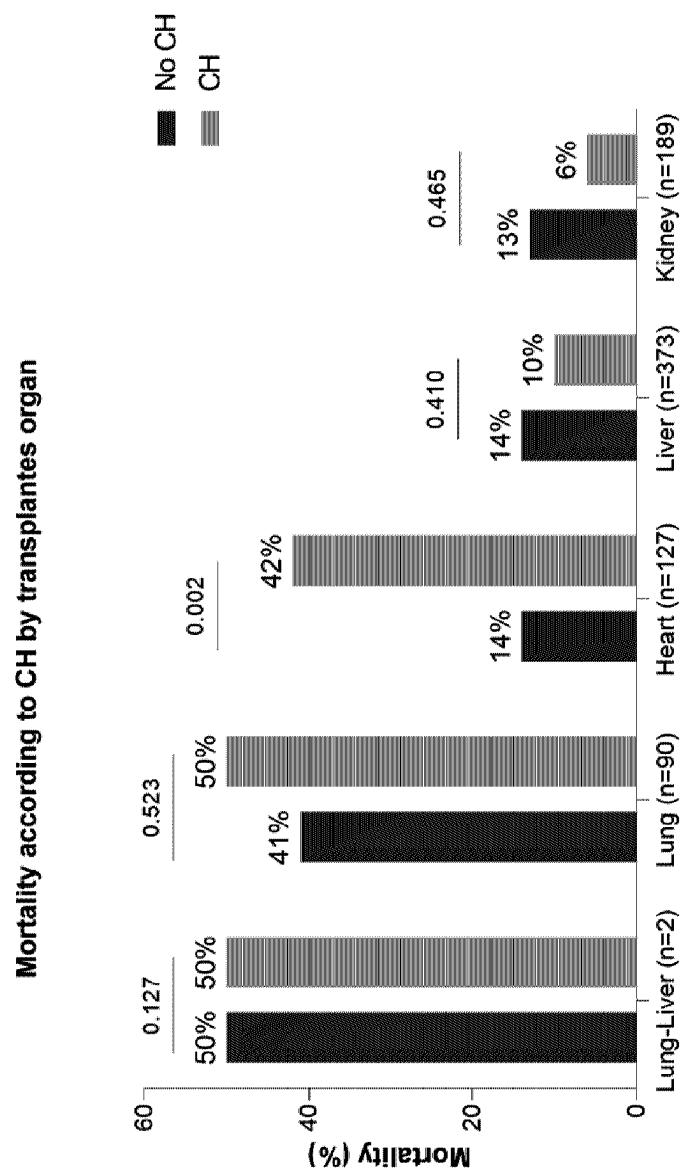


Figure 21

## CLONAL HEMATOPOIESIS AS A BIOMARKER

### RELATED APPLICATIONS

[0001] This application claims priority to U.S. Provisional Application No. 63/333,628 filed on Apr. 22, 2022, which is hereby incorporated by reference in its entirety.

### FIELD OF THE INVENTION

[0002] The invention relates to the measurement of clonal haematopoiesis for the purposes of assessing the risk associated with various disease states, particularly relating to solid organs and/or cancer.

### BACKGROUND OF THE INVENTION

[0003] Clonal haematopoiesis (CH) is the acquisition of mutations in hematopoietic stem cells that results in selective clonal expansion leading to enhanced systemic inflammation.<sup>5</sup> While early studies had shown that at least 10% of individuals harbour CH mutations in their seventies,<sup>5</sup> more sensitive techniques have demonstrated that CH mutations are ubiquitous in healthy middle-age adults.<sup>6,7</sup> Despite these mutations increasing the risk of haematological cancer development, progression to malignancy is low.<sup>8</sup>

[0004] Interestingly, CH is also associated with elevated cardiovascular risk;<sup>5,9,10</sup> more than most traditional risk factors.<sup>11</sup> The presence of CH mutations is linked to a 25% increase in the incidence of de novo heart failure (HF) and a 2-fold increase in mortality in patients with pre-existing HF.<sup>9,12</sup> In animal models of HF, mice harbouring CH mutations developed adverse left ventricular (LV) remodelling with fibrosis and a concomitant increase in IL-6 and IL-1 $\beta$ .<sup>13</sup>

[0005] However, the incidence of CH in more specific cardiac diseases, specific cancers and diseases in other organs, and its impact in clinical outcomes, remains unknown.

[0006] For example, cardiogenic shock (CS) is a life-threatening condition with markedly reduced cardiac output resulting in multi-organ failure.<sup>1</sup> Despite increasing recognition of CS and implementation of intensive therapies, morbidity and mortality remain exceedingly high.<sup>2</sup> The evolving epidemiological descriptions of CS patients illustrate that there is a large variability in the underlying aetiology, response to medical therapy, and outcomes.<sup>1,3</sup> The association of a systemic inflammatory response syndrome with worse outcomes in CS<sup>3</sup> could be a key to understanding the heterogeneity in the natural history of CS and uncover new pathways to target for treatment.<sup>4</sup>

[0007] Further, orthotopic heart transplant (OHT) is the treatment of choice for patients with advanced heart failure to improve quality of life and survival.<sup>51</sup> In the United States, over 80,000 HT were performed in the past three decades and over 5,000 yearly worldwide.<sup>s2, s3</sup> However, despite the improvement in donor and recipient pre-transplant care, post-transplant survival is affected by a number of complications including infections due to long-term immunosuppression therapy, cancer development and cardiac allograft vasculopathy (CAV).<sup>s4, s5</sup> OHT recipients require extensive monitoring after transplantation with endomyocardial biopsies (EMB) for rejection vigilance, viral detection for opportunistic infection, echocardiograms and coronary angiography for allograft function and CAV assessment to instill early treatment and improve survival.<sup>4</sup>

Despite this intensive care, new non-invasive surveillance methods that could improve morbidity and reduce mortality are still warranted.<sup>s6</sup> The increased inflammatory cytokine/chemokine production linked to CH could also affect outcomes in OHT recipients, but this association has never been evaluated.<sup>s8, s15</sup>

[0008] There remains a need to study the link between CH and various disease states, including those listed above.

### SUMMARY OF THE INVENTION

[0009] We hypothesized that the enhanced inflammatory environment associated with CH may play a significant role in various disease outcomes and its related complications. Therefore, we evaluated the prevalence of CH in patients with various cardiac diseases, solid organ diseases and specific cancers.

[0010] In an aspect, there is provided a method of predicting the risk of a disease condition of a solid organ in a patient, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis; comparing the degree of clonal hematopoiesis in the patient to a control degree; and determining the patient is at an elevated risk of the disease condition if the degree of clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner.

[0011] In an aspect, there is provided a kit comprising a library of probes library comprising at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

[0012] In an aspect, there is provided a method of predicting the benefit of immunotherapy in a patient with melanoma, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis in TET2; comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and determining the patient would benefit from immunotherapy if the degree of TET2 clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner. Preferably, the method further comprises treating the patient with immunotherapy.

[0013] In an aspect, there is provided a method of predicting metastatic risk in a patient with a non-hematological cancer, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis in TET2; comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and determining the patient is at a lower risk of metastasis if the degree of TET2 clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner. Preferably, the method further comprises treating the patient with a treatment and monitoring regimen reflective of a low risk of metastasis.

### BRIEF DESCRIPTION OF FIGURES

[0014] These and other features of the preferred embodiments of the invention will become more apparent in the following detailed description in which reference is made to the appended drawings wherein:

[0015] FIG. 1. Study design. Cardiogenic shock patients were screened for eligibility and those with available biospecimen and consent were included. Ambulatory heart

failure patients were screened on a digital database and those with complete data for age, sex, ejection fraction and aetiology of heart failure, available biospecimen and consent were included. Cardiogenic shock and ambulatory heart failure patients were matched on a 1:1 ratio for age, sex, ejection fraction, and aetiology. Ambulatory heart failure and cardiogenic shock patients were sequenced for clonal haematopoiesis related genes and its prevalence was estimated. A survival analysis was performed in each group. A survival analysis for specific genes mutations and a cytokine profile were assessed in cardiogenic shock patients.

[0016] FIG. 2. Somatic variant characteristics in cardiogenic shock cohorts and ambulatory heart failure. Panel A shows the number of mutations for the 10 most frequently mutated genes according to each cohort. Panel B shows the number of mutations per patient in those where a clonal haematopoiesis mutation was identified. Panel C shows the variant allele frequency boxplot for patients with a mutation with a VAF $\geq$ 2%. No differences were observed between cohorts ( $P=0.87$ ). Panel D shows the number of patients with CH mutation according to age in both cohorts. Filled columns represent those with CH mutations, and unfilled those without.

[0017] FIG. 3. Survival according to clonal haematopoiesis and specific gene mutations. Panels A, B and C shows the reduced survival in CS patients with CH mutations in 30-day, 90-day and 3-year survival respectively. Panels D, E and F shows the reduced survival in CS patients according to specific CH-related mutations (DNMT3A, ASXL1 and TET2) in 30-day, 90-day and 3-year survival respectively. All figures represents VAD/OHT censored survival analysis.

[0018] FIG. 4. Inflammatory cytokines in CS patients with TET2 and ASXL1 mutations. Panel A shows the differences in SCD40L, IFN $\gamma$ , IL-4, TNF- $\alpha$  and abundance in plasma of patients with or without TET2 mutations of variant allele frequency  $\geq$ 2%. Panel B shows the differences in CCL7 in patients with or without ASXL1 mutations with a variant allele frequency  $\geq$ 2% ( $P=0.03$ ).

[0019] FIG. 5. Somatic clonal hematopoiesis gene mutations prevalence and characteristics in orthotopic heart transplant recipients. Panel A shows the frequency of CH in OHT recipients. Panel B shows the number of mutations according to genes related to CH. Panel C shows the number of patients with one, two, three, five and six CH mutations. Panel D shows the number of patients with CH mutations according to age. (CH, clonal hematopoiesis; OHT, orthotopic heart transplant).

[0020] FIG. 6. Survival analysis in orthotopic heart transplant recipients according to the presence of clonal hematopoiesis gene mutations. (CH, clonal hematopoiesis) FIG. 7. Somatic mutations related to clonal hematopoiesis in patients with hypertrophic cardiomyopathy. Panel A shows the number of mutations in the most common affected genes in the cohort. Panel B shows the number of mutations per patients in those with clonal hematopoiesis. Panel C shows the number of patients with clonal hematopoiesis according to the decade of the assessment. (CH, clonal hematopoiesis; HCM, hypertrophic cardiomyopathy).

[0021] FIG. 8. Survival in patients with hypertrophic cardiomyopathy stratified according to the presence of clonal hematopiesis. Panel A shows the survival according to the presence of clonal hematopiesis among HCM patients. Panel B shows the survival according to the presence of clonal hematopiesis in the DNMT3A, TET2, and

ASXL1 genes among HCM patients. Panel C shows the survival according to the presence of clonal hematopoiesis among HCM patients with sarcomeric mutations. Panel D shows the survival according to the presence of clonal hematopiesis in the DNMT3A, TET2, and ASXL1 genes among HCM patients with sarcomeric mutations. (CH, clonal hematopoiesis; HCM, hypertrophic cardiomyopathy).

[0022] FIG. 9. Troponin I, cytokines and chemokines levels among HCM patients with sarcomeric mutations according to the presence of clonal hematopoiesis. (CH, clonal hematopoiesis; HCM, hypertrophic cardiomyopathy).

[0023] FIG. 10. TET2-mutant clonal hematopoiesis is associated with clinical benefit from immunotherapy in melanoma. A) 569 patients with melanoma, bladder cancer, renal cell carcinoma (RCC), or non-small cell lung cancer (NSCLC) treated with immune-checkpoint blockade were screened for clonal hematopoiesis using publicly-available exome sequencing, with at least one mutation of variant allele frequency (VAF) $>0.02$  detected in 74 patients (datasets EGAD00001006632, SRP064805, SRP067938, SRP072934, SRP090294, SRP095809, SRP115658, SRP128156). B) TET2-mutant clonal hematopoiesis is associated with significantly higher odds of clinical benefit 6 months after receiving immunotherapy in melanoma patients (Odds Ratio=5.98), but not bladder cancer, renal cell carcinoma, or non-small cell lung cancer patients ( $p$  value from Firth's multivariate logistic regression adjusted for patient age, sex, study, and immune checkpoint). C) In an animal model of immunotherapy, mice with Tet2-mutant hematopoiesis—mimicking TET2-mutant clonal hematopoiesis—show enhanced response to PD-1 immune checkpoint blockade, while isotype control (ISO) treated tumours show identical growth kinetics (\* $p<0.05$  by Mann-Whitney Test).

[0024] FIG. 11. TET2-mutant clonal hematopoiesis is associated with lower risk of metastatic disease in patients with non-hematological cancers. A) 16,744 patients with metastatic or non-metastatic solid tumours from Nguyen et al. Cell, 2022 were tested for clonal hematopoiesis in Bolton et al. Nature Genetics, 2020 using the MSK-IMPACT targeted sequencing panel. CH mutations with variant allele frequency of at least 0.02 were detected in 19.5% of patients. B) The 5 most commonly detected clonal hematopoiesis mutations from A) are shown. C) Exposure to TET2-mutant CH is associated with lower risk of having metastatic cancer in patients from A) as assessed by multivariate logistic regression adjusted for age, sex, smoking status, and chemotherapy treatment. D) Exposure to TET2-CH is associated with significantly lower risk of having metastases in patients from A) with Non-Small Cell Lung and Breast Cancer, with a trend towards lower risk of metastases in colorectal and bladder cancer, as assessed by multivariate logistic regression adjusted for age, sex, smoking status, and chemotherapy treatment. Patients in A) with TET2-mutant CH have significantly few metastases detected on clinical imaging (E) and have fewer overall sites/organs involved with metastatic disease (F),  $p$  values from Wilcoxon Rank Sum Test.

[0025] FIG. 12. Clonal hematopoiesis prevalence among the 782 transplant recipients.

[0026] FIG. 13. Clonal hematopoiesis prevalence according to transplanted organ.

[0027] FIG. 14. Clonal hematopoiesis mutated genes among the 782 transplant recipients.

[0028] FIG. 15. Clonal hematopoiesis mutated genes among the 127 heart transplant recipients.

[0029] FIG. 16. Clonal hematopoiesis mutated genes among the 90 lung transplant recipients.

[0030] FIG. 17. Clonal hematopoiesis mutated genes among the 189 kidney transplant recipients.

[0031] FIG. 18. Clonal hematopoiesis mutated genes among the 374 liver transplant recipients.

[0032] FIG. 19. Mortality according to the transplanted organ.

[0033] FIG. 20. Mortality according to clonal hematopoiesis.

[0034] FIG. 21. Mortality according to clonal hematopoiesis by transplanted recipients.

#### DETAILED DESCRIPTION

[0035] In the following description, numerous specific details are set forth to provide a thorough understanding of the invention. However, it is understood that the invention may be practiced without these specific details.

[0036] As noted above, we investigated the role that the enhanced inflammatory environment associated with CH may play in various disease outcomes and its related complications.

[0037] In one example, we studied cardiogenic shock (CS) and its association with variable systemic inflammation and whether it may be responsible for the patient heterogeneity and the exceedingly high mortality rate. Cardiovascular events have been associated with clonal haematopoiesis (CH) where specific gene mutations in hematopoietic stem cells lead to clonal expansion and the development of inflammation. This study aims to assess the prevalence of CH and its association with survival in a population of CS patients in a quaternary centre.

[0038] We compared the frequency of CH mutations among 341 CS patients and 345 ambulatory heart failure (HF) matched for age, sex, ejection fraction, and HF aetiology. The association of CH with survival and levels of circulating inflammatory cytokines was analysed. We detected 266 CH mutations in 149 of 686 (22%) patients. CS patients had a higher prevalence of CH-related mutations than HF patients (OR 1.5; 95% CI 1.0-2.1, P=0.02) and was associated with decreased survival (30-days: HR 2.7; 95% CI 1.3-5.7, P=0.006; 90-days: HR 2.2; 95% CI 1.3-3.9, P=0.003; and 3-years: HR 1.7; 95% CI 1.1-2.8, P=0.01). TET2 or ASXL1 mutations were associated with lower survival in CS patients at all-time points (P≤0.03). CS patients with TET2 mutations had higher circulating levels of SCD40L, IFNγ, IL-4, and TNFα (P≤0.04), while those with ASXL1 mutations had decreased levels of CCL7 (P=0.03).

[0039] CS patients have high frequency of CH, notably mutations in TET2 and ASXL1. This was associated with reduced survival and dysregulation of circulating inflammatory cytokines in those CS patients with CH.

[0040] Novel risk stratification and non-invasive surveillance methods are also needed in orthotopic heart transplant (OHT) to reduce morbidity and mortality post-transplant, and this was thus the focus of another example. The purpose of this study was to investigate the association between CH and OHT. Blood samples were collected from 127 OHT recipients. Error-corrected sequencing was used to detect CH-associated mutations. We evaluated the association between CH and acute cellular rejection, CMV infection,

cardiac allograft vasculopathy (CAV), malignancies, and survival. CH mutations were detected in 26 (20.5%) patients, mostly in DNMT3A, ASXL1, and TET2. Patients with CH showed a higher frequency of CAV grade 2 or 3 (0% vs. 18%, P<0.001). Moreover, a higher mortality rate was observed in patients with CH [11 (42%) vs. 15 (15%), P=0.008] with an adjusted hazard ratio of 2.9 (95% CI, 1.4-6.3; P=0.003). CH was not associated with acute cellular rejection, CMV infection or malignancies. The prevalence of CH in OHT recipients is higher than previously reported for the general population of the same age group, with an associated higher prevalence of CAV and mortality.

[0041] Similar studies were conducted with respect to hypertrophic cardiomyopathy, lung transplant, immunotherapy benefit in myeloma and metastatic risk of a non-hematological cancer.

[0042] Accordingly, in an aspect, there is provided a method of predicting the risk of a disease condition of a solid organ in a patient, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis; comparing the degree of clonal hematopoiesis in the patient to a control degree; and determining the patient is at an elevated risk of the disease condition if the degree of clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner.

[0043] As used herein, the term “control” refers to a specific value or dataset that can be used as a reference to classify a measured value e.g. the wild type or frequency of mutations in a cohort. A person skilled in the art will appreciate that the comparison between the measurement in the test sample and the reference values in the control will depend on the control used.

[0044] As used herein “hematopoietic stem cell” refers to cells capable of developing into any blood cell, including mature myeloid and/or lymphoid cells. These cells are typically bone marrow, liver, spleen or cord blood in origin. Myeloid and lymphoid lineages both are involved in dendritic cell formation. Myeloid cells include monocytes, macrophages, neutrophils, basophils, eosinophils, erythrocytes, and megakaryocytes to platelets. Lymphoid cells include T cells, B cells, natural killer cells, and innate lymphoid cells.

[0045] The term “sample” as used herein refers to any fluid, cell or tissue sample from a subject that can be assayed for the mutations in hematopoietic stem cells described herein.

[0046] In some embodiments, the degree of clonal hematopoiesis is measured using a variant allele frequency of mutations determined to be associated with clonal hematopoiesis. Preferably, the variant allele frequency (VAF) is ≥2%. Further preferably, the VAF is ≥5%.

[0047] In some embodiments, the following genes are sequenced in the sample: TET2, DNMT3A, and ASXL1, and optionally one or more of, but preferably all of, BCOR, BRAF, CALR, CBL, CEBPA, EZH2, FLT3A, GATA1, GATA2, GNAS, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TP53, U2AF1, WT1, and ZRSR2.

[0048] In some embodiments, the sequencing is performed using single-molecule molecular inversion probes (sm-MIPs). The smMIPs technique is an assay that combines single molecule tagging with multiplex targeted capture to

enable practical and highly sensitive detection of low-frequency or subclonal variation.

[0049] In some embodiments, the mutations associated with clonal hematopoiesis are detectable by the probes listed in Table A.

[0050] In some embodiments, the mutations associated with clonal hematopoiesis are detected using a library comprising at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

[0051] In some embodiments, the mutations associated with clonal hematopoiesis are detected using a library consisting of at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

[0052] In some embodiments, the mutations associated with clonal hematopoiesis are detected using a library consisting of substantially all of the probes listed in Table A.

[0053] In some embodiments, the mutations associated with clonal hematopoiesis are detected using a library consisting of the probes listed in Table A.

[0054] In some embodiments, the solid organ is a heart.

[0055] In some embodiments, the disease condition is cardiogenic shock. In some embodiments, an elevated risk of cardiogenic shock is associated with an elevated risk of death. Preferably, the method further comprises treating or preventatively treating the patient for cardiogenic shock.

[0056] In some embodiments, the disease condition is an adverse outcome after orthotopic heart transplant (OHT). In some embodiments, the adverse outcome is an elevated risk of mortality and/or elevated risk of cardiac allograft vasculopathy. Preferably, the method further comprises treating or preventatively treating the patient for cardiac allograft vasculopathy.

[0057] In some embodiments, the disease condition is hypertrophic cardiomyopathy. Preferably, the method further comprises treating or preventatively treating the patient for hypertrophic cardiomyopathy.

[0058] In some embodiments, the solid organ is a lung. In some embodiments, the disease condition is an adverse outcome, including death, after lung transplant. Preferably, the method further comprises treating or preventatively treating the patient for the adverse outcome after lung transplant.

[0059] In an aspect, there is provided a kit comprising a library of probes library comprising at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

[0060] In some embodiments, the kit comprises a library consisting of at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

[0061] In some embodiments, the kit comprises a library consisting of substantially all of the probes listed in Table A.

[0062] In some embodiments, the kit comprises a library consisting of the probes listed in Table A.

[0063] In an aspect, there is provided a method of predicting the benefit of immunotherapy in a patient with melanoma, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis in TET2; comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and determining the patient would benefit from immunotherapy if the degree of TET2 clonal hematopoiesis in the patient is higher than the control

degree in a statistically significant manner. Preferably, the method further comprises treating the patient with immunotherapy.

[0064] In an aspect, there is provided a method of predicting metastatic risk in a patient with a non-hematological cancer, the method comprising: receiving a sample from the patient containing hematopoietic stem cells; sequencing the sample to detect a degree of clonal hematopoiesis in TET2; comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and determining the patient is at a lower risk of metastasis if the degree of TET2 clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner. Preferably, the method further comprises treating the patient with a treatment and monitoring regimen reflective of a low risk of metastasis.

[0065] The advantages of the present invention are further illustrated by the following examples. The examples and their particular details set forth herein are presented for illustration only and should not be construed as a limitation on the claims of the present invention.

#### Example 1

##### Materials and Methods

###### Patient Selection

[0066] We performed a retrospective study to evaluate the prevalence of CH in CS patients and compared it to matched stable ambulatory HF patients. Stable ambulatory HF patients were chosen as controls as there is a known relationship with CH. We screened 1,315 consecutive patient admission with CS admitted to the cardiac intensive care unit (CICU) at the Toronto General Hospital (Ontario, Canada) from January 2014 to December 2020, identifying 341 patients with suitable biospecimens and consent. CS was diagnosed based on international consensus.<sup>14</sup> Only the first CICU admission was considered for inclusion into the study. We also screened 9,485 ambulatory HF patients with no previous history of CS, orthotopic heart transplant (OHT), durable ventricular assist device (VAD), or HF admission in the 12 months prior to biospecimen collection and clinical evaluation (N=583). We included all patients aged ≥18 years, with biospecimens stored in the Peter Munk Cardiac Centre Cardiovascular Biobank. We excluded patients with incomplete digital records, those who withdrew consent during follow-up, or low biospecimen quality (FIG. 1).

###### Definition of Clinical States of Enrolled Patients

[0067] Cardiogenic shock diagnosis was based on international consensus criteria<sup>14</sup> which required a systolic blood pressure≤90 mmHg for more than 30 minutes, or the need for inotrope/vasopressor support, signs of end-organ failure (clammy skin, capillary filling time >3 seconds, urine output <0.5 mL/kg/h, lactate level >4 mmol/L), or a low cardiac output (<2.2 L/min/m<sup>2</sup> if receiving inotropes/vasopressors or <1.8 L/min/m<sup>2</sup> without inotropes/vasopressors). In contrast, we defined stable ambulatory HF as patients with HF, with no history of OHT or VAD, or HF admission in the 12 months up to the time-point of biospecimen collection.

### Data Collection

**[0068]** Clinical and laboratory data for CS patients were collected within the first 24 hours of CICU admission. The Society for Cardiovascular Angiography and Intervention (SCAI) CS stage<sup>14</sup> was calculated at 24 hours after CICU admission. Data collected after this time were related to in-hospital outcomes such as use of mechanical circulatory support (MCS), renal replacement therapy, mechanical ventilation and death. Data for ambulatory HF patients were collected as close to the biospecimen collection date as possible. All study data were collected from electronic records and prior to CH sequencing.

### Follow-Up and Outcomes

**[0069]** All CS patients were followed until death or their last visit to our institution after hospital discharge. Follow-up time for the ambulatory HF group was defined from the time of biospecimen collection until the last visit to our institution or notice of death. As OHT and VAD substantially increase survival, a patient was right censored at the time of VAD, OHT or last follow-up, whichever was earlier. We reported event-free survival at 30-day, 90-day and 3-year. Similar to other studies,<sup>9</sup> we defined CH-related mutations at a VAF cut-off  $\geq 2\%$ .

### Biospecimens and Analysis

**[0070]** Biospecimens were collected from patients during their admission to the CICU unit of the Toronto General Hospital with deferred consent. In the case that a patient, or their substitute decision-maker, denied consent at a later time point, the biospecimens were discarded. Biospecimens from ambulatory HF patients were obtained during routine heart function clinic visits at our institution. All samples were stored at  $-80^{\circ}\text{C}$ . at the Peter Munk Cardiac Centre biobank.

**[0071]** For patients with CS, biospecimens were collected within a median of 10 (interquartile range, IQR 67) days from CS admission. In the ambulatory HF patient group, 89% of biospecimens were collected on the same day as clinical evaluation. We felt the timing of biospecimen collection was appropriate as changes in clonal haematopoiesis do not occur over days, but rather over years.

### Genetic Sequencing Procedures

**[0072]** Next-generation sequencing library construction was conducted with smMIPs.<sup>15</sup>

### Cytokine Analysis

**[0073]** To define whether cytokine levels can be potential markers of inflammation, the analysis was restricted to those samples obtained during the admission to the CICU.

### Statistical Analysis

**[0074]** All analyses on the frequency and associations with CH were performed with a variant allele frequency (VAF) cut-off  $\geq 2\%$ . For specific gene analysis, we compared patients with no mutation with those with a mutation in one of the three more common mutations (DNMT3A, TET2, or ASXL1) with a VAF  $\geq 2\%$  but with no overlap mutations. We also transformed VAF and cytokines levels using the logarithm function to reduce the distribution skewness.

**[0075]** A sample size of 345 patients for each group would detect a ratio of 1.5 in CH frequency between CS and ambulatory HF groups with a power of 87.5% and alpha of 0.05. There were 345 CS patients and 583 stable HF patients selected after initial screening. The CS and stable HF groups were one-to-one matched by age, sex, aetiology of HF, and ejection fraction. A nearest neighbour method was applied without replacement. After matching, there were 345 patients in each group. FIG. 1 summarizes sample selection.

**[0076]** All variables were tested for normality with histogram analysis and Shapiro-Wilk test. Normal and non-normal continuous variables are presented as mean  $\pm$  standard deviation or median (interquartile range), and categorical variables with frequencies. Between-cohort differences in continuous variables were evaluated with a Student's t-test or Mann-Whitney accordingly. Between-cohort differences in categorical variables were evaluated with a chi-square test. Logistic regression was performed to quantify the association of the prevalence of CH between CS and ambulatory heart failure patients in terms of odds ratios. Next, we separately characterized the 30-day, 90-day and 3-year event-free survival for each cohort using the Kaplan-Meier survival method. Furthermore, within each cohort, we contrasted event-free survival in patients with and without CH in terms of hazard ratios (HR) using Cox proportional hazards regression and evaluated the survival differences using log-rank tests. The HRs in this descriptive analysis were not adjusted for covariates. Subsequently, we also quantified the association between CS and mortality both with age only and with other clinically relevant covariates (i.e., age, sex, aetiology, use of mechanical circulatory support, creatinine, sodium, and white blood count). The model was validated by the proportional hazard assumption test based on Schoenfeld residual. Finally, as a sensitivity analysis, we repeated the previous analyses on all-cause mortality without right censoring patients at the time of OHT and VAD implantation. We described and explored the event-free survival and the levels of 48 cytokines in patients with a single gene mutation in the three most commonly mutated genes to patients without any mutations. We used a statistical significance of 0.05 for all analyses and a two-sided p-value. All analyses were performed using SPSS, version 25.0 (SPSS Inc., NY, USA).

### Results and Discussion

**[0077]** In this study, 341 patients were included in the CS group and 345 in the ambulatory HF group. Four (1%) patients were excluded from the CS group due to poor biospecimen quality (FIG. 1). All characteristics included in the case-control study were similar between groups (Table 1). Our study population consisted mostly of males with a predominance of non-ischemic cardiomyopathy. Patients with CS, however, had a lower body mass index, more frequent history of smoking, lower incidence of pre-existing chronic HF, higher admission serum creatinine and higher BNP when compared with ambulatory HF patients.

**[0078]** In the CS group, the most common aetiology was acute decompensation of chronic HF in 225 (66%) patients, followed by new onset HF in 93 (27%), myocardial infarction in 10 (3%) and myocarditis in 11 (3%). The majority were classified at SCAI stage D (285 patients, 83%) and pulmonary artery catheter was used in 178 (52%) patients confirming disease severity. Fifty-two (15%) patients required temporary MCS with intra-aortic balloon pump

being the most commonly used ( $n=26$ , 8%), followed by extra-corporeal life support ( $n=18$ , 5%), and Impella Device® (Abiomed Inc., Massachusetts, USA) ( $n=8$ , 2%). Mechanical ventilation was needed in 63 (18%) patients and renal replacement therapy in 35 (10%). Clinical characteristics are summarized for both CS patients (Table 2) and ambulatory HF (data not shown). CS patients were followed for a median of 676 (1289) days, while ambulatory HF patients were followed for 1246 (884) days.

[0079] In the CS group, 104 (30%) underwent OHT, 79 (23%) required durable VAD, 132 (39%) died during follow-up with 59 (17%) patients dying during the index hospitalization and 73 (21%) after hospital discharge. In the ambulatory HF group, 19 (6%) patients had OHT, seven (2%) were referred for durable VAD, and 35 (10%) patients died.

#### Prevalence and Distribution of CH Mutations in the Study Groups

[0080] Overall, 422 mutations were identified in 28 genes, of which 266 (63%) mutations had a VAF  $\geq 2\%$  and were included in the analysis (data not shown), affecting 149 (22%) of the 686 patients. The most common mutation type was missense, followed by frameshift, nonsense and splice site (data not shown). The most mutated gene was DNMT3A in 84 (32%), followed by TET2 in 48 (18%), and ASXL1 in 30 (11%) patients, with a similar distribution in mutations observed in both the CS and ambulatory HF groups (FIG. 2A). Among all patients with CH, 83 (56%) had a single mutation, 35 (23%) had two and 31 (21%) had three or more (FIG. 2B). The VAF distribution was similar in both populations (FIG. 2C). As expected, an age-associated increase in CH prevalence (FIG. 2D) was observed in both groups; however, the overall frequency of CH was significantly higher in CS patients, as compared with ambulatory HF patients (25.2% versus 18.3%; odds ratio, 1.5; 95% CI 1.0-2.1,  $P=0.02$ ). CS patients with CH were older than those without mutations, and had a higher frequency of dyslipidaemia, lower sodium, and white blood count (Table 2). The frequency of CH in CS patients with previous HF was similar than those without out [24 (26%) vs. 24 (23%),  $P=0.54$ ]. Ambulatory HF patients with CH were older and more likely to have ischemic cardiomyopathy (data not shown).

#### Association Between CH and Survival

[0081] The presence of CH in the CS group was associated with an increased risk of death in a multivariable adjusted analysis for age, sex, aetiology of CS, use of mechanical circulatory support, creatinine, sodium, and white blood count and censored for VAD/OHT: 17 patients (20%) with CH died in the first 30-days compared with only 17 (7%) without mutations (hazard ratio, (HR), 2.7; 95% CI 1.3 to 5.7,  $P=0.006$ ; FIG. 3A). A similar ratio was seen at 90-days (HR, 2.2; 95% CI 1.3 to 3.9,  $P=0.003$ ; FIG. 3B). At 3 years, 36 patients (42%) with CH had died compared with 47 (18%) without detectable CH at initial admission for CS (HR, 1.7, 95% CI 1.1 to 2.8,  $P=0.01$ ; FIG. 3C). Similar results were observed with the unadjusted and age-adjusted analysis for both uncensored and VAD/OHT censored (data not shown). There were no differences in survival between CH and non-CH groups in the ambulatory HF patients uncensored or VAD/OHT censored (data not shown). In addition, when considering VAF as a continuous variable,

there was no association with death. However, analysis of VAF categorized as  $\geq 2$  to  $<5\%$  and  $\geq 5\%$  was associated with a higher risk of death in those with VAF  $\geq 5\%$ , at 90-days and 3-years. Increasing number of mutated genes was not associated with death (data not shown).

[0082] We then stratified the CS group according to the three most mutated genes (DNMT3A, TET2, and ASXL1, FIGS. 3D, 3E, 3F) and found an association for TET2 and ASXL1 mutations with decreased 30-day, 90-day, and 3-year survival compared with patients who had no CH mutations. Results for survival censored for VAD/OHT had similar results. DNMT3A mutations had no effect on survival at 30-day, 90-day or 3-year follow-up.

#### Cytokine Expression in Cardiogenic Shock

[0083] To assess changes in the inflammatory milieu associated with CH, we compared 48 cytokines in the plasma of CS patients with mutations in the three most mutated genes, to those without CH. CS patients with TET2 mutations exhibited higher circulating levels of SCD40L, IFN $\gamma$ , IL-4, and TNF $\alpha$  (FIGS. 4A, 4B, 4C and 4D), and those with ASXL1 mutations had lower levels of CCL7 (FIG. 4E) compared with patients lacking CH mutations. There were no differences in the cytokine profiles of patients with DNMT3A mutations (data not shown).

#### DISCUSSION

[0084] CH mutations are associated with increased risk for adverse cardiovascular events in specific populations of patients with atherosclerosis and heart failure.<sup>5,9,10</sup> We found that patients with CS had a 1.5-fold higher prevalence of CH as compared to ambulatory HF patients, with an associated decrease in 30-day, 90-day, and 3-year survival. The observed prevalence of CH in ambulatory HF patients (18.3%) is consistent with other reported findings, emphasizing the comparability of the methodology applied.<sup>9,16</sup> Importantly, our data shows that CH may be considered as risk factor for CS admission regardless of prior HF. Of note, mutations specifically in TET2 and ASXL1 impacted the prognosis of CS and were associated with distinct circulating inflammatory cytokine profiles, compared with those patients without CH mutations. While the retrospective nature of this study may have introduced a survival bias, as CS patients who did not survive the first hours of presentation were less likely to have biospecimens taken, our study likely underestimates the prevalence of CH in CS. To our knowledge, this is the first study to show the higher prevalence of CH and lower survival in patients admitted with CS.

[0085] DNMT3A was the most common mutated gene in both groups, followed by TET2 and ASXL1. These genes are epigenetic regulators with a role in altering DNA methylation to potentially promote stem cell self-renewal and clonal expansion.<sup>17</sup> While DNMT3A is responsible for de novo DNA methylation, TET2 promotes demethylation.<sup>11</sup> ASXL1 has a role in chromatin regulation, promoting myeloid leukemogenesis.<sup>18</sup> Although the mechanisms ascribed to these genes are still poorly understood, they likely boost systemic inflammation which may have an impact in CS.<sup>10,13,17</sup> TET2 mutations were associated with a significant decrease in both short- and long-term survival in CS patients. These findings mirror previous work showing higher pathogenicity of mutations in TET2, compared to DNMT3A in the broader setting of HF.<sup>9,10,16,19</sup> Addition-

ally, ASXL1 mutations have been related to increased risk for myocardial infarction<sup>10</sup> but its role in HF was unknown prior to our study. Here, we report a decrease of short- and long-term survival in ASXL1 carriers admitted with CS. DNMT3A mutations have been associated with HF hospitalization and death<sup>16</sup>, but this was not seen in our analysis. Mutations in DNMT3A may have lower pathogenicity in CS, explaining their higher frequency in this population.

[0086] CS is associated with acute systemic inflammation, which has been shown to increase mortality.<sup>4,20</sup> Augmentation of this inflammatory state could explain the increased risk of death seen in CS patients with CH mutations. In our study, patients with CS harbouring TET2 mutations had elevated circulating levels of SCD40L, IFN $\gamma$ , IL-4, and TNF- $\alpha$ . SCD40L has a pro-inflammatory, pro-coagulant function associated with cardiovascular events related to atherosclerosis.<sup>21,22</sup> IL-4 leads to tissue macrophage accumulation,<sup>23</sup> and increases IFN $\gamma$  expression, which has a key role in the adaptive immune response<sup>24</sup>, and promotes myelopoiesis in response to inflammation<sup>24,25</sup>. TNF- $\alpha$  is primarily produced by macrophages and can induce apoptosis in hematopoietic cells.<sup>26,27</sup> Additionally, ASXL1 mutations in CS patients were associated with lower circulating levels of CCL7, a chemokine that is a potent chemoattractant for myeloid cells.<sup>28</sup> The differential regulation of cytokines promoted by specific CH mutation could enhance the immune response leading to reduced survival in TET2 and ASXL1 mutation carriers. The lack of any dysregulation of circulating cytokines with DNMT3A mutations offers an explanation why survival was not affected in our CS patients.

[0087] Clinically, the increasing incidence of CS remains a major limitation in patient management.<sup>2</sup> The association of CH mutations with higher mortality could provide a new biomarker to help identify patients at elevated risk, establishing a new paradigm of risk assessment in CS. The fact that CH patients were older does not explain the dramatic increase in mortality in CH patients, as the age-adjusted analysis showed similar results. Also, similar age differences between study populations were described in previous studies showing the impact of CH in cardiovascular outcomes.<sup>9,19</sup> Mechanistically, the increased risk due to CH likely occurs through augmentation of the acute inflammatory state in CS. The altered cytokine profile may provide potential therapeutic targets in these patients. Prior studies have shown that decreased IL-6 receptor activity improved outcomes in patients with CH.<sup>29</sup> The development of smMIP-sq for CH assessment in our study should overcome the barrier to clinical implementation of other sequencing methods.<sup>16,19</sup> Furthermore, the 2% VAF cut-off remains controversial. VAF reflects the size of the expanded clone evaluated in the peripheral blood and it is reasonable to hypothesize that risk increases with an increase in VAF.<sup>11,16,17</sup> However, we did not find a difference in the VAF between CS patients and ambulatory HF, and its use as a continuous variable was not associated with increased mortality in CS patients. We did find that CH-associated risk increased with a categorized higher VAF cutoff.<sup>16</sup> This may be explained by the highly-skewed distribution of VAF.

[0088] CS patients had a 50% higher prevalence of CH mutations than stable ambulatory HF patients. These mutations were associated with a 2-fold reduction in survival of CS patients. Specifically, mutations in TET2 and ASXL1 genes were shown to be more lethal than DNMT3A in this

context and were associated with an altered profile of circulating inflammatory cytokines that may suggest a mechanism for CH to affect patient outcomes.

## Example 2

### Materials and Methods

#### Study Population

[0089] We performed a retrospective study of 127 patients that underwent OHT in the Toronto General Hospital from 2005 to 2021. Only patients older than 18 with available biospecimens and complete clinical evaluation were included. No patients with active malignancies were included because it is considered a criteria for heart transplant candidacy.

#### Data Collection

[0090] The clinical chart and pre-transplant assessment of OHT recipients were reviewed from the patients' digital health records. We collected demographic data, medical history, laboratory assessment, date of OHT, transplant-related treatment at the time of the procedure and the immunosuppressive regimen at 1-year post-OHT, the occurrence and grade of acute cellular rejection episodes, CMV infection, CAV, any malignancy and death. All baseline characteristics regarding demographic and comorbidities were collected as close as possible to the biospecimens collection date because of its relationship with CH mutations.

#### Follow-Up and Outcomes

[0091] Patients were followed from the time of OHT procedure to the last visit at our institution or death. The patients were evaluated for the following outcomes: the first occurrence of acute cellular rejection, CMV infection, de novo post-transplant malignancy, CAV, and death.

[0092] Cellular rejection episode was diagnosed and classified according to the International Society for Heart and Lung Transplantation (ISHLT).<sup>34</sup> A positive cellular rejection episode was defined as the occurrence of 2R and 3R classification in EMB performed routinely or due to clinical suspicion of cellular rejection. As a routine, patients are routinely evaluated for rejection in weeks 1-4, 6, 8, 10 and months 3-6, 9, 12, 18, 24. Gene-expression profiling was also used for rejection surveillance in low-risk patients at our center, with a gene-expression derived high-risk score verified by confirmatory EMB. CMV assessment was performed when infection was suspected or when prophylaxis was discontinued. CMV infection was defined as positive PCR in peripheral blood regardless of clinical symptoms. Post-OHT malignancy vigilance is performed routinely by our centre and the diagnosis is based on tissue biopsy showing malignant neoplastic cells. OHT recipients have coronary angiography performed with intravascular ultrasound at 3 months, 12 months, 1-year and 5-years post OHT, though this may be deferred if intercurrent illness or significant kidney disease is present. The findings are graded according to the ISHLT criteria for CAV and considered positive in the presence of CAV2 or CAV3.<sup>34</sup> In the survival analysis, we considered death from any cause in the end of follow-up.

### Genetic Sequencing Procedures

**[0093]** Peripheral blood samples were collected with patient consent during clinical visits to Toronto General Hospital and were stored in the Peter Munk Cardiac Centre biobank. 100 ng of DNA was used to construct sequencing libraries using single molecule Molecular Inversion Probes (smMIP) as previously described.<sup>516</sup> Paired-end 150 bp sequencing reads were generated using the Illumina Novaseq platform (Illumina Inc., California, USA).

### Statistical Analysis

**[0094]** All variables were tested for normality using the Shapiro-Wilk test. Normal and non-normal continuous variables are presented as mean±standard deviation or median (interquartile range). Difference among groups were evaluated with a Student's t-test or Mann-Whitney accordingly. Group differences in categorical variables were evaluated with a chi-square test or Fisher's exact test as appropriate. The hazard ratios (HR) for the event-free survival for OHT patients with or without CH was calculated using the Cox proportional hazards regression. An adjusted Cox proportional hazards regression including age, sex, primary heart failure diagnosis (ischemic, non-ischemic and congenital) and chronic kidney disease was also calculated to estimate the impact of CH on survival. The model was ascertained by the proportional hazard assumption test based on Schoenfeld residual and found to be valid. The survival function is represented graphically using Kaplan-Meier curves and compared according to the presence of CH mutations using log-rank test. We used a statistical significance of 0.05 for all analyses and a two-sided p-value. All analyses were performed using SPSS, version 25.0 (SPSS Inc., NY, USA).

### Results and Discussion

#### Study Participants

**[0095]** Between 2005 and 2021, 589 patients underwent OHT at our institution. 127 patients (21.5%) were included in this study. 97 males and 30 females. Their mean age was 49±14 years. The most common comorbidities were prior smoking (n=34, 27%), hypertension (n=33, 26%), dyslipidemia (n=33, 26%) and type 2 diabetes (n=28, 22%). 90 patients (71%) were diagnosed with underlying non-ischemic HF prior to OHT while 28 patients (22%) had ischemic heart disease. Transplantation was conducted in 44 (35%) patients with a ventricular assist devices (VAD). All patients received induction therapy, with the vast majority (n=123, 97%) receiving rabbit anti-thymocyte globulin. The most common immunosuppressive therapy regimen at hospital discharge included tacrolimus (n=119, 94%), sodium mycophenolate (n=123, 97%) and corticosteroids (n=127, 100%). Table 3 summarizes the patient's baseline characteristics.

#### Evaluation of CH in OHT Recipients

**[0096]** The targeted sequencing of CH genes was successfully performed in all patients. In 87 (68%) cases, samples were collected before the procedure with a median time from sample to procedure of 200 (IQR 428) days, and in 40 (32%) cases the sample was collected after the transplant, with a median time from the procedure to the sample collection of 114 (IQR 624) days. We observed 46 CH mutations in 26 (20%) OHT recipients (FIG. 1A) with a median variant allele frequency (VAF) of 8.6% (3.2-35.9).

The most commonly affected genes were DNMT3A in 11 (9%), ASXL1 in 5 (4%), and TET2 in 4 (3%). TP53, PPM1D, and CEBPA affected two (2%) patients each, while JAK2, IDH2, SF3B1 and SMC1A were found in one (1%) patient each (FIG. 2B). Most patients (N=16, 62%) with CH had only one mutation (FIG. 3C). Clinical characteristics of patients with specific CH mutations were summarized (data not shown). The list of variants detected can be found in Table 5. Gene mutations and the VAF according to immunosuppressive regimen at hospital discharge were summarized (data not shown).

**[0097]** OHT patients with CH were older than those without mutation (54±13 vs 48±14 years, P=0.04) and were followed for a longer period after OHT (4.3±3.9 vs. 2.9±2.1, P=0.01). CH carriers also received an organ from EBV+ donor less frequently than those without CH [16 (62%) vs. 81 (80%), P=0.02]. At hospital discharge, CH patients were less likely to receive tacrolimus [22 (85%) vs. 97 (96%) P=0.03], and sodium mycophenolate [23 (89%) vs. 100 (99%), P=0.006]. There were no statistically significant differences in the prevalence of cardiovascular risk factors (diabetes, hypertension, BMI, smoking, dyslipidemia) or pre-OHT HF etiology between patients with and without CH (Table 3).

CH is Associated with Increase Mortality in the Setting of OHT

**[0098]** The mean follow-up post-OHT was 3.2±2.6 years. Primary graft dysfunction occurred in 19 (15%) with an in-hospital mortality post-OHT of 9%. During follow-up, 59 (46%) patients had CMV infection, 69 (54%) had at least one 2/3R acute cellular rejection episode, 11 (9%) had post-transplant malignancy, 4 (3%) CAV grade 2 or 3, and 26 (20%) died.

**[0099]** All four CAV diagnosis occurred OHT recipients with CH (18%; P<0.001), but no CAV was found among those without CH. The number of patients assessed for CAV with coronary angiogram was similar between patients with CH and those without CH [17 (65%). Vs. 68 (67%), P=0.85], and also time from OHT to first coronary angiogram 441 (1192) days vs. 399 (107) days, P=0.19. Patients with CH showed a higher mortality rate than those without CH [11 (42%) vs. 15 (15%), P=0.008], with an unadjusted hazard ratio (HR) of 3.1 (95% CI 1.4-6.7), P=0.005, and an adjusted HR of 2.9 (95% CI 1.4-6.3; P=0.003). The clinical characteristics and cause of death of patients with and without CH were summarized (data not shown). Because CH patients had a trend towards more Cyclosporine prescription at discharge and at the end of the first year after OHT, we performed a sensitivity analysis with age and type of immunosuppressive drugs in the of the 1<sup>st</sup> year. The adjusted model showed that CH was associated with increased mortality with an HR of 5.9 (95% CI 1.7-19.9), P=0.004. FIG. 2 shows the Kaplan-Meier survival analysis with an increased mortality in those with CH (P log-rank=0.003). The evaluation of outcomes according to specific gene mutation showed that more acute cellular rejection 2/3R were observed in those with DNMT3A, more CAV grade 2/3 in patients with DNMT3A and with TET2, and higher mortality in those with TET2 gene mutation (data not shown). We did not observe a higher mortality in patients with a VAF≥10% (n=14) in comparison to those with VAF<10% (N=113) [5 (35.7%) vs. 21 (18.6%), P=0.31]. Considering our results, we undertook a post-hoc power calculation. With a sample size of 127 patients and a hazard

ratio of 3.1 for OHT survival, given an alpha of 0.05, we would have a power of 99.2% of detecting such a difference. No differences were observed between OHT patients with or without CH regarding CMV infection, 2/3R acute cellular rejection or post-transplant malignancy. Both cases of post-OHT malignancy in patients with CH were diagnosed with squamous cell carcinoma of the skin, and one also developed lung carcinoma. No patients developed PTLD. Table 4 summarizes outcomes in OHT recipients according to CH.

## DISCUSSION

**[0100]** CH has been linked to inflammatory conditions, increased mortality and incidence of cardiovascular diseases, but data in the setting of solid organ transplantation is scarce.<sup>s8, s17</sup> We showed that the CH prevalence in OHT recipients is higher than expected for the same age in the general population. CH mutations are associated CAV and a 3-fold increase in mortality after OHT. These findings suggests a new biomarker in post-transplantation risk assessment.

**[0101]** The detection of CH is an exceedingly common feature of aging, with a prevalence of 10% by the 7<sup>th</sup> decade of life and an overall prevalence of 4-5%.<sup>s7</sup> In this study, 20% of OHT recipients were found to have a CH mutation in a younger population, mainly in DNMT3A, ASXL1 and TET2 genes, with most patients harboring a single mutation. Previously, HF patients were shown to have an 18.5% frequency in CH mutations at a median age of 65 years.<sup>s10, s14</sup> Similarly, the median VAF in our cohort was 12%, which is much higher than the reported ≈4-6% in non-advanced HF cohorts.<sup>s10, s14</sup> Additionally, CH patients have been consistently reported to be older than those without these mutation, similar to our study. While concerns can be raised about CH being a risk marker of aging instead of a disease-driving factor, several studies have shown that CH is independently associated with increased cardiovascular risk after adjusting for age.<sup>s10, s14</sup> CH has also been shown to have a causal effect in mice harboring either Dnmt3a, Tet2, Jak2, Tp53, and Ppm1d mutations with adverse LV remodeling, lower LV ejection fraction and worsening degree of fibrosis post-myocardial infarction.<sup>s15, s18-s21</sup>

**[0102]** CH mutations have been shown to be associated with atherosclerosis, myocardial infarction, stroke and HF.<sup>s8-s10, s14</sup> A similar background of inflammation driving clinical outcomes would be expected in OHT recipients. In our study, CH was associated CAV grade 3. Experimental models have shown that Tet2-deficient mice have larger atherosclerotic plaque size and increased levels of several inflammatory cytokines.<sup>s8, s22</sup> Higher levels of coronary artery disease have been observed in patients with CH.<sup>s8</sup> The pathways involved in atherosclerosis development overlap with the inflammatory background of CH, but the pathophysiology of CAV comprises a complex interaction of immune and non-immune factors which contribute to a pro-inflammatory state and ultimately result in endothelial injury, vascular cell proliferation, fibrosis, and remodeling.<sup>s23-s25</sup> The increased inflammatory cytokines expressed in patients with CH could have a role in CAV development, but further studies are needed to confirm this hypothesis, especially due to the low number of CAV diagnosis in the sample.

**[0103]** The complex relationship of immune phenomena and inflammation promoted by CH could be responsible for other outcomes in OHT recipients. The innate immune

system can be activated by several different cytokines resulting in rejection episode<sup>s26, s27</sup>, and activation of IL-1R pathway has a central role in ischemic reperfusion injury.<sup>s28</sup> However, despite the overall higher proportion of CH patients experiencing acute cellular rejection, it failed to reach statistical significance. One possibility is that based on the 16% absolute increase observed, a sample size of over 400 patients would be required to reach statistical significance. CH has also been associated with the occurrence of infections and malignancies.<sup>s11, s12</sup> We observed only a small number of such events which may explain the lack of association of CH with these outcomes. Nevertheless, CH was associated with a 3-fold increase in mortality in OHT recipients even after adjustment for confounding factors. Cardiovascular events in CH patients have been shown to be related with ischemic events and progression to heart failure, but these are not common in OHT recipients.<sup>s8, s10, s14</sup> The cause of death in this study was related to allograft dysfunction, acute rejection episode, CAV, and septic shock. The mechanisms responsible for the observed high mortality rate remains unclear, yet previous work have shown that non-survivors after OHT were more likely to present with sustained inflammation.<sup>s29</sup> Nonetheless, patients with CH were older, and, despite not being statistically significant, also had higher frequency of hypertension, dyslipidemia and smoking that could have an impact in our results.

**[0104]** In summary, we demonstrated that CH is associated with, and a potential risk factor, for CAV and mortality in OHT recipients. The complex interaction of the inflammatory cytokines promoted by CH and the immune system could drive several other potential outcomes such as rejection, infections and malignancies. A prior case series of graft versus host disease in transplanted liver patients showed that 71% had CH, highlighting the possible association with these somatic mutations to adverse outcomes.<sup>s30</sup>

## Example 3

### Methods and Materials

**[0105]** We investigated a cohort of patients with hypertrophic cardiomyopathy (HCM) submitted to targeted sequencing for detecting CH. We included 799 patients who were ≥18 years of age, with a clinical diagnosis of HCM by current guidelines<sup>s2</sup>, cardiac magnetic resonance imaging (MRI) and available biospecimens from the PMCC Biobank. We excluded patients with incomplete records, those that withdraw consent, or low biospecimen quality.

**[0106]** Among the 799 included patients, CH was found in 183 (22.9%). HCM patients with genotype-positive and CH were found to be more symptomatic and with a higher burden of fibrosis. CH was associated with major cardiovascular event (MACE) in HCM patients [adjusted HR of 3.46 (95% CI 1.25-9.52; p=0.016)], with the highest risk among genotype-positive and DNMT3A, TET2 and ASXL1 mutated genes [adjusted HR of 7.23 (95% CI 1.79-29.13) p=0.005]. Several cytokine and chemokines (IL-1ra, IL-6, IL-17F, TGF $\alpha$ , CCL21, CCL1, CCL8, and CCL17), and also troponin I were upregulated in those genotype-positive with CH. Fibrosis, a hallmark of HCM, was found to be increased in those with CH, as well as ABPR at exercise. CH was also associated with a higher mortality and major cardiovascular events (MACE). These results indicate that CH is frequent among HCM patients and associated with a worse clinical phenotype and outcomes.

### Definitions

**[0107]** HCM was defined as the presence of maximal LV wall thickness (MLVWT)  $\geq 15$  mm. Also included were patients with MLVWT  $\geq 13$  mm and a P/LP genetic variant or a family history of HCM in the absence of other causes for hypertrophy. MLVWT was defined as the higher LV wall measure on echocardiogram or cardiac MRI. The assessment of P/LP variants was conducted using a previously published strategy by our group<sup>23</sup>. Evaluation for non-sustained ventricular tachycardia (NSVT) or abnormal blood pressure response (ABPR) at exercise were performed according to the attending clinician discretion. All patients with HCM underwent cardiac MRI with late gadolinium enhancement (LGE) for quantification of fibrosis. The LGE was assessed visually and quantified manually as previously validated<sup>8</sup>. LGE extent was defined as the LGE mass percentage of the total LV mass. We were able to quantify LGE in (84.1%) of patients with MRI. In the remaining 127 (15.9%) patients, we only included the qualitative measure of LGE as present or not.

### Clonal hematopoiesis and cytokine assessment

**[0108]** The full method on CH and cytokines evaluation was performed substantially as described in earlier examples. Briefly, we used a single molecule molecular inversion probe (smMIP) method including 35 myeloid genes related to CH and smMIP-tools to call mutations and reported those with variant allele frequency (VAF), a measure of clone size,  $\geq 2\%$  for all analysis. The cytokine analysis was performed using a human cytokine/chemokine 71-plex assay with the Luminex™ 200 system by Eve Technologies Corp. (Alberta, Canada) and included brain natriuretic peptide (BNP) and cardiac troponin I (cTnI).

### Results and Discussion

#### Clonal Hematopoiesis Prevalence and Characteristics

**[0109]** Overall characteristic of cohort is summarized in Table 7. The median time from biospecimen collection to the echocardiogram was 0 (0-16) days and median time from biospecimen to MRI assessment was 2.2 (0.2-5.6) years.

**[0110]** All patients had an assessment of CH performed and all samples passed quality control specifications. CH mutations were observed in 183 (22.9%) patients with a median VAF of 6.7 (2.8-40.8) %, being 136 (17.0%) in the three most common genes: DNMT3A in 70 (8.8%), TET2 in 51 (6.3%), and ASXL1 in 24 (3.0%), comprising 73.8% of all CH mutations. All other genes included in the smMIP panel were present in less than 1% of patients. Most patients (158, 19.8%) harbored a single mutation, while two mutations were found in 18 (2.3%) patients, 4 (0.5%) three mutations, and 3 (0.3%) four or more mutations. Among the 183 patients with CH, 135 (73.7%) were over 50 years old. However, among the 54 patients  $< 30$  years, CH was present in 14 (25.9%). In relation to the age of HCM diagnosis, 27 (14.8%) patients with CH were diagnosis before 30 years of age, while 62 (33.8%) within 31-50 years, and the majority, 94 (51.3%), were diagnosed after 50 years old. FIG. 7 summarizes CH mutations characteristics. Overall clinical characteristics of CH patients were similar to those without CH (Table 7).

**[0111]** We then analyzed the association of CH with the HCM phenotype. No differences were found in those with or without CH on echocardiographic parameter such as

MLVWT ( $18.3 \pm 4.2$  mm vs.  $18.8 \pm 5.1$  mm,  $p=0.256$ ), left atrium diameter ( $36.7 \pm 14.5$  mm vs.  $38.1 \pm 12.7$  mm,  $p=0.208$ ) and LVOT gradient ( $24.1 \pm 36.2$  mmHg vs.  $22.1 \pm 34.6$  mmHg,  $p=0.491$ ). Cardiac MRI parameters, including the presence of fibrosis evaluated by LGE, as well as other HCM features such as syncope, ABPR at exercise, among others were also similar between groups. However, apical aneurysm [33 (5.4%) vs. 14 (7.7) %,  $p=0.004$ ] and death or need for orthotopic heart transplant was higher among patients with CH [4 (0.6%) vs. 6 (3.3%),  $p=0.005$ ]. MACE was also more frequent among patients with CH [12 (2.0%) vs. 9 (5.2%),  $p=0.026$ ], with an unadjusted HR of 2.72 (95% CI 1.14-6.49;  $p=0.023$ ), and adjusted HR of 3.46 (95% CI 1.25-9.52;  $p=0.016$ ). CH patients showed a worse survival in comparison to those without CH as shown in the Kaplan-Meier curve (Log-Rank  $P=0.018$ ) (FIG. 8A).

#### Clonal Hematopoiesis Related to DNMT3A, TET2 and ASXL1

**[0112]** We evaluated whether somatic mutations in 3 genes (DNMT3A, TET2 and ASXL1) alone are sufficient to drive poor HCM patient outcome. We found that patients harboring DNMT3A, TET2 and ASXL1 mutations were older than their counterparts [55.3 (14.5%) vs. 58.1 (14.5%),  $p=0.042$ ] and were more likely to have a family history of SCD [28 (4.2%) vs. 9 (6.7%),  $p=0.038$ ]. As we noted in the wider CH analysis, these patients were more likely to have hypertension, a P/LP germline HCM related mutation, a pacemaker and treated with a non-dihydropyridine calcium channel blocker (Table 6).

**[0113]** While patients with DNMT3A, TET2 and ASXL1 CH mutations, exhibited a similar HCM phenotype to those without CH, patients with CH showed a higher mortality or need for orthotopic heart transplant [4 (0.6%) vs. 6 (4.4%),  $p<0.0001$ ] and MACE [13 (2.0%) vs. 8 (6.2%),  $p=0.008$ ]. The unadjusted HR for MACE was 3.19 (95% CI 1.32-7.73;  $p=0.010$ ) and adjusted HR 3.97 (95% CI 1.39-11.28;  $p=0.010$ ). FIG. 8B shows the Kaplan-Meir curve with worse survival for patients with CH (Log-Rank  $p=0.006$ ).

#### Clonal Hematopoiesis in HCM Patients with a Sarcomeric Mutation

**[0114]** HCM patients harboring a sarcomeric gene mutation are associated with early age at diagnosis, higher MLVWT and worse outcomes<sup>25</sup>. Because this subtype of HCM patients have a distinct clinical profile, we sought to investigate if there could be a distinct interaction with CH. The overall characteristics shown among those with or without CH were recorded (data not shown). A trend of a higher burden of symptoms (NYHA class II to IV) [15 (40.5%) versus 47 (28.0%),  $p=0.132$ ] among those with CH, but it was not statistically significant. However, CH was associated with a higher burden of fibrosis as reflected by LGE in  $>15\%$  of the LV mass [11 (29.7%) versus 26 (15.3%),  $p=0.044$ ], with an odds ratio of 2.32 (95% CI 1.00-5.38,  $p=0.048$ ), there was a trend towards a higher amount of fibrosis in the LV of those with CH [15.6% (10.4-24.6)] in comparison to those without CH [12.2% (7.7-17.6)],  $p=0.068$ . CH patients also showed a higher frequency of ABPR at exercise [25 (29.8%) vs. 10 (62.5%),  $p=0.012$ ]. Finally, CH was associated with worse outcomes with higher mortality or orthotopic heart transplant [3 (8.1%) versus 2 (1.2%), ( $p=0.013$ )]. This was also observed for MACE in patients with CH [5 (13.5%) versus 5 (3.0%),  $p=0.008$ ], with an unadjusted HR of 5.28 (95% CI 1.51-18.4,

$p=0.009$ ), and adjusted HR of 6.89 (95% CI 1.78-26.6,  $p=0.005$ ). FIG. 8C shows the Kaplan-Meier survival curve showing a worse survival for those with CH (log-rank  $p=0.003$ ).

[0115] We then stratified the HCM phenotype and clinical outcomes in those with sarcomeric mutations and specifically the presence of DNMT3A, TET2, and ASXL1 mutations. Baseline characteristics was similar between groups. The amount of fibrosis assessed by LGE was higher in those with CH [21.2% (13.7-41.8) versus 12.2% (7.7-17.5),  $p=0.014$ ], whereas LGE $\geq 15\%$  was not statistically different in HCM patients with and without CH [7 (35.0%) vs. 30 (18.3%),  $p=0.09$ ]. However, CH patients showed a higher frequency of abnormal blood pressure response (ABPR) with exercise than those without CH [8 (66.7%) vs. 27 (30.7%),  $p=0.014$ ]. Finally, mortality or orthotopic heart transplant was more common in the CH group than in those without CH [3 (13.0%) vs. 2 (1.1%),  $p<0.0001$ ], as well as MACE [4 (17.4%) vs. 6 (3.2%),  $p=0.004$ ]. MACE was associated with CH with an unadjusted HR of 5.04 (95% CI 1.39-18.28)  $p=0.014$  and adjusted HR of 7.23 (95% CI 1.79-29.13)  $p=0.005$ . FIG. 8D shows the Kaplan-Meier survival curve showing a worse survival for those with CH (log-rank  $p=0.007$ ).

#### Biomarkers and Cytokines/Chemokines

[0116] A panel of 71 cytokines and chemokines, BNP and cardiac troponin I were evaluated in patients with a sarcomeric mutation and levels were compared among those with ( $N=37$ ) or without CH ( $N=169$ ). It was observed that troponin I ( $p=0.008$ ), IL-1ra ( $p=0.037$ ), IL-6 ( $p=0.028$ ), IL-17F ( $p=0.006$ ), TGFa ( $p=0.005$ ), CCL21 ( $p=0.036$ ), CCL1 ( $p=0.002$ ), CCL8 ( $p=0.036$ ), and CCL17 ( $p=0.047$ ) were all upregulated in patients with CH. FIG. 9 shows levels measured among those with and without CH. We then sought to investigate if specific CH mutations were associated with specific cytokines/chemokines. In HCM patients with sarcomeric mutations, those with CH due to DNMT3A ( $N=16$ ) mutations showed higher levels of IL-9 ( $p=0.031$ ) and CXCL12 ( $p=0.046$ ). TET2 CH carriers ( $N=6$ ) showed higher levels of troponin I ( $p=0.013$ ), IL-5 ( $p=0.012$ ), IL-10 ( $p=0.010$ ), CXCL10 ( $p=0.001$ ), CXCL9 ( $p=0.012$ ), CCL4 ( $p=0.037$ ), VEGF-A ( $p=0.041$ ), CCL21 ( $p=0.013$ ), CXCL13 (BCAP=0.012) and CCL1 ( $p=0.007$ ). Finally, CH due to ASXL1 ( $N=2$ ) did not show any differences in comparison to those without CH.

#### Discussion

[0117] In this study, we showed that CH prevalence among HCM patients is higher than described in the general population. Fibrosis, a known SCD risk factor, was more prevalent among CH patients with HCM sarcomeric gene mutations. We also observed higher burden of symptoms and higher frequency of ABPR during exercise among CH patients. Finally, CH was associated with higher mortality or orthotopic heart transplant and MACE. Several cytokines, chemokines and troponin were differently expressed in HCM patients with CH, highlighting a plausible causal relationship with the phenotype and outcomes. This is the first cohort in which there is an association between CH prevalence, HCM phenotype and clinical outcomes.

[0118] To our knowledge, this is the first study to evaluate the prevalence of CH in patients with HCM. In this study, we found that 22.9% of HCM patients harbored CH.

[0119] When restricting analysis to the three specific genes DNMT3A, TET2 and ASXL1, we observed that 17% of HCM patients harbored CH mutations.

[0120] Fibrosis was more common in those patients with HCM who have a sarcomeric mutation and specific DNMT3A, TET2 and ASXL1 mutations. This is an important finding as fibrosis is linked to SCD in patients with HCM<sup>40</sup>. In addition, ABPR at exercise, a known marker of SCD risk and worse outcomes<sup>41-43</sup>, was also more frequent among those with CH and HCM with sarcomeric mutations. This result potentially illustrates that CH could affect the HCM phenotype and promote adverse outcomes in patients with HCM.

[0121] We showed that, in subsets of HCM patients and evaluating for overall CH or specific CH mutations, the mortality or need for orthotopic heart transplant is increased among CH patients even when adjusting for confounding factors. Moreover, condensing important major cardiovascular events in HCM, such as stroke, sudden cardiac death, appropriate ICD shock, death or orthotopic heart transplant, CH increases its risk in all subsets of patients, reaching the highest risk among those with sarcomeric mutations and with specific CH genes. Our results show that CH is a new risk factor among HCM patients. In fact, HCM patients with sarcomeric mutations with CH on the most common genes showed the worse survival (17%), contrasting to recent cohorts showing that HCM patients have a low mortality.<sup>9</sup> Our results do not show a clear evidence of which mechanisms CH increase mortality in HCM, but its strong association with ageing<sup>13</sup> leads us to hypothesize that the epigenetic ageing and the inflammatory milieu may have a causal relationship with the reduced survival.

[0122] Among HCM with sarcomeric mutations, CH was associated with several inflammatory cytokines and chemokines such as IL-1ra, IL-6, IL-17F, TGFa, CCL21, CCL1, CCL8, and CCL17, but also with troponin I, a marker of myocyte injury that is associates with clinical outcomes in HCM.<sup>47</sup> However, specific CH mutations may have distinct prognosis and inflammatory profiles.<sup>14,34</sup> We observed that DNMT3A driven CH was associated with IL-9 and CXCL12. TET2 driven CH was associated with the higher number of differently expressed cytokines/chemokines including troponin I among all tested genes. DNMT3A was associated with LV remodeling and worse outcomes, but the high frequency CH mediated by this gene in the population could be explained by its low lethality and lower burden of inflammation, introducing a survival bias.<sup>11,19,28,29,34</sup> Cardiac aging processes mediated by TET2 have shown to produce an enhanced inflammatory background that could be related to hypertrophy and fibrosis, but the worse prognosis associated with TET2 could also explain its lower frequency in studies.<sup>11,17,29</sup> ASXL1 carriers did not show different levels of expressed cytokines, chemokines, BNP or Troponin I. We believe that the low number of patients with this specific mutation could explain the results.

#### Example 4

[0123] We also investigated TET2 mutant clonal hematopoiesis and its association with the benefit of immunotherapy, as well as metastasis of non-hematological cancers. Referring to FIG. 10, TET2-mutant clonal hematopoiesis is associated with clinical benefit from immunotherapy in melanoma. FIG. 10A shows 569 patients with melanoma, bladder cancer, renal cell carcinoma (RCC), or non-small

cell lung cancer (NSCLC) treated with immune-checkpoint blockade were screened for clonal hematopoiesis using publicly-available exome sequencing, with at least one mutation of variant allele frequency (VAF)>0.02 detected in 74 patients (datasets EGAD00001006632, SRP064805, SRP067938, SRP072934, SRP090294, SRP095809, SRP115658, SRP128156). FIG. 10B shows TET2-mutant clonal hematopoiesis is associated with significantly higher odds of clinical benefit 6 months after receiving immunotherapy in melanoma patients (Odds Ratio=5.98), but not bladder cancer, renal cell carcinoma, or non-small cell lung cancer patients ( $p$  value from Firth's multivariate logistic regression adjusted for patient age, sex, study, and immune checkpoint). FIG. 10C shows in an animal model of immunotherapy, mice with Tet2-mutant hematopoiesis—mimicking TET2-mutant clonal hematopoiesis—show enhanced response to PD-1 immune checkpoint blockade, while isotype control (ISO) treated tumours show identical growth kinetics (\* $p$ <0.05 by Mann-Whitney Test).

[0124] Referring to FIG. 11, TET2-mutant clonal hematopoiesis is associated with lower risk of metastatic disease in patients with non-hematological cancers. FIG. 11A shows 16,744 patients with metastatic or non-metastatic solid tumours from Nguyen et al. Cell, 2022 were tested for clonal hematopoiesis in Bolton et al. Nature Genetics, 2020 using the MSK-IMPACT targeted sequencing panel. CH mutations with variant allele frequency of at least 0.02 were detected in 19.5% of patients. FIG. 11B shows the 5 most commonly detected clonal hematopoiesis mutations from FIG. 11A are shown. FIG. 11C shows exposure to TET2-mutant CH is associated with lower risk of having metastatic cancer in patients from FIG. 11A as assessed by multivariate logistic regression adjusted for age, sex, smoking status, and chemotherapy treatment. FIG. 10D shows exposure to TET2-CH is associated with significantly lower risk of having metastases in patients from FIG. 11A with Non-Small Cell Lung and Breast Cancer, with a trend towards lower risk of metastases in colorectal and bladder cancer, as assessed by multivariate logistic regression adjusted for age, sex, smoking status, and chemotherapy treatment. Patients in FIG. 11A with TET2-mutant CH have significantly few metastases detected on clinical imaging (FIG. 11E) and have fewer overall sites/organs involved with metastatic disease (FIG. 11F),  $p$  values from Wilcoxon Rank Sum Test.

#### Example 5

[0125] Applicant further sought to investigate the prevalence of CH among solid organ transplant (SOT) recipients (heart, lung, liver and kidney), study the association with specific CH-related genes and the impact on outcomes.

#### Methods and Materials

##### Study Population

[0126] We conducted a retrospective study of 1,500 patients who underwent SOT at the Toronto General Hospital between 2005 and 2021. The inclusion criteria were patients aged 18 years or older with available biospecimens and complete clinical evaluation. Patients with active malignancies were excluded, as it is a criterion for solid organ transplant candidacy.

#### Data Collection

[0127] The electronic health records of the SOT recipients were reviewed to collect demographic data, medical history, laboratory assessments, date of SOT, transplant-related treatment at the time of the procedure, and the immunosuppressive regimen at one year post-SOT. Baseline characteristics, including demographic data and comorbidities, were collected as close as possible to the biospecimens collection date due to their relationship with CH mutations.

#### Follow-Up and Outcomes

[0128] Patients were followed from the time of SOT procedure until the last visit at our institution or death. The following outcomes were evaluated: the first occurrence of acute cellular rejection, CMV infection, de novo post-transplant malignancy, CAV, and death.

#### Genetic Sequencing

[0129] Peripheral blood samples from patients who had provided consent during their visits to Toronto General Hospital. These samples were stored in the biobank of the Peter Munk Cardiac Centre. To construct the sequencing libraries, 100 ng of DNA was utilized, and single molecule Molecular Inversion Probes (smMIP) were employed. The smMIPs were utilized to capture 35 genes known to be recurrently mutated in myeloid neoplasms. Sequencing was performed using the Illumina Novaseq platform, and an in-house computational pipeline was used to reduce artifacts and false-positive mutation calls. Alleles were filtered based on a P-value cut-off of 0.05 and were manually inspected based on several criteria, including base-pair change, annotation in COSMIC, minor allele frequency, and number of reads supporting the alternative allele. The resulting variants were analyzed and manually inspected to avoid selecting false positives.

#### Statistical Analysis

[0130] The normality of all variables was assessed using the Shapiro-Wilk test, and both normal and non-normal continuous variables are reported as mean±standard deviation or median (interquartile range). Student's t-test or Mann-Whitney test were used to evaluate differences among groups depending on the normality of the data. Categorical variables were assessed using chi-square test or Fisher's exact test. All analyses were performed using SPSS, version 25.0 (SPSS Inc., NY, USA), with a statistical significance level of 0.05 and a two-sided  $p$ -value.

#### Results and Discussion

[0131] Out of the 1,500 patients enrolled, 782 have been sequenced as of the current date. Among these patients, 127 (16.2%) underwent heart transplant, 90 (11.5%) underwent lung transplant, 189 (24.2%) underwent kidney transplant, 374 (47.8%) underwent liver transplant, and 2 (0.3%) underwent lung-liver transplant. The average age of the entire cohort was  $54.2\pm12.7$  years, with a majority of male patients (52.9%). The age distribution varied significantly across organ groups ( $p<0.0001$ ), with lung-liver transplant patients being the youngest ( $47\pm12.7$ ), followed by heart ( $49.2\pm14.0$ ), kidney ( $53.7\pm13.3$ ), lung ( $54.4\pm15.1$ ) and liver ( $56.1\pm10.8$ ) transplant patients. Sex also differed among the organ groups ( $p=0.05$ ), with all lung-liver transplant recipients

being male, and a majority of heart (76.4%), kidney (76.2%), liver (66.5%), and lung (58.9%) transplant recipients being male. For a summary of the overall cohort characteristics, refer to Table 8.

[0132] CH was observed in 123 (15.7%) patients. CH prevalence was similar across the organ groups (FIG. 12), except for kidney (8%) that was lower than heart (20%), lung (19%), and (liver 18%), p=0.007. Lung-liver showed a 50% of CH, but the low number of patients may explain this result.

[0133] We then analyzed the specific mutated genes among patients with CH. In the literature, DNMT3A is the most common mutated gene in the general population, followed by TET2. [13] In our cohort, DNMT3A was the most commonly mutated gene (n=45, 5.7%), followed by TET2 (n=40, 5.1%) and ASXL1 (n=20, 2.5%). Notably, DNMT3A was the most commonly mutated gene among heart transplant recipients (FIG. 15) and among kidney recipients (FIG. 17), while TET2 was the most common mutated gene among lung (FIG. 16) and liver (FIG. 18) recipients. These findings suggest that TET2 may play a role in lung and liver end-stage disease, but further clinical validation is required.

[0134] The overall mortality rate in our cohort was 18.3%. Mortality differed across the different SOT (p<0.0001), with

the highest mortality observed in lung-liver recipients (50%), followed by lung (43.3%), heart (20.5%), liver (14.2%), and kidney (12.7%) recipients (FIG. 19). We observed a trend in mortality according to the presence of CH (17.4% vs. 23.4%) (FIG. 20). Among solid organ transplant recipients, those who received a heart transplant showed a higher mortality rate when developing CH (14% vs. 42%, p=0.002) with a trending shown for lung. CH did not affect the mortality of recipients of kidney or liver (FIG. 21).

[0135] The study partial results shows that CH was observed in 15.7% of patients, with similar prevalence across most organ groups except for kidney, which had a lower prevalence. DNMT3A was the most commonly mutated gene among heart and kidney transplant recipients, while TET2 was the most common in lung and liver recipients. Heart transplant recipients had a higher mortality rate when developing CH.

[0136] Although preferred embodiments of the invention have been described herein, it will be understood by those skilled in the art that variations may be made thereto without departing from the spirit of the invention or the scope of the appended claims. All documents disclosed herein, including those in the following reference list, are incorporated by reference.

TABLE 1

CHARACTERISTICS OF THE PATIENTS AT BASELINE <sup>A</sup>			
	Cardiogenic Shock (N = 341)	Ambulatory HF (N = 345)	P value
<u>Matched variables</u>			
Age (years)	55 ± 15	57 ± 15	0.25
- median (range)	58 (19)	58 (19)	
Male sex	249 (73%)	247 (72%)	0.64
Heart failure aetiology			
Ischemic cardiomyopathy	107 (31%)	106 (31%)	0.85
Non-ischemic cardiomyopathy	221 (65%)	225 (65%)	0.91
Congenital disease	13 (4%)	14 (4%)	0.86
Ejection fraction (%)	26 ± 12	27 ± 10	0.09
<u>Other baseline characteristics</u>			
Body mass index (kg/m <sup>2</sup> ) <sup>b</sup>	26 ± 6	29 ± 6	<0.001
Hypertension	125 (37%)	109 (32%)	0.16
Dyslipidaemia	115 (34%)	122 (35%)	0.65
Diabetes	99 (29%)	78 (23%)	0.05
Prior/current smoker	101 (30%)	82 (24%)	<0.001
Prior history of cancer	33 (10%)	41 (12%)	0.35
Prior coronary revascularization	69 (20%)	84 (24%)	0.19
Previous cerebrovascular disease/transient ischemic attack	39 (11%)	33 (10%)	0.42
Atrial Fibrillation/Flutter	122 (36%)	101 (29%)	0.06
Chronic Heart Failure	237 (70%)	345 (100%)	<0.001
Implantable cardioverter-defibrillator	85 (25%)	106 (31%)	0.09
Cardiac resynchronization therapy	69 (20%)	70 (20%)	0.98
White blood count (×10 <sup>9</sup> /L)	10.7 ± 6.6	7.3 ± 2.4	<0.001
Creatinine (μmol/L)	179 ± 128	110 ± 73	<0.001
Sodium (mmol/L)	135 ± 6	138 ± 3	<0.001
B-type natriuretic peptide (pg/mL)	1,428 (1730)	168 (337)	<0.001

<sup>A</sup>Plus-minus are means ± SD.<sup>b</sup>The body-mass index is the weight in kilograms divided by the square of the height in meters.

TABLE 2

	All cardiogenic shock (N = 341)	No clonal haematopoiesis (N = 256)	Clonal haematopoiesis (N = 85)	P value
Age (year)	55 ± 15	54 ± 15	60 ± 14	0.002
Male sex	249 (73%)	188 (73%)	61 (72%)	0.76
Body mass index (kg/m <sup>2</sup> ) <sup>b</sup>	26 ± 6	26 ± 6	26 ± 6	0.50
Hypertension	125 (37%)	87 (34%)	38 (44%)	0.09
Dyslipidaemia	115 (34%)	78 (30%)	37 (44%)	0.03
Diabetes	99 (29%)	72 (28%)	27 (31%)	0.57
Prior/current smoker	101 (30%)	75 (29%)	25 (29%)	0.89
Prior history of cancer	33 (10%)	25 (10%)	9 (11%)	0.86
Prior coronary revascularization	69 (20%)	52 (20%)	17 (20%)	0.90
Previous cerebrovascular disease/transient ischemic attack	39 (11%)	27 (11%)	12 (14%)	0.39
Cardiogenic shock aetiology				
Acute decompensation of chronic heart failure	225 (66%)	168 (66%)	57 (67%)	0.94
New onset of heart failure	93 (27%)	72 (28%)	21 (25%)	0.27
Myocardial infarction	10 (3%)	6 (2%)	4 (5%)	0.87
Myocarditis	11 (3%)	8 (3%)	3 (4%)	0.58
SCAI classification <sup>c</sup>				
B	27 (8%)	21 (8%)	6 (7%)	0.73
C	27 (8%)	20 (8%)	7 (8%)	0.90
D	285 (83%)	213 (83%)	72 (85%)	0.74
E	2 (1%)	2 (1%)	0	0.41
Number of inotropes or vasopressors	1.7 ± 1.0	1.6 ± 1.0	1.8 ± 1.0	0.24
Pulmonary artery catheter	178 (52%)	134 (52%)	44 (52%)	0.92
Temporary mechanical circulatory support				
Intra-aortic balloon pump	26 (8%)	20 (8%)	6 (7%)	0.50
Impella device ®	8 (2%)	8 (3%)	0	0.09
Extra-corporeal life support	18 (5%)	16 (6%)	3 (4%)	0.59
Mechanical ventilation	63 (18%)	45 (18%)	18 (21%)	0.45
Renal replacement therapy	35 (10%)	24 (9%)	11 (13%)	0.34
White blood count ( $\times 10^9/L$ )	7.3 ± 2.4	11.1 ± 7.2	9.4 ± 4.3	0.01
Creatinine ( $\mu\text{mol}/L$ )	110 ± 73	176 ± 129	188 ± 124	0.44
Sodium (mmol/L)	138 ± 3	135 ± 6	133 ± 5	0.02
Peak lactate (mmol/L)	3.4 ± 3.2	3.4 ± 3.1	3.4 ± 3.1	0.86
B-type natriuretic peptide (pg/mL)	1428 (1730)	1446 (1712)	1350 (1737)	0.42

<sup>a</sup>plus-minus are mean ± SD.<sup>b</sup>The body-mass index is the weight in kilograms divided by the square of the height in metres.

<sup>c</sup>Patients were classified according to the Society for Cardiovascular Angiography & Interventions. Briefly, Class B are patients at beginning of shock; Class C is classic cardiogenic shock; Class D is deteriorating and failure to respond to initial interventions; and Class E is extreme shock on patients supported by multiple interventions who may be experiencing cardiac arrest and/or extracorporeal life support.

TABLE 3

Characteristics	All (N = 127)	No CH (N = 101)	CH (N = 26)	P value
Age - year	49 ± 14	48 ± 14	54 ± 13	0.04
Median (range)	53 (23)	52 (24)	58 (21)	0.03
Male sex - no. (%)	97 (77%)	79 (78%)	18 (69%)	0.33
Body mass index - kg/m <sup>2</sup> <sup>†</sup>	25 ± 6	25 ± 6	25 ± 5	0.97
Hypertension - no. (%)	33 (26%)	25 (25%)	8 (31%)	0.53
Dyslipidemia - no. (%)	33 (26%)	24 (24%)	9 (35%)	0.26
Diabetes - no. (%)	28 (22%)	23 (23%)	5 (19%)	0.69
Prior smoker - no. (%)	34 (27%)	25 (25%)	9 (35%)	0.31
Prior neoplasia- no. (%)	8 (6%)	8 (8%)	None	0.20
Heart failure etiology- no. (%)				0.41

TABLE 3-continued

Characteristics	Clinical characteristics of OHT recipients and according to CH status.			P value
	All (N = 127)	No CH (N = 101)	CH (N = 26)	
Ischemic cardiomyopathy	28 (22%)	20 (20%)	8 (31%)	
Non-ischemic	90 (71%)	73 (72%)	17 (65%)	
cardiomyopathy- no. (%)				
Congenital disease- no. (%)	9 (7%)	8 (8%)	1 (4%)	
Previous VAD - no. (%)	44 (35%)	37 (37%)	7 (27%)	0.35
White blood count ( $\times 10^9/L$ )	8.8 $\pm$ 4.4	7.9 $\pm$ 4.5	6.9 $\pm$ 3.5	0.11
Sodium (mmol/L)	134 $\pm$ 5	136 $\pm$ 5	135 $\pm$ 6	0.53
Creatinine (mmol/L)	117 (92)	122 (86)	116 (127)	0.65
Induction therapy				
Thymoglobulin	123 (97%)	97 (96%)	26 (100%)	0.30
Basiliximab	4 (3%)	4 (4%)	None	
Primary graft dysfunction	19 (15%)	17 (17%)	2 (8%)	0.24
In-hospital death post OHT	12 (9%)	10 (10%)	2 (8%)	0.73
MCS post-OHT	18 (14%)	17 (17%)	1 (4%)	0.09
Follow-up from OHT, years	3.2 $\pm$ 2.6	2.9 $\pm$ 2.1	4.3 $\pm$ 3.9	0.01
Donor CMV+	57 (46%)	45 (46%)	12 (46%)	0.98
Recipient CMV+	80 (65%)	63 (64%)	17 (65%)	0.91
Donor EBV+	97 (14%)	81 (80%)	16 (62%)	0.02
Recipient EBV+	115 (93%)	89 (91%)	26 (100%)	0.10
Immunosuppressive therapy at discharge post-OHT				
Tacrolimus	119 (94%)	97 (96%)	22 (85%)	0.03
Sodium mycophenolate	123 (97%)	100 (99%)	23 (89%)	0.006
Steroids	127 (100%)	101 (100%)	26 (100%)	—
MTOR inhibitor	1 (1%)	None	1 (4%)	0.04
Cyclosporine	6 (5%)	3 (3%)	3 (12%)	0.06
Azathioprine	1 (1%)	None	1 (4%)	0.04
Immunosuppressive therapy at 1 year after OHT				
Tacrolimus	80 (86%)	64 (87%)	16 (84%)	0.79
Sodium mycophenolate	71 (77%)	58 (80%)	13 (68%)	0.30
Steroids	87 (94%)	68 (82%)	19 (100%)	0.19
MTOR inhibitor	17 (19%)	11 (15%)	6 (32%)	0.09
Cyclosporine	8 (9%)	5 (7%)	3 (16%)	0.21
Azathioprine	2 (2%)	1 (1%)	1 (5%)	0.30

CH, clonal hematopoiesis; CMV, cytomegalovirus; EBV, Epstein-barr virus; HF, heart failure MCS, mechanical circulatory support; OHT, orthotopic heart transplant; VAD, ventricular assist device; VAF, variant allele frequency;

TABLE 4

	Clinical outcomes in patients with OHT according to CH mutations			P-value
	All (N = 127)	No CH (N = 101)	CH (N = 26)	
CMV infection	59 (46%)	48 (47.5%)	11 (42.3%)	0.63
Acute cellular rejection	69 (54%)	51 (53%)	18 (69%)	0.14
2/3R				
Post-transplant malignancy	11 (9%)	9 (9%)	2 (8%)	0.84
CAV grade 2 or 3	4 (3%)	None	4 (18%)	<0.001
Mortality	26 (20%)	15 (15%)	11 (42%)	0.008

CAV, cardiac allograft vasculopathy; CH, clonal hematopoiesis; CMV, cytomegalovirus

TABLE 5

List of clonal hematopoiesis mutations detected among orthotopic heart transplant recipients.						
Sample ID	Gene	Chromosome	Start position	End position	Variant type	Variant type
②CHCVD_0004	CEBPA	chr19	33792312	33792312	Missense_Variant	SNV
②CHCVD_0006A	ASXL1	chr20	31023894	31023894	Missense_Variant	SNV

TABLE 5-continued

List of clonal hematopoiesis mutations detected among orthotopic heart transplant recipients.

②CHCVD_0010B	DNMT3A	chr2	25463562	25463562	Frame_Shift_Del	indel
②CHCVD_0010B	DNMT3A	chr2	25467086	25467086	Frame_Shift_Del	indel
②CHCVD_0010B	FLT3	chr13	28608064	28608064	Missense_Variant	SNV
②CHCVD_0011	DNMT3A	chr2	25463187	25463187	Missense_Variant	SNV
②CHCVD_0014	ASXL1	chr20	31024221	31024221	Missense_Variant	SNV
②CHCVD_0017	ASXL1	chr20	31022344	31022344	Missense_Variant	SNV
②CHCVD_0017	BCOR	chrX	39933074	39933074	Missense_Variant	SNV
②HCVD_0017	DNMT3A	chr2	25470612	25470612	Missense_Variant	SNV
②CVD_0017	SF3B1	chr2	198266552	198266552	Missense_Variant	SNV
②HCVD_0017	TP53	chr17	7577127	7577127	Stop_Gained	SNV
②HCVD_0029	DNMT3A	chr2	25469086	25469086	Missense_Variant	SNV
②CHCVD_0038	DNMT3A	chr2	25468174	25468174	Missense_Variant	SNV
②CHCVD_0038	TP53	chr17	7578371	7578371	Missense_Variant	SNV
ARCHCVD_0038	TP53	chr17	7578380	7578380	Missense_Variant	SNV
ARCHCVD_0041	TP53	chr17	7578380	7578380	Missense_Variant	SNV
ARCHCVD_0043	IDH2	chr15	90631946	90631946	Missense_Variant	SNV
ARCHCVD_0046	DNMT3A	chr2	25470590	25470590	Missense_Variant	SNV
ARCHCVD_0055	TET2	chr4	106158134	106158134	Missense_Variant	SNV
ARCHCVD_0060	ASXL1	chr20	31023667	31023667	Missense_Variant	SNV
ARCHCVD_0060	TET2	chr4	106158560	106158560	Missense_Variant	SNV
ARCHCVD_0096	TET2	chr4	106157326	106157326	Stop_Gained	SNV
ARCHCVD_0100	DNMT3A	chr2	25463568	25463568	Missense_Variant	SNV
ARCHCVD_0100	PTPN11	chr12	112910785	112910785	Missense_Variant	SNV
ARCHCVD_0114	DNMT3A	chr2	25467491	25467491	Missense_Variant	SNV
②CHCVD_0117	DNMT3A	chr2	25467124	25467124	Frame_Shift_Ins	indel
②CHCVD_0117	PPM1D	chr17	58740549	58740549	Frame_Shift_Del	indel
②CHCVD_0117	PPM1D	chr17	58740604	58740607	Frame_Shift_Del	indel
②CHCVD_0117	PPM1D	chr17	58740714	58740714	Frame_Shift_Del	indel
②CHCVD_0117	PPM1D	chr17	58740732	58740732	Frame_Shift_Del	indel
②CHCVD_0117	TP53	chr17	7577526	7577526	Missense_Variant	SNV
②CHCVD_0128	DNMT3A	chr2	25469633	25469633	Missense_Variant	SNV
②CHCVD_0128	TP53	chr17	7577556	7577556	Missense_Variant	SNV
②CHCVD_0147	ASXL1	chr20	31023190	31023190	Missense_Variant	SNV
②CHCVD_0149	DNMT3A	chr2	25463196	25463197	Frame_Shift_Del	indel
②CHCVD_0165	TP53	chr17	7577120	7577120	Missense_Variant	SNV
②CHCVD_0166	DNMT3A	chr2	25463236	25463238	Frame_Shift_Del	indel
②HCVD_0166	DNMT3A	chr2	25463586	25463586	Missense_Variant	SNV
②HCVD_0166	DNMT3A	chr2	25464455	25464455	Missense_Variant	SNV
②HCVD_0170	DNMT3A	chr2	25463583	25463583	Missense_Variant	SNV
②HCVD_0200	PHF6	chrX	133549136	133549136	Stop_Gained	SNV
②CHCVD_0210	SMC1A	chrX	53431967	53431967	Stop_Gained	SNV
②CHCVD_0227	DNMT3A	chr2	25462078	25462078	Missense_Variant	SNV
ARCHCVD_0227	PPM1D	chr17	58740522	58740522	Frame_Shift_Del	indel
ARCHCVD_0241	RUNX1	chr21	36252975	36252975	Missense_Variant	SNV
ARCHCVD_0296	DNMT3A	chr2	25458637	25458637	Stop_Gained	SNV
ARCHCVD_0331	DNMT3A	chr2	25470583	25470583	Stop_Gained	SNV
ARCHCVD_0398	ASXL1	chr20	31022341	31022341	Missense_Variant	SNV
ARCHCVD_0456	GATA2	chr3	128200154	128200154	Missense_Variant	SNV
ARCHCVD_0492	TET2	chr4	106157803	106157810	Frame_Shift_Del	indel
ARCHCVD_0563	BCOR	chrX	39933121	39933121	Missense_Variant	SNV
ARCHCVD_0563	EZH2	chr7	148506185	148506185	Missense_Variant	SNV
ARCHCVD_0568	EZH2	chr7	148504787	148504787	Missense_Variant	SNV
ARCHCVD_0568	STAG2	chrX	123220456	123220456	Missense_Variant	SNV
②CHCVD_0585	TP53	chr17	7578278	7578278	Missense_Variant	SNV
②CHCVD_0603	JAK2	chr9	5073739	5073739	Missense_Variant	SNV
②CHCVD_0614	TET2	chr4	106197039	106197039	Missense_Variant	SNV
②CHCVD_0629	CEBPA	chr19	33792987	33792987	Missense_Variant	SNV
②CHCVD_0636	DNMT3A	chr2	25457243	25457243	Missense_Variant	SNV
②CHCVD_0636	DNMT3A	chr2	25469096	25469096	Frame_Shift_Del	indel
②CHCVD_0636	DNMT3A	chr2	25469162	25469162	Stop_Gained	SNV
②CHCVD_0644	TET2	chr4	106155429	106155429	Missense_Variant	SNV
②CHCVD_0657	BCOR	chrX	39933039	39933039	Frame_Shift_Del	indel
②CHCVD_0673	PPM1D	chr17	58740698	58740698	Stop_Gained	SNV
②CHCVD_0680	ASXL1	chr20	31021109	31021109	Missense_Variant	SNV

Sample ID	Ref. Allele	Alt. Allele	Protein change	Alt. reads	Ref. reads	VAF
②CHCVD_0004	T	A	p.Thr337Ser	442	656	0.67378049
②CHCVD_0006A	G	A	p.Asp1127Asn	2559	13221	0.19355571
②CHCVD_0010B	C	-	p.Gly707fs	791	32884	0.02405425
②CHCVD_0010B	G	-	p.Arg597fs	277	92757	0.0029863

TABLE 5-continued

List of clonal hematopoiesis mutations detected among orthotopic heart transplant recipients.

②CHCVD_0010B	T	A	p.Lys634Asn	19623	42835	0.45810669
②CHCVD_0011	A	G	p.Ile769Thr	496	16037	0.03092848
②CHCVD_0014	T	G	p.Ser1236Ala	6179	37380	0.1653023
②CHCVD_0017	G	A	p.Gly610Asp	1265	7311	0.17302695
②CHCVD_0017	A	G	p.Trp509Arg	745	46356	0.01607127
②HCVD_0017	G	A	p.Arg288Trp	1350	4998	0.27010804
②CVD_0017	C	T	p.Ala762Thr	734	24252	0.03026555
②HCVD_0017	C	A	p.Glu271*	619	6642	0.09319482
②HCVD_0029	G	A	p.Arg458Trp	416	4097	0.10153771
②CHCVD_0038	T	C	p.Asn501Ser	9671	29430	0.32861026
②CHCVD_0038	C	G	p.Gly187Arg	133	17741	0.00749676
ARCHCVD_0038	C	G	p.Asp184His	133	17740	0.00749718
ARCHCVD_0041	C	G	p.Asp184His	142	20782	0.00683284
ARCHCVD_0043	T	C	p.Asn136Ser	2076	5343	0.38854576
ARCHCVD_0046	A	T	p.Leu295Gln	570	8500	0.06705882
ARCHCVD_0055	C	T	p.Pro1012Leu	3565	9098	0.39184436
ARCHCVD_0060	G	A	p.Arg1051His	841	9827	0.08558054
ARCHCVD_0060	A	G	p.Asn1154Ser	2104	7665	0.27449446
ARCHCVD_0096	C	T	p.Gln743*	200	28409	0.00704002
ARCHCVD_0100	A	G	p.Ile705Thr	375	12290	0.03051261
ARCHCVD_0100	G	A	p.Arg265Gln	238	21688	0.01097381
ARCHCVD_0114	C	T	p.Asp529Asn	170	10755	0.0158066
②CHCVD_0117	T	+	p.Tyr584fs	1599	36285	0.0440678
②CHCVD_0117	G	-	p.Ile486fs	77	24796	0.00310534
②CHCVD_0117	AACA	-	p.Asn505fs	70	29465	0.0023757
②CHCVD_0117	A	-	p.Glu540fs	362	22820	0.01586328
②CHCVD_0117	T	-	p.Leu546fs	262	22819	0.01148166
②CHCVD_0117	A	T	p.Leu252His	278	15061	0.01845827
②CHCVD_0128	G	A	p.Arg379Cys	4474	62094	0.07205205
②CHCVD_0128	C	T	p.Cys242Tyr	422	40218	0.01049281
②CHCVD_0147	C	A	p.Ser892Tyr	228	36353	0.00627183
②CHCVD_0149	TT	-	p.Lys766fs	1027	37205	0.02760382
②CHCVD_0165	C	G	p.Arg273Pro	4705	12830	0.36671863
②CHCVD_0166	A	-	p.Trp753fs	1226	55482	0.02209726
②HCVD_0166	C	T	p.Gly699Asp	658	13363	0.04924044
②HCVD_0166	G	C	p.Asp686Glu	145	12401	0.01169261
②HCVD_0170	G	A	p.Pro700Leu	172	15467	0.01112045
②HCVD_0200	C	T	p.Arg274*	895	62494	0.01432137
②CHCVD_0210	G	A	p.Arg725*	697	13878	0.05022338
②CHCVD_0227	G	A	p.Pro777Ser	547	19125	0.02860131
ARCHCVD_0227	A	-	p.Asn477fs	728	13283	0.0548069
ARCHCVD_0241	C	T	p.Leu129Leu	203	40261	0.0050421
ARCHCVD_0296	G	A	p.Gln846*	196	7986	0.02454295
ARCHCVD_0331	C	T	p.Trp297*	152	14952	0.01016586
ARCHCVD_0398	C	T	p.Thr609Ile	5571	12858	0.43327112
ARCHCVD_0456	C	G	p.Arg384Thr	127	47555	0.00267059
ARCHCVD_0492	AGAA	-	p.Asn903fs	240	70735	0.00339295
ACCA						
ARCHCVD_0563	C	T	p.Gly493Asp	58	29158	0.00198916
ARCHCVD_0563	C	G	p.Glu725Gln	59	24362	0.0024218
ARCHCVD_0568	G	C	p.Ala736Gly	134	25452	0.00526481
ARCHCVD_0568	G	C	p.Trp1038Leu	99	40520	0.00244324
②CHCVD_0585	G	C	p.Pro191Ala	118	31392	0.00375892
②CHCVD_0603	C	A	p.His606Gln	9294	25742	0.36104421
②CHCVD_0614	C	G	p.Ser1791Cys	146	29756	0.00490657
②CHCVD_0629	G	T	p.Pro112Thr	128	130	0.98461538
②CHCVD_0636	G	A	p.Arg882Cys	6936	287680	0.02411012
②CHCVD_0636	G	-	p.Lys456fs	659	100672	0.00654601
②CHCVD_0636	G	C	p.Tyr432*	897	91092	0.00984719
②CHCVD_0644	G	T	p.Lys110Asn	476	19776	0.02406958
②CHCVD_0657	G	-	p.Asn520fs	461	41910	0.01099976
②CHCVD_0673	A	T	p.Lys535*	3230	36839	0.08767882
②CHCVD_0680	T	A	p.Ser370Thr	12555	20108	0.62437836

② indicates text missing or illegible when filed

TABLE 6

Clinical phenotype and outcomes according to CH among HCM patients with sarcomeric mutations						
	All-CH		DNMT3A, TET2, ASXL1			
	No CH (N = 169)	CH (N = 37)	p	No CH (N = 182)	CH (N = 23)	p
<b>Echocardiogram</b>						
MLVWT, mean (SD), mm	17.3 (4.6)	17.6 (5.1)	0.765	17.4 (4.7)	17.5 (4.9)	0.874
LA diameter, mm	3.9 (1.2)	3.8 (1.1)	0.651	3.9 (1.2)	3.7 (1.4)	0.642
LAVi, ml/m <sup>2</sup>	38.5 (30.8)	41.3 (20.7)	0.599	39.5 (30.2)	35.6 (20.3)	0.547
LV EF, %	58.2 (15.3)	62.4 (6.2)	0.106	58.5 (14.8)	63.0 (7.3)	0.156
LVOT maximal gradient, mm Hg	17.2 (26.6)	22.5 (40.3)	0.316	17.6 (27.4)	22.6 (43.5)	0.442
SAM, No. (%)	76 (45.0)	21 (56.8)	0.193	84 (45.9)	13 (56.5)	0.336
Moderate-severe MR, No. (%)	7 (4.1)	1 (2.7)	0.681	8 (4.4)	0	0.306
Cardiac MRI						
LV mass, g	137.3 (52.9)	143.1 (61.4)	0.601	137.8 (52.9)	142.3 (65.5)	0.728
LV mass index, g/m <sup>2</sup>	72.1 (25.5)	74.7 (27.2)	0.622	72.5 (25.3)	73.1 (30.2)	0.920
MLVWT, mm	18.9 (6.4)	19.2 (5.6)	0.814	19.0 (6.4)	19.0 (5.8)	0.980
LV EF, %	60.8 (8.3)	62.1 (6.2)	0.390	61.0 (8.2)	61.1 (5.8)	0.979
LGE, No (%)	134 (79.3)	27 (73.0)	0.400	144 (78.7)	17 (73.9)	0.601
LGE >15%, No (%)	26 (17.7)	11 (33.3)	0.044	30 (18.8)	7 (35.0)	0.090
LV mass % of LGE <sup>1</sup> , %	12.2 (7.7-17.6)	15.6 (10.4-24.6)	0.068	12.2 (7.7-17.5)	21.2 (13.7-41.8)	0.014
Apical Aneurysm, No (%)	1 (0.6)	1 (2.7)	0.145	2 (1.1)	0	0.613
Syncope, No (%)	6 (3.6)	3 (8.1)	0.219	7 (3.8)	2 (8.7)	0.281
ABPR at exercise, No. (%) (85/15)	25 (29.8)	10 (62.5)	0.012	27 (30.7)	8 (66.7)	0.014
NVST, No. (%) (145/21)	52 (37.7)	11 (39.3)	0.873	56 (37.6)	7 (41.2)	0.772
Stroke, No. (%)	2 (1.2)	2 (5.4)	0.092	3 (1.6)	1 (4.3)	0.375
Appropriate ICD shock, No. (%)	2 (1.2)	0	0.506	2 (1.1)	0	0.614
Cardiac arrest, No. (%)	0	0	n/a	0	0	n/a
Death or orthotopic heart transplant, No. (%)	2 (1.2)	3 (8.1)	0.013	2 (1.1)	3 (13.0)	<0.0001
MACE, No. (%)	5 (3.0)	5 (13.5)	0.008	6 (3.4)	4 (17.4)	.004

<sup>1</sup>Quantified LGE >5%.

ABPR, abnormal blood pressure response;

EF, ejection fraction;

LA, left atrium diameter;

LAVi, left atrium volume index;

ICD, implantable cardioverter defibrillator;

LGE, late gadolinium enhancement;

LV, left ventricle;

LVOT, left ventricular outflow tract;

MACE, major cardiovascular events;

MLVWT, maximal left ventricular wall thickness;

MR, mitral regurgitation;

MRI, magnetic resonance imaging;

NVST, non-sustained ventricular tachycardia;

SAM, systolic anterior motion;

TABLE 7

Overall characteristics of the HCM cohort and between those with or without CH.				
	All (N = 799)	No CH (N = 616)	CH (N = 183)	P
Age, mean (SD), years	55.7 (14.6)	55.3 (14.5)	57.2 (14.8)	0.126
Age at diagnosis, mean (SD), years	47.8 (15.8)	47.3 (15.6)	49.6 (16.3)	0.089
Male sex, No. (%)	547 (68.5)	424 (68.8)	123 (67.2)	0.679
Body mass index <sup>1</sup> , mean (SD), kg/m <sup>2</sup>	29.0 (6.9)	29.0 (7.1)	29.2 (6.2)	0.647
Hypertension, No. (%)	315 (39.4)	233 (37.8)	82 (44.8)	0.093
Diabetes, No. (%)	104 (13.0)	78 (12.6)	26 (14.2)	0.863
Prior/current smoker, No. (%)	155 (19.3)	119 (19.3)	36 (19.6)	0.637
Coronary artery disease, No. (%)	73 (9.1)	61 (9.9)	12 (6.5)	0.166
Atrial fibrillation, No. (%)	143 (17.8)	107 (17.3)	36 (19.6)	0.493
Genetic testing, No. (%)	712 (89.1)	554 (89.9)	158 (86.3)	0.170
Pathogenic/Likely pathogenic variant, No. (%)	206 (25.8)	169 (30.5)	37 (23.4)	0.083
MYH7, No. (%)	53 (25.7)	43 (25.6)	10 (27.0)	0.664
MYBPC3, No. (%)	127 (61.6)	106 (63.1)	21 (56.8)	
Other, No. (%)	26 (12.6)	20 (11.8)	6 (16.2)	
Family history of HCM, No. (%)	251 (31.4)	194 (31.5)	57 (31.1)	0.087
Family history of SCD, No. (%)	37 (4.6)	26 (4.2)	1 (5%)	0.30
Implantable cardioverter defibrillator, No. (%)	111 (13.9)	89 (14.4)	22 (12.0)	0.405

TABLE 7-continued

Overall characteristics of the HCM cohort and between those with or without CH.				
	All (N = 799)	No CH (N = 616)	CH (N = 183)	P
Pacemaker, No. (%)	13 (1.6)	6 (1.0)	7 (3.8)	0.007
NYHA II-IV, No. (%)	235 (29.4)	182 (29.5)	53 (28.9)	0.803
Beta-blocker, No. (%)	421 (52.7)	321 (52.1)	100 (54.6)	0.547
Non-dihydropyridine calcium channel blocker, No. (%)	116 (14.5)	77 (12.5)	39 (21.3)	0.003
Disopyridine, No (%)	67 (8.4)	51 (8.3)	16 (8.7)	0.842
Diuretic, No (%)	81 (10.1)	59 (9.5)	22 (12.0)	0.303
Septal reduction therapy, No. (%)	76 (9.5)	53 (8.6)	23 (12.5)	0.130

Abbreviations: CH, clonal hematopoiesis; HCM, hypertrophic cardiomyopathy; SCD, sudden cardiac death

<sup>1</sup>Body mass index calculated as weight (kg)/height<sup>2</sup>(m)

TABLE 8

Clinical characteristics of OHT recipients and according to CH status.				
Characteristics	All (N = 782)	No CH (N = 659)	CH (N = 123)	P value
Age - year	54.2 ± 12.7	54.1 ± 12.8	54.4 ± 12.3	0.795
Median (range)		57 (48-63)	58 (46-63)	
Male sex	52.9%	68%	67.3%	0.882
Organ				
Heart	127 (16.2%)	101 (15.3%)	26 (21.1%)	0.007
Lung	90 (11.5%)	73 (11.1%)	17 (13.8%)	

TABLE 8-continued

Clinical characteristics of OHT recipients and according to CH status.				
Characteristics	All (N = 782)	No CH (N = 659)	CH (N = 123)	P value
Kidney	189 (24.2%)	174 (26.4%)	15 (12.2%)	
Liver	374 (47.8%)	310 (47.0%)	64 (52%)	
Lung-Liver	2 (0.3%)	1 (0.2%)	1 (0.8%)	

TABLE A

SmMIP Probe List									
>mip_key	logistic_score	ext_probe_start	ext_probe_stop	ext_probe_copy	ext_probe_copy	ext_probe_sequence	SEQ_ID	lig_probe_stop	lig_probe_copy
1 : 43814899-43815068/26, 18/-	0.78875	1	43815043	43815068	1	TGGTCCACCGCAGCTCCCTGCCCTGG	1	43814916	1
1 : 115256459-115256628/21, 23/+	0.981109	1	115256459	115256479	1	GATGGCAAATACACAGAGAA	2	115256628	1
1 : 115258635-115258804/21, 23/-	0.951804	1	115258784	115258804	1	CAACAGGTTCTGTGGTGTG	3	115258657	1
2 : 25457124-25457293/22, 22/+	0.833844	2	25457124	25457145	2	TACCTAGATTGCCCATGTC	4	25457293	1
2 : 25457152-25457321/20, 24/-	0.839643	2	25457302	25457321	2	TCACCCCTGCCCTCTGCCT	5	25457175	1
2 : 25458549-25458718/20, 24/-	0.96996	2	25458699	25458718	2	TCCTCTTTCTCTCTCAT	6	25458572	1
2 : 25459749-25459918/21, 23/-	0.860238	2	25459898	25459918	1	GTATCCAGGTTCTTTGTT	7	25459771	1
2 : 25461967-25462136/22, 22/-	0.90969	2	25462115	25462136	1	GCTGTTCATGCTCCTCTTGG	8	25461988	1
2 : 25463123-25463292/20, 24/+	0.881523	2	25463123	25463142	1	AGGTAGAACCATAGTGA	9	25463292	1
2 : 25463185-25463354/20, 24/-	0.871458	2	25463325	25463354	2	GCCCCAGCTGATGGCTTCT	10	25463208	1
2 : 25463484-25463653/20, 24/+	0.917457	2	25463484	25463503	1	GTGGAGGGAAAGATGGTA	11	25463653	1
2 : 25464510-25464629/20, 24/+	0.808999	2	25464510	25464529	1	TCCTCAACACCTCCAGGC	12	25464629	1
2 : 25464407-25464566/24, 20/-	0.825581	2	25464543	25464566	1	GCTGAGGACTTGGAATTAGGT	13	25464426	1
2 : 25466743-25466912/20, 24/-	0.909729	2	25466893	25466912	1	GCTGGTGGAGCTTGGAC	14	25466766	1
2 : 25467012-25467163/20, 24/+	0.81207	2	25467012	25467031	1	CCAGGACTCAAAATCCT	15	25467163	1
2 : 25466901-25467110/22, 22/-	0.807386	2	25467089	25467110	1	AAGGGTACCTAGGGCTGTC	16	25467012	1
: 25467117-25467237/22, 22/-	0.81286	2	25467216	25467237	1	GTCTCCCTGTCACCTGGCT	17	25467138	1
2 : 25467383-25467552/23, 21/-	0.896693	2	25467530	25467552	1	GTGGTTCTGACCCCTCCGCTG	18	25467403	1
2 : 25468100-25468249/20, 24/+	0.927609	2	25468100	25468119	1	TCCTGGTGGCTCTGCTACTCT	19	25468249	1
2 : 25468075-25468224/23, 21/-	0.855948	2	25468202	25468224	1	CATCCCCTCCCTCTGTTCCAG	20	25468095	1
2 : 25468817-25468986/24, 20/+	0.721162	2	25468817	25468840	1	CTTCCTPAAGTGCTCTGCTACTCT	21	25468986	1
2 : 25468993-25469162/20, 24/+	0.826636	2	25468993	25469012	2	TCCTGGTGGCCACCTCTCCA	22	25469162	1
2 : 25469087-25469256/24, 20/+	0.953003	2	25469087	25469110	1	GGGCTTTGGCTGGTGAAGGTG	23	25469256	1

TABLE A-continued

SmmIP Probe List						
2 : 25469510-25469676/20, 24/+	0 .700311	2	25469510	25469529	1	TAGGGCCAGAAGGCTGGAAAG
2 : 25469385-25469551/22, 22/-	0 .787747	2	25469530	25469551	1	TGATTGAATGGCCCTGGGG
2 : 2546926-25470095/23, 21/+	0 .871049	2	25469926	25469948	1	GACTCTGTAGATGGCTTTGGGT
2 : 25469859-25470028/22, 22/-	0 .898607	2	25470007	25470028	1	GGTGTGTTGTTGAGAACGTGATG
2 : 25470436-25470599/22, 22/+	0 .833016	2	25470436	25470457	1	CTACTGCCAAACCCACAACATT
2 : 25470523-25470685/23, 21/-	0 .911389	2	25470663	25470685	1	ATGGGGGATCAGGGTGGCAGGG
2 : 25470913-25471078/26, 18/+	0 .711861	2	25470913	25470938	1	TCTGGCTCGTCATCGCTGTTGGT
2 : 198266544-198266713/20, 24/+	0 .804959	2	198266544	198266563	1	GTAGTTGGCATATCTGCAT
2 : 198266417-198266586/23, 21/-	0 .890112	2	198266564	198266586	1	TGGGTATCTTATTCTCTATGG
2 : 198266730-198266899/20, 24/-	0 .956695	2	198266880	198266899	1	TAGGTAATGTTGGGGATAG
2 : 198267419-198267588/22, 22/+	0 .934101	2	198267419	198267440	1	GGGCAATAAGGAATGCC
2 : 198267315-198267494/21, 23/-	0 .947509	2	198267464	198267484	1	CCTAACACAAACGCTAGAGCT
2 : 209113063-209113232/24, 20/+	0 .895571	2	209113063	209113086	1	CAAATCACATTATGCCAACATG
3 : 128200021-128200186/21, 23/-	0 .950888	3	128200166	128200186	1	TCTGAAACACTGGTTGCCT
3 : 128200661-128200783/24, 20/+	0 .899098	3	128200661	128200684	1	CATTTGGCAGCTTGTTAGTAGGGC
3 : 128202705-128202871/20, 24/-	0 .848532	3	128202852	128202871	2	TGTCTCTCCCTGTCCTG
4 : 5558697-55589866/23, 21/+	0 .941587	4	55589697	55589719	1	GTTGCTGAGGTTCAGGACTC
4 : 5559221-5559390/20, 24/-	0 .944773	4	55599371	55599390	1	GCAGGAGCTGTCAAGGAGA
4 : 106155115-106155234/21, 23/+	0 .928618	4	106155115	106155135	1	ACCAACCATGTTGAGGCAAC
4 : 106155243-106155367/20, 24/+	0 .976973	4	106155243	106155262	1	AAATGGAGAACCAAGTGGC
4 : 106155161-106155308/20, 24/-	0 .963051	4	106155289	106155308	1	TGGCTTCCTTCATAGGG
4 : 106155408-106155577/22, 22/+	0 .954287	4	106155408	106155429	1	CTCTGGGCTCCTTCAGATCAAG
4 : 106155297-106155466/23, 21/-	0 .967386	4	106155444	106155466	1	GTCCTTCTCCATTAGCTTTGG
4 : 106155628-106155777/18, 26/+	0 .954069	4	106155628	106155645	1	CCAGAGCTTCAGATCTG
4 : 106155497-106155666/20, 24/-	0 .964361	4	106155647	10615666	1	ACTTTCCCTCCTGTCAT

TABLE A-continued

SmmIP Probe List									
4 : 106155827-106155996/20,	24/+	0.947632	4	106155827	106155846	2	AGAAAACCACATCTCACATA	49	106155996
4 : 106155708-106155877/20,	24/-	0.944218	4	106155858	10615877	1	ACTCATTAAGTACCTGACTG	50	106155731
4 : 106156035-106156184/25,	19/+	0.927737	4	106156035	106156059	1	TACCTGTCCCTTCAGAACAGAA	51	106156184
4 : 106155947-106156116/22,	22/-	0.98082	4	106156095	106156116	1	GTTATTCTCGAGGAGATGGG	52	106155968
4 : 106156251-106156420/22,	22/+	0.902481	4	106156251	106156272	1	CTCAGTGTTCACTAAGGATTC	53	106156420
4 : 106156143-106156312/25,	19/-	0.903718	4	106156288	106156312	1	GCAATTGTGATGGTGGTGGTGT	54	106156161
4 : 106156470-106156639/22,	22/+	0.946747	4	106156470	106156491	1	ACCAACCTCCAGAGTCCTAAT	55	106156639
4 : 106156348-106156517/20,	24/-	0.958324	4	106156498	106156517	1	GAAGGGCTGCATACTGTGT	56	106156371
4 : 106156694-106156863/20,	24/+	0.907492	4	106156694	106156713	1	TGATGAGAAAACAAGCAA	57	106156863
: 106156579-106156748/20,	24/-	0.965115	4	106156729	106156748	1	CCTGTTGCTCCTTGTCCTG	58	106156602
4 : 106156916-106157085/23,	21/+	0.951204	4	106156916	106156938	1	CTGGAAATTCGAAACATGCCTGG	59	106157085
4 : 106156809-106156978/21,	23/-	0.972677	4	106156958	106156978	1	GCTGTGTTGTTCTGGTGT	60	106156831
4 : 106157149-106157318/21,	23/+	0.947906	4	106157149	106157169	1	CAACAAAGGAGGATTCCAA	61	106157318
4 : 106157036-106157205/20,	24/-	0.962137	4	106157186	106157205	1	GTGCTGTTCAACACTGGGG	62	106157059
4 : 106157399-106157568/18,	26/+	0.930675	4	106157399	106157416	1	ATGATCAGCAAAGAGAG	63	106157568
4 : 106157269-106157438/18,	26/-	0.968587	4	106157421	106157438	1	TTAGTCTGCCAAAGAAT	64	106157294
4 : 106157597-106157766/21,	23/+	0.921979	4	106157597	106157617	1	CTTGTCAAACATAACACC	65	106157766
4 : 106157482-106157651/20,	24/-	0.953483	4	106157632	106157651	1	GGATGTGTTAGTCTGTCCTT	66	106157505
4 : 106157839-106158008/21,	23/+	0.951954	4	106157839	106157859	1	CTTGTCAAGCAAGGTACTTG	67	106158008
4 : 106157718-106157892/22,	22/-	0.959552	4	106157871	106157892	1	ACGCACAGGAAAAACATTGCA	68	106157739
4 : 106158007-106158176/18,	26/+	0.886265	4	106158007	106158024	1	ACTGAGTCCTGCACATGT	69	106158176
4 : 106157931-106158100/23,	21/-	0.983485	4	106158078	106158100	1	TGTTCCTGGTGGTGTGTGC	70	106157951
4 : 106158223-106158378/21,	23/+	0.956903	4	106158223	106158243	1	GACCATTAAGGCTCTTACTCTC	71	106158378
4 : 106158127-106158296/22,	22/-	0.950701	4	106158275	106158296	1	GTCAAAACTGTGACTGGCCCTG	72	106158148
4 : 106158415-106158589/20,	24/+	0.882262	4	106158415	106158434	1	GAGTCACCTCCAAATTACT	73	106158589
4 : 106158315-106158478/20,	24/-	0.979383	4	106158459	106158478	1	GAGTCITGACAGGTGATCC	74	106158338

TABLE A-continued

SmmIP Probe List						
4 :	106162450-106162619/20 , 24/+	0 . 88601	4	106162450	106162469	1
4 :	106163956-106164125/22 , 22/+	0 . 980266	4	106163956	106163977	4
4 :	106164761-106164930/21 , 23/+	0 . 926757	4	106164761	106164781	1
4 :	106164674-106164843/20 , 24/-	0 . 873669	4	106164824	106164843	1
4 :	106164852-106165021/21 , 23/-	0 . 899251	4	106165001	106165021	1
4 :	106180720-106180839/24 , 20/+	0 . 846203	4	106180720	106180743	1
4 :	106180786-106180955/20 , 24/-	0 . 931831	4	106180936	106180955	1
4 :	106182895-106183049/19 , 25/+	0 . 697024	4	106182895	106182913	1
4 :	106190771-106190940/20 , 24/+	0 . 930131	4	106190771	106190790	1
4 :	106190690-106190859/21 , 23/-	0 . 810744	4	106190839	106190859	1
4 :	106193771-106193940/22 , 22/+	0 . 917879	4	106193771	106193792	1
4 :	106193686-106193855/20 , 24/-	0 . 956667	4	106193836	106193855	3
4 :	106193946-106194115/20 , 24/+	0 . 908902	4	106193946	106193965	1
4 :	106193871-106194040/22 , 22/-	0 . 986116	4	106194019	106194040	1
4 :	106196177-106196316/24 , 20/+	0 . 915559	4	106196177	106196200	1
4 :	106196361-106196530/21 , 23/+	0 . 913618	4	106196361	106196381	1
4 :	106196262-106196431/20 , 24/-	0 . 95844	4	106196412	106196431	1
4 :	106196561-106196730/20 , 24/+	0 . 846784	4	106196561	106196580	1
4 :	106196462-106196631/21 , 23/-	0 . 977129	4	106196611	106196631	1
4 :	106196781-106196950/20 , 24/+	0 . 993805	4	106196781	106196800	1
4 :	106196677-106196846/21 , 23/-	0 . 987067	4	106196826	106196846	1
4 :	106196887-106197056/21 , 23/+	0 . 931081	4	106196887	106196907	1
4 :	106196980-106197149/20 , 24/+	0 . 893803	4	106196980	106196999	1
4 :	106197193-106197362/24 , 20/+	0 . 908112	4	106197193	106197216	1
:	106197071-106197240/18 , 26/-	0 . 907301	4	106197223	106197240	1

TABLE A-continued

SmMIP Probe List							
4 :	106197400-106197569/20,	24/+	0 .975927	4	106197400	106197419	1
4 :	106197289-106197458/24,	20/-	0 .959564	4	106197435	106197458	1
4 :	106197523-106197692/20,	24/-	0 .923275	4	106197673	106197692	1
5 :	170837475-170837644/22,	22/-	0 .943775	5	170837623	170837644	17
7 :	140453073-140453242/20,	24/+	0 .916227	7	140453073	140453092	1
7 :	148504716-148504885/20,	24/+	0 .944239	7	148504716	148504735	1
7 :	148506108-148506277/22,	22/-	0 .949232	7	148506256	148506277	1
7 :	148506397-148506516/24,	20/+	0 .969517	7	148506397	148506420	1
7 :	148507392-148507561/23,	21/-	0 .965315	7	148507539	148507561	1
7 :	148508689-148508859/20,	24/-	0 .923191	7	148508839	148508858	2
7 :	148511097-148511266/23,	21/+	0 .841123	7	148511097	148511119	1
7 :	148510995-148511164/20,	24/-	0 .869647	7	148511145	148511164	1
7 :	148511955-148512124/20,	24/-	0 .889269	7	148512105	148512124	1
7 :	148512532-148512701/22,	22/-	0 .917806	7	148512680	148512701	1
7 :	148516641-148516810/20,	24/-	0 .763635	7	148516791	148516810	1
7 :	148523639-148523808/20,	24/+	0 .843345	7	148523639	148523658	1
7 :	148523519-148523688/20,	24/-	0 .900594	7	148523669	148523688	1
7 :	148526795-148526954/21,	23/-	0 .896884	7	148526934	148526954	1
8 :	117864762-117864931/20,	24/-	0 .909931	8	117864912	117864931	1
8 :	117864807-117864976/23,	21/-	0 .857987	8	117864954	117864976	17
8 :	117866456-117866633/21,	23/+	0 .779265	8	117866456	117866476	1
8 :	117866573-117866742/24,	20/-	0 .877384	8	117866719	117866742	1
8 :	117868372-117868549/24,	20/-	0 .808009	8	117868526	117868549	31
9 :	5069922-5070091/20,	24/-	0 .88135	9	5070072	5070091	1
9 :	5073712-5073881/20,	24/+	0 .965559	9	5073731	5073742	1
9 :	5069922-5070091/20,	24/-	0 .88135	9	5070072	5070091	1
9 :	5073712-5073881/20,	24/+	0 .965559	9	5073731	5073742	1

TABLE A-continued

SmmIP Probe List									
10 : 112350147-112350316/21, 23/+	0.883234	10	112350147	112350167	1	TTTCATTCTGACAACTTAC	125	112350316	1
10 : 112350217-112350386/21, 23/-	0.943637	10	112350366	112350386	1	TAAGCTATTCTTATCCCTCT	126	112350239	1
10 : 112350706-112350875/22, 22/+	0.9222256	10	112350706	112350727	1	CCTGAGTACCAATAAGATTG	127	112350875	1
10 : 112350813-112350982/20, 24/-	0.959726	10	112350963	112350982	1	GTTGATAGTGCTGGCACT	128	112350836	1
10 : 112352791-112352960/22, 22/+	0.980092	10	112352791	112352812	1	CTGTTGTGATCCTCTGTG	129	112352960	1
10 : 112352887-112353056/21, 23/-	0.892519	10	112353036	112353056	1	CGCCCAGCCAGATATATGTT	130	112352909	1
10 : 112356126-112356295/20, 24/+	0.893075	10	112356126	112356145	1	ACAGACCTATTACATATGTT	131	112356295	1
11 : 32413487-32413656/20, 24/+	0.897861	11	32413487	32413506	1	GA AAAAATAATGTGAGAAA	132	32413656	1
11 : 32414159-32414328/20, 24/-	0.930567	11	32414309	32414328	1	TCAAATAGAATATGTGTT	133	32414182	1
11 : 32417866-32418035/20, 24/+	0.938676	11	32417866	32417885	1	GGTAAGCACACATGAGGG	134	32418035	1
11 : 32417752-32417921/20, 24/-	0.91638	11	32417902	32417921	1	TCTGTACGGTGGCATCTG	135	32417775	1
11 : 32421472-32421637/20, 24/+	0.93191	11	32421472	32421491	1	TGGGCCTGTCGTGCTC	136	32421637	1
11 : 119148811-119148980/23, 21/+	0.851218	11	119148811	119148833	1	CTGTTAACATTATAATTGCACT	137	119148980	1
11 : 119148895-119149064/20, 24/-	0.92696	11	119149045	119149064	1	TACCGATTTCACAGTTA	138	119148918	1
11 : 119149175-119149344/20, 24/+	0.895932	11	119149175	119149194	2	AGTATTTCTGATGATCTG	139	119149344	1
2 : 25378504-25378673/20, 24/-	0.9111124	12	25378654	25378673	1	GTACCTATGGTCCTAATAGG	140	25378527	1
12 : 25380216-25380385/20, 24/-	0.967652	12	25380366	25380385	1	TGGACTGTAATAATCAGAC	141	25380239	1
12 : 25398165-25398334/20, 24/-	0.933725	12	25398315	25398334	1	ATAAGGCCTGCTGAAATGA	142	25398188	1
12 : 112888093-112888262/23, 21/-	0.916866	12	112888240	112888262	3	CCATCTCTCTCTTTTAATTGCC	143	112888113	1
12 : 112910715-112910880/22, 22/+	0.894139	12	112910715	112910736	1	CACGTATAATATGACTTTC	144	112910880	1
12 : 112915411-112915580/20, 24/-	0.966125	12	112915561	112915580	1	GGCTAGAAATGTGTTGTCAG	145	112915434	1
12 : 112926198-112926363/20, 24/-	0.918085	12	112926344	112926363	2	CATAAACTAAACAGAAC	146	112926221	1
12 : 112926812-112926981/20, 24/+	0.957582	12	112926812	112926831	1	GATGTTTCCTTGTGTAATGTT	147	112926981	1
13 : 28592560-28592729/20, 24/+	0.919768	13	28592560	28592579	1	CACAAATAGCGTATAAAA	148	28592729	1
13 : 28602295-28602464/16, 29/+	0.881258	13	28602295	28602310	2	TTTCGTGGAAGTGGG	149	28602464	1

TABLE A-continued

SnpMIP Probe List									
13 : 28607990-28608155/20, 24/-	0.927129	13	28608136	28608155	1	GCACGTACTCACCATTGTC	150	28608013	1
13 : 28608205-28608374/20, 24/+	0.894916	13	28608205	28608224	1	CATTCCATTCCTTACCAACT	151	28608374	1
13 : 28608170-28608339/20, 24/-	0.920908	13	28608320	28608339	1	GAAGCCAGCTACAGATGGT	152	28608193	1
13 : 28608401-28608570/20, 24/+	0.891863	13	28608401	28608420	1	AGAGGAAGAAATAATGATT	153	28608570	1
13 : 28609586-28609755/21, 23/+	0.98033	13	28609586	28609616	1	GTTGGGATTCTCTGATGTTGG	154	28609755	1
13 : 28609701-28609870/20, 24/+	0.946119	13	28609701	28609720	1	ACCCTTTATGGCTTCACTC	155	28609870	1
13 : 2861048-28610217/20, 24/+	0.916878	13	28610048	28610067	1	AAGGGATCATGTCCATA	156	28610217	1
15: 90631745-90631914/20, 24/+	0.801172	15	90631745	90631764	1	AAGAGGATGGCTAGGGAGG	157	90631914	1
15: 90631845-90632014/20, 24/+	0.93351	15	90631845	90631864	1	TGGTGAATGGCTTGGTCAG	158	90632014	1
17: 7572870-7573039/21, 23/+	0.981202	17	7572870	75728890	1	AGGGAGGGAGGAGATGGGT	159	7573039	1
17: 7573933-7574112/22, 22/-	0.910933	17	7574091	7574112	1	CAAACAAATGTAACITGAACCA	160	7573966	1
17: 7576792-7576961/24, 20/-	0.847926	17	7576938	7576961	1	TTCACTTTATGACCTTCCCTGTC	161	7576811	1
17: 7577075-7577244/24, 20/+	0.980151	17	7577075	7577098	1	TTCTCTTCTCTGTCGCCGCT	162	7577244	1
17: 7576963-7577132/21, 23/-	0.924868	17	7577112	7577132	1	GCTTTGAGGTGCGTGTGTTG	163	7576988	1
17: 7577438-7577602/20, 24/+	0.897643	17	7577438	7577457	1	AGAGGAAAGCAGGGCTGGG	164	7577602	1
17: 7577529-7577693/22, 22/-	0.959787	17	7577672	7577693	14	AAAAAAAAAAAAAGGCCTCC	165	7577550	1
17: 7578169-7578338/23, 21/+	0.893158	17	7578169	7578191	1	AACCAGACCTCAGGGCTCAT	166	7578338	1
17: 7578093-7578262/23, 21/-	0.937736	17	7578240	7578262	1	GAATGGAGGAAATTGCGTGTG	167	7578113	1
17: 7578393-7578562/18, 26/+	0.843508	17	7578393	7578410	1	ATGGTGGGGCAGGCCT	168	7578562	1
17: 7578334-7578453/18, 26/-	0.833295	17	7578436	7578453	1	CATGGCCATCTACAAAGCA	169	7578359	1
17: 7578469-7578628/26, 18/-	0.890436	17	7578603	7578628	1	CTGCCGCTTCCAGTTCCTTATCTG	170	7578486	1
17: 7579238-7579407/20, 24/+	0.809488	17	7579238	7579257	1	CAAACAAAAGAATGCAGGG	171	7579407	1
17: 7579298-7579467/21, 23/+	0.74921	17	7579298	7579318	1	TAGGGAAACTAACCGTGCAA	172	7579467	1
17: 7579416-7579577/20, 24/+	0.784204	17	7579416	7579435	2	AGGAGGGGGCTGGTCAGGG	173	7579577	1
17: 7579495-7579664/21, 23/-	0.900055	17	7579644	7579664	2	TGGGACCTGGAGGGCTGGGG	174	7579517	1
17: 7579802-7579971/24, 20/-	0.866469	17	7579948	7579971	1	TCATGGCTGATCCCCACACTTTCTC	175	7579821	1

TABLE A-continued

SmmIP Probe List						
17:	58740425-58740594/22, 22/+	0.952631	17	58740425	58740446	1
17:	58740303-58740472/20, 24/-	0.827005	17	58740453	58740472	1
17:	58740633-58740802/21, 23/+	0.979392	17	58740633	58740653	1
17:	58740506-58740675/21, 23/-	0.853213	17	58740655	58740675	1
17:	58740833-58741002/20, 24/+	0.902941	17	58740833	58740852	1
7:	58740728-58740897/21, 23/-	0.938281	17	58740877	58740897	1
17:	74732929-74733008/24, 20/+	0.924881	17	74732929	74732952	1
18:	42531843-42532012/21, 23/+	0.911291	18	42531843	42531863	1
19:	13054585-13054754/20, 24/+	0.937952	19	13054585	13054604	1
19:	13054480-13054649/24, 20/-	0.794174	19	13054626	13054649	1
19:	33792231-33792385/16, 27/-	0.810719	19	33792370	33792385	12
19:	33792335-33792504/20, 24/-	0.830437	19	33792485	3379254	1
19:	33792732-33792851/16, 26/+	0.652911	19	33792732	33792747	19
19:	33792942-33793051/16, 24/-	0.849634	19	33793036	33793051	2
19:	33793045-33793154/16, 29/+	0.8992	19	33793045	33793060	10
19:	33793184-33793288/16, 26/+	0.876116	19	33793184	33793199	12
20:	31021052-31021221/21, 23/+	0.922229	20	31021052	31021072	1
20:	31021242-31021411/22, 22/+	0.940116	20	31021242	31021263	1
20:	31021151-31021320/24, 20/-	0.925719	20	31021297	31021320	1
20:	31021437-31021606/20, 24/+	0.888392	20	31021437	31021456	1
20:	31021362-31021531/23, 21/-	0.82328	20	31021509	31021531	1
20:	31021534-31021703/20, 24/+	0.939897	20	31021534	31021553	1
20:	31022183-31022352/22, 22/+	0.894333	20	31022183	31022204	1
20:	31022389-31022533/16, 25/+	0.740488	20	31022389	31022404	2
20:	31022292-31022441/20, 24/-	0.670733	20	31022422	31022441	1

TABLE A-continued

TABLE A-continued

SmMIP Probe List						
X: 39911542-39911711/21, 24/+	0.734511	21	36164530	36164549	1	GGTTGGGAGGCCTGGGTTG
X: 36164619-36164747/21, 23/+	0.781897	21	36164619	36164639	2	ACCATGGAGAACCTGGTAGG
X: 36164705-36164815/20, 24/+	0.711885	21	36164705	36164724	1	TTGCGAGGAGCCGGGTAGG
X: 36164717-36164857/23, 21/+	0.828908	21	36164717	36164739	1	GGGGTAAAGGCCGGCAGGTAGG
X: 36164802-36164956/19, 25/+	0.794232	21	36164802	36164820	1	GTCGGGAGTAGGTGAAGG
X: 36171528-36171697/21, 23/-	0.841039	21	36171677	36171697	1	TCCATTGCCTCTCTGTG
X: 36171646-36171815/22, 22/-	0.879815	21	36171794	36171815	1	CATTTTTAACCCACCCAC
X: 36206622-36206777/23, 21/+	0.865415	21	36206622	36206644	1	GGGAAGGTGTGCAATGGGG
X: 36206730-36206885/21, 23/+	0.735902	21	36206730	36206750	1	GGGTAAAGGCAGTGAGTGG
X: 36206799-36206954/23, 21/-	0.791705	21	36206932	36206954	15	TCTTCCTCCCTCCCTCCCTCCC
X: 36231732-36231901/22, 22/-	0.873923	21	36231880	36231901	1	TTTGTCTCTATGTCCTCC
X: 36252801-36252970/23, 21/+	0.943161	21	36252801	36252823	1	TGGTTTGTGCGATGAACGTG
X: 36252916-36252085/21, 23/-	0.94378	21	36253065	36253085	1	ATCACATACACAATGCCCCAA
X: 36259108-36259222/16, 29/+	0.817091	21	36259108	36259123	15	CTGTCTCCCCACCAAC
X: 36259159-36259263/22, 22/+	0.706198	21	36259159	36259180	3	GTCTTGTGCGAGGCCATGCG
X: 44514729-44514898/22, 22/-	0.933507	21	44514877	44514898	2	TTTCGCGTGAAGAATGCGG
X: 44524416-44524585/20, 24/+	0.94191	21	44524416	44524435	1	CAAACAAACCTGGCTAACG
X: 15833872-15834041/20, 24/+	0.979296	X	15833872	15833891	2	AATGGAGCAGTGCAGGAGGG
X: 15833745-15833914/20, 24/-	0.924197	X	15833895	15833914	2	GCTTGCCTCAGGTCAATGT
X: 15836657-15836826/21, 23/-	0.93315	X	15836806	15836836	1	AACAGAAACAGAACAAAC
X: 15838303-15838483/23, 21/+	0.712992	X	15838303	15838325	1	GCATATCATTGATTTGGTT
X: 39911340-39911509/20, 24/+	0.940705	X	39911340	39911359	1	GTACATGGGGTCCAGACTT
X: 39911542-39911711/21, 23/+	0.932675	X	39911542	39911562	1	TTCTGGCTCTGGAAATGGGAC
X: 39911448-39911617/20, 24/-	0.941736	X	39911598	39911617	1	GAAATGAAAATGTCCTCCC
X: 39911595-39911476/20, 24/+	0.919934	X	399114595	399114614	1	AGACCAATTCTGAACTTTG

TABLE A-continued

SmmIP Probe List									
X: 39914691-39914860/24, 20/-	0.9663337	X	39914837	39914860	1	TGCCAGCTTGCCTGTTTT	251	39914710	1
X: 39932843-39933012/24, 20/+	0.82704	X	39932843	39932866	1	TCCGTGGTTGGCCATCTG	252	39933012	1
X: 39933079-39933348/20, 24/+	0.945629	X	39933079	39933098	1	GAGGGCAGTGCTGATGAT	253	39933248	1
X: 39932964-39933133/20, 24/-	0.933519	X	39933114	39933133	1	CTCAGGAAATGGTTGCT	254	39932987	1
X: 48649464-48649633/16, 29/+	0.856993	X	48649464	48649479	14	TTCTGTTGCTGAGGA	255	48649633	1
X: 48649495-48649864/21, 23/+	0.897556	X	48649695	48649715	1	TGGCTACTAAGGGACGCTG	256	48649864	1
X: 48649576-48649745/20, 24/-	0.823488	X	48649726	48649745	1	TGGAGTACCTGGGAGGT	257	48649599	1
X: 53431899-53432068/20, 24/+	0.892295	X	53431899	53431918	1	TGTGTTGGATGGCTTGGAG	258	53432068	1
X: 53432011-53432180/22, 22/+	0.897516	X	53432011	53432032	1	ATCTGGAGTCATGGGCTGAG	259	53432180	1
X: 53432104-53432273/23, 21/+	0.897847	X	53432104	53432126	1	GCTAGGGTAAAGGTGGCTG	260	53432273	1
X: 53432228-53432397/24, 20/+	0.904552	X	53432228	53432251	1	TTTCATCCAGCGCGTGCCT	261	53432397	1
X: 53432336-53432505/20, 24/+	0.904126	X	53432336	53432355	1	GGGGAGAGAGAGAGGGG	262	53432505	1
: 53432548-53432717/23, 21/+	0.873273	X	53432548	53432570	1	ATCAATCACTAGCTTGGCCCT	263	53432717	1
X: 53432438-53432607/22, 22/-	0.912547	X	53432586	53432607	1	CAGGTGAAGCCTAACATGAGA	264	53432459	1
X: 53432775-53432944/23, 21/+	0.945673	X	53432775	53432797	1	GCCTGTTCTCGAGTCACAA	265	53432944	1
X: 53432662-53432831/22, 22/-	0.898153	X	53432810	53432831	1	ACCAAGGTTGGCAAAGAAC	266	53432683	1
X: 123181234-123181403/20, 24/+	0.95047	X	123181234	123181253	1	TGGACTAAATCTTAGCAT	267	123181403	1
X: 123181157-123181326/20, 24/-	0.9185	X	123181307	123181326	1	GCCTCTCATGGCTGTTTT	268	123181180	1
X: 123182833-123183002/20, 24/+	0.820783	X	123182833	123182852	1	GAATGATGTTGTTTTAC	269	123183002	1
X: 123184006-123184184/21, 23/+	0.907704	X	123184006	123184026	1	TTATGCATCGTTTCTCTCC	270	123184184	1
X: 123184910-123185079/20, 24/+	0.833242	X	123184910	123184929	1	GAAGTGAAAATACTAGAG	271	123185079	1
X: 123185026-123185195/22, 22/+	0.858971	X	123185026	123185047	1	AAGAGCTTAATCACAATGGG	272	123185195	1
X: 123185116-123185285/20, 24/+	0.932372	X	123185116	123185135	5	CTTTCCTCTGCTTCTCTTT	273	123185285	1
X: 123189951-123190120/21, 23/-	0.874373	X	123190100	123190120	1	GCCTTAGAAAATGAGTAACAG	274	123189973	1
X: 123220363-123220532/20, 24/+	0.871879	X	123220363	123220382	1	GTATCAAAGCTAACAGTTTC	275	123220532	1
X: 123220475-123220644/20, 24/-	0.7772	X	123220625	123220644	1	AAAAGAAATAATTATPATCC	276	123220498	1

TABLE A-continued

SmmIP Probe List					
lig_probe_sequence	SEQ_ID	miP_scan_start_position	miP_name		
TCAACTTGGCCACCC	286	43814917	MPL_001_Myeloid_Panel		
GTGTTGGAAAGGTAAAGGGCAGGG	287	115256480	NRAS_001_Myeloid_Panel		
GTAGCCCCGTCACCTGATCCGT	288	115258658	NRAS_002_Myeloid_Panel		
ACTGGAAACCAAATAACCTGG	289	25457146	DNMT3A_001_Myeloid_Panel		
GCTGAAGGAGTATTGCGTGTGT	290	25457176	DNMT3A_002_Myeloid_Panel		
CCCGGGTTGTCGTCGCACTGGCT	291	25458573	DNMT3A_003_Myeloid_Panel		
GCAGGGAAAGGGAGGGAGGAT	292	25459772	DNMT3A_004_Myeloid_Panel		
GCTCTGGCCCTGGGGCGTGT	293	25461989	DNMT3A_005_Myeloid_Panel		
GCGATCATGCGAGGGCGTGA	294	25463143	DNMT3A_006_Myeloid_Panel		
GGTTAGTACAACAGGGACATCT	295	25463239	DNMT3A_007_Myeloid_Panel		
GCTGTCAGGGCACAGGGAGACA	296	25463504	DNMT3A_008_Myeloid_Panel		
TTGAGGCCATCTCCCTGGACCTT	297	25464530	DNMT3A_009_Myeloid_Panel		
GTCATGCTGTGGGGCGTGA	298	25464427	DNMT3A_010_Myeloid_Panel		
GTGAGGGGTGAGGCCAAGAGGT	299	25466767	DNMT3A_011_Myeloid_Panel		

TABLE A-continued

SmmIP_Probe_List	
CTTCCTTAATGGCTGCCCTGGCAG	25467032 DNMT3A_012_Myeloid_Panel
GCTTGCGGCGGGCTCGAGCT	25467013 DNMT3A_013_Myeloid_Panel
CCCTGAAACTGTACATGTGC	25467119 DNMT3A_014_Myeloid_Panel
GCTGTTGCTGCCCTCAGTGGT	25467404 DNMT3A_015_Myeloid_Panel
GGTAGTACACCGAAGGCCCTCT	25468120 DNMT3A_016_Myeloid_Panel
TGCCGTTAGGCCGCCCTTC	25468096 DNMT3A_017_Myeloid_Panel
CCGGCTCTCCCTCGGATG	25468841 DNMT3A_018_Myeloid_Panel
CACATGTCGGTACACTCTTTC	25469013 DNMT3A_019_Myeloid_Panel
TCCCCCACCCCTCGTTACAG	25469111 DNMT3A_020_Myeloid_Panel
GTGACACCGCAGGGTTGGGTGTT	25469530 DNMT3A_021_Myeloid_Panel
GGCTGCCAACGCCCTCCACAGAG	25469407 DNMT3A_022_Myeloid_Panel
CACCAACCCATGCCTGGAA	25469949 DNMT3A_023_Myeloid_Panel
GCACTAGGGGCCCTGGAAGTTG	25469881 DNMT3A_024_Myeloid_Panel
TTCCCCAACCAAGCTCCCCAA	25470458 DNMT3A_025_Myeloid_Panel
GTGTCTTGGGGATGACGGGC	25470544 DNMT3A_026_Myeloid_Panel
CGGCCCCGGTTTCTCTT	25470939 DNMT3A_027_Myeloid_Panel
AGGTAATGGGGATTACCTTTTC	198266564 SF3B1_001_Myeloid_Panel
CTGGATAATTTCATGGTCT	198266438 SF3B1_002_Myeloid_Panel
GTGTTAAAGCCCTTATGGAGGGT	198266754 SF3B1_003_Myeloid_Panel
GAAAGGACAGTCATGAGTGGT	198267441 SF3B1_004_Myeloid_Panel
CTTATGGCTGTGCCATCTGCC	198267318 SF3B1_005_Myeloid_Panel
GGTCCCATTTGGTATTTC	209113087 IDH1_001_Myeloid_Panel
TGCAGGAAAGTCATCCCCCTTC	128200044 GATA2_001_Myeloid_Panel
GGTGGCGGCTCTCTGGCG	128200685 GATA2_002_Myeloid_Panel
CACTCATTAAGCCAAAGCGAAGAC	128202729 GATA2_003_Myeloid_Panel
GTCCAGGAAACTGAGCAGGAGT	55589720 KIT_001_Myeloid_Panel

TABLE A-continued

	SmmIP_Probe_List
GTTGAAATAACACTATTAGGTGGAGG	326
GCCCCACTGCCTGAGAGAGTCAT	327
GTAGAGGGTATTCCAAAGTGTGCG	328
GTTCTGTCTGGCAAATGGAGGTG	329
TCTGTAGGCCAAGAAAAATGAG	330
CGACTATCTGGCTTCCCTTC	331
TGGACACACACATGGTGAACCTCTG	332
CATTGGTGACTGCTTCACCTG	333
GTGAGTGAGGCCCTGTGATGCTGAT	334
GCACCATAGGCATTAGCACTGCC	335
CCAGCAGCAATTGCAAGC	336
GCACCTGCTTGCAGGACCT	337
CACCACTACCCAAACCAAA	338
TGAACAGAAATTCTCACCA	339
CCATGTCGAAZACCTZAGC	340
GCTTTTCTCTCTGAAGGAAGCTG	341
CGTATGAGGCATCACTGCATCA	342
CCAAATGGAACAGTCATTGTCCC	343
CCCTCACACAGGTGCACTTC	344
GGGATTCCGCTTGTGAAGAGA	345
TCCAGAGATTCACATCTCCTCA	346
GGAACCTGGAGATGGTCACCTG	347
GAAATTCCCTTATAGT2AGACCATG	348
GGTTGTGTTGTGCTGCTGTTATG	349
GCTTTCAAAAACAGGAGAAG	350
	55599245
	TET2_001_Myeloid_Panel1
	106155136
	106155263
	106155195
	106155430
	106155318
	106155646
	TET2_006_Myeloid_Panel1
	106155521
	TET2_007_Myeloid_Panel1
	106155847
	TET2_009_Myeloid_Panel1
	106156060
	TET2_010_Myeloid_Panel1
	106155949
	TET2_011_Myeloid_Panel1
	106156273
	TET2_012_Myeloid_Panel1
	106156162
	TET2_013_Myeloid_Panel1
	106156422
	TET2_014_Myeloid_Panel1
	106156372
	TET2_015_Myeloid_Panel1
	106156714
	TET2_016_Myeloid_Panel1
	106156663
	TET2_017_Myeloid_Panel1
	106156939
	TET2_018_Myeloid_Panel1
	106156822
	TET2_019_Myeloid_Panel1
	106157170
	TET2_020_Myeloid_Panel1
	106157255
	TET2_023_Myeloid_Panel1
	106157618
	TET2_024_Myeloid_Panel1

TABLE A-continued

SmmIP Probe List	
GACATTATGAGTCAGACTCGCT	351 TET2_025_Myeloid_Panel
CAGCAAAACAGCAACCCAAAC	352 106157860 TET2_026_Myeloid_Panel
GTGAGAAAGATCTGCTTGGG	353 106157740 TET2_027_Myeloid_Panel
AATGTGCAACAAAGGCAATCATGA	354 106158025 TET2_028_Myeloid_Panel
GCAGGATGTTTGTAGTGCC	355 106157952 TET2_029_Myeloid_Panel
CTTCTCAAAAAAGACACCAAACC	356 106158244 TET2_030_Myeloid_Panel
CACAGCTTGCAGGGGATCTC	357 106158149 TET2_031_Myeloid_Panel
CTTCAGATAATGGGATTTCCTCT	358 106158435 TET2_032_Myeloid_Panel
GCTGGGTTGTGGCTATCAAGTCT	359 106158339 TET2_033_Myeloid_Panel
GCAAGGGCAAGGGCAGATTAAAG	360 106162470 TET2_034_Myeloid_Panel
GCTTTGGCTTAAATCTTGGG	361 106163978 TET2_035_Myeloid_Panel
CCAATCGGGGTGCCCCCTTGAAAT	362 106164782 TET2_036_Myeloid_Panel
CCCCCAACCCAAACAAACAAA	363 106164698 TET2_037_Myeloid_Panel
GCTCGAGTAGAGTTGTCAAGCC	364 106164875 TET2_038_Myeloid_Panel
TTGCCAGAAGCAAGATCCC	365 106180744 TET2_039_Myeloid_Panel
TTCGGATCCAGCCCCGACAGGC	366 106180810 TET2_040_Myeloid_Panel
GGCAGCAATTGTAAACAATTACTTG	367 106182914 TET2_041_Myeloid_Panel
GAGGACAGCTTAGGAGCTTGAG	368 106190791 TET2_042_Myeloid_Panel
GAAACTCACTAGTATTAGACC	369 106190713 TET2_043_Myeloid_Panel
GTCAGAGACTTGCAGAACAGGA	370 106193793 TET2_044_Myeloid_Panel
GTAGACACATTACAGCCTCAACTAC	371 106193710 TET2_045_Myeloid_Panel
GCATTGTAGATAAATGTGTTGTG	372 106193966 TET2_046_Myeloid_Panel
GCGAAAAGAAACTGAGTACCTG	373 106193893 TET2_047_Myeloid_Panel
CCCCAGCAGCAGGAGCCACA	374 106196201 TET2_048_Myeloid_Panel
CCATGAAACCCCTAACCTGGGCTT	375 106196382 TET2_049_Myeloid_Panel
GCTGGGCTGTGGTGGCTGCTCT	376 106196286 TET2_050_Myeloid_Panel

TABLE A-continued

	SmmIP_Probe_List
GCCAAAGGTTGGAAATAGCCAGAG	377
CCTGCAGGTTGAGATGAGGTGGA	378
GGTGAACATCATCACCTCTCAC	379
GTCATGCGATGGGTGGTAGACTG	380
GCTTTCACACAGCTAATGGGT	381
GTGATGCTTAATGGTCAGAAAAAGC	382
TCACCCCCACCAAGGATCTCC	383
GCAGTTCTATCATGGTTAAGAGCTGG	384
CAGAGCCCACCTAACCTGGTTCA	385
GCAGCTCACGGCTTGCAAC	386
GAAGTTTCAATGGGCTAGCAGGGC	387
CCAAACACTCTATAGACATCA	388
CAGTAGATCTCATTTCTATCAG	389
CACACAAAGCCTGAGATAG	390
GGCTTTCTACTGGATGTG	391
GTAAAGCAZAGCCCAAGTGAAAT	392
GCTGGGAGGCAGTSGAGTCCT	393
GGCZCTGATAACCTGTATTCAGGT	394
GGAGGTTCTCACTCATACC	395
GTAGTTAGTATTAGTGTGCAA	396
GCATGAGAACTAAATAGGTCTTGT	397
GCTTGTTCATTGTGTTAG	398
GCAGAGGGTACTTGAGGAACTTT	399
GTTTCTAAAGGTTCCATGTGTT	400
CGTTTCTATTTCATCTTTGTG	401
TET2_051_Myeloid_Panel1	106196581
TET2_052_Myeloid_Panel1	106196485
TET2_053_Myeloid_Panel1	106196801
TET2_054_Myeloid_Panel1	106196700
TET2_055_Myeloid_Panel1	106196908
TET2_056_Myeloid_Panel1	106197000
TET2_057_Myeloid_Panel1	106197217
TET2_058_Myeloid_Panel1	106197097
TET2_059_Myeloid_Panel1	106197420
TET2_060_Myeloid_Panel1	106197309
TET2_061_Myeloid_Panel1	106197547
NPM1_001_Myeloid_Panel1	170837497
BRAF_001_Myeloid_Panel1	140453093
EZH2_001_Myeloid_Panel1	148504736
EZH2_002_Myeloid_Panel1	148506130
EZH2_003_Myeloid_Panel1	148506421
EZH2_004_Myeloid_Panel1	148507413
EZH2_005_Myeloid_Panel1	148508713
EZH2_006_Myeloid_Panel1	148511120
EZH2_007_Myeloid_Panel1	148511049
EZH2_008_Myeloid_Panel1	1485111919
EZH2_009_Myeloid_Panel1	148512554
EZH2_010_Myeloid_Panel1	148516655
EZH2_011_Myeloid_Panel1	148523659
EZH2_012_Myeloid_Panel1	148523543

TABLE A-continued

SmmIP Probe List	
GAGCCATATGCCCTTCCTGG	402 148526818 EZH2_013_Myeloid_Panel
TGIFTCTGTGGAATAGTCCCTTG	403 117864786 RAD21_001_Myeloid_Panel
GAGGACCAACAGCAGCAT	404 117864828 RAD21_002_Myeloid_Panel
GAATAATCACTAAGTGGCTCT	405 117866477 RAD21_003_Myeloid_Panel
GGATCTGGACGCCACCA	406 117866593 RAD21_004_Myeloid_Panel
CCTTAGATTATAACAGCAT	407 117868392 RAD21_005_Myeloid_Panel
AGACTAGAAAGTTGATTATCTG	408 5069946 JAK2_001_Myeloid_Panel
CAGGATCACAGCTAGGTGTCAGTG	409 5073732 JAK2_002_Myeloid_Panel
CTTCTACACATGGTGGAGTC	410 112350168 SMC3_001_Myeloid_Panel
GCTGGTTATTCCCTTTCACGG	411 112350240 SMC3_002_Myeloid_Panel
GTTAGATGTCAGGGATAAGCC	412 112350728 SMC3_003_Myeloid_Panel
AGTAACCTCTCCAGGAAGATTCAT	413 112350837 SMC3_004_Myeloid_Panel
CAGCTGGCCCGTGTTCACTA	414 112352813 SMC3_005_Myeloid_Panel
GAGCTTTCAAAAGACATGTTTG	415 112352910 SMC3_006_Myeloid_Panel
GCAAAGCTCAATGAAAACTGC	416 112356146 SMC3_007_Myeloid_Panel
GCTCGCCCCCTAACATGGGCA	417 32413507 WT1_001_Myeloid_Panel
GCTGTGTTCCCTGGCTAGGGTT	418 32414183 WT1_002_Myeloid_Panel
GTCITGAGGAGACTGAGACTGG	419 32417886 WT1_003_Myeloid_Panel
GCAAACATGGTCAAGAGCTCCTT	420 32417776 WT1_004_Myeloid_Panel
AGGCCTCAAGTGGCTCAAGTCGC	421 32421492 WT1_005_Myeloid_Panel
GAGCCCTGTGGACACCTCATG	422 119148834 CBL_001_Myeloid_Panel
GTTGGAAATGGAGCCCATCTCAC	423 119148919 CBL_002_Myeloid_Panel
GAGGCAAGGAGCAGGGAGCTCC	424 119149195 CBL_003_Myeloid_Panel
CACAGATCTGTTCTGAAAATC	425 25378528 KRAS_001_Myeloid_Panel
GACTGGGAGGGCTTTCTTGTGT	426 25380240 KRAS_002_Myeloid_Panel
GCATATTACTGGTGCAAGGACCAT	427 25398189 KRAS_003_Myeloid_Panel

TABLE A-continued

	SmmIP_Probe_List
GTCCATTGGAAAGGGAGCAA	428
TCCGCTCAGTAATAGTCACTCT	429
GGTACATAAGTCCTGGACTGCTT	430
GGAAACAGAATCATTCAATGGGG	431
GCGCAGGATTGAAAGAACAGGT	432
GGCCAGGTCTCTGTGAAACACACTG	433
AAGGAGCATTAAAAATGAAACTCAAGT	434
GTGGAAGGACAGCAACAAAGATGC	435
GCTTCAGAGATGAAATGATGAGTC	436
TCTGAGGCAATTCTTTCCATTGG	437
GCAAAAGAGTGTCACTCAGCG	438
CTGCTCACACCCACTGTCAA	439
GCTGTCACTAGATGGAAAGTTAGG	440
CGTGTGAAATAAGTCACTGGCTG	441
GCAGATGATGGCTCCGGAAAGAC	442
GAGTAATAATGTTCCCCTACTGCCAG	443
GACGAAAGCAGGGAGGAGATG	444
GCTGGAAAGGAGCCAGGGGGAA	445
GTCTAACACTCAAATGCG	446
ACCGGGCTCATCTACTCC	447
GTAGTGGATGGTGTACAGTCAGA	448
GCGGATGACCGAGGCCAT	449
CCTGGGACCCCTGGCAACCA	450
GTGAGCAATGGGGGGCTTTC	451
	452
PTPN11_001_Myeloid_Panel1	112888114
PTPN11_002_Myeloid_Panel1	112910737
PTPN11_003_Myeloid_Panel1	112915435
PTPN11_004_Myeloid_Panel1	112926222
PTPN11_005_Myeloid_Panel1	112926832
FLT3_001_Myeloid_Panel1	28592580
FLT3_002_Myeloid_Panel1	28602311
FLT3_003_Myeloid_Panel1	28608014
FLT3_004_Myeloid_Panel1	28608225
FLT3_005_Myeloid_Panel1	28608194
FLT3_006_Myeloid_Panel1	28608421
FLT3_007_Myeloid_Panel1	28609607
FLT3_008_Myeloid_Panel1	28609721
FLT3_009_Myeloid_Panel1	28610068
IDH2_001_Myeloid_Panel1	90631765
IDH2_002_Myeloid_Panel1	90631865
TP53_001_Myeloid_Panel1	7572891
TP53_002_Myeloid_Panel1	7573955
TP53_003_Myeloid_Panel1	7576812
TP53_004_Myeloid_Panel1	7577099
TP53_005_Myeloid_Panel1	7576986
TP53_006_Myeloid_Panel1	7577458
TP53_007_Myeloid_Panel1	7577551
TP53_008_Myeloid_Panel1	7578152
TP53_009_Myeloid_Panel1	7578114

TABLE A-continued

SmmIP Probe List	
GTTGAGGGAGGGAGTACTGTAGGA	453
GGGTGGAGAGACAGACAGGGCTGTT	454
TTCCACACCCCGCCCG	455
TTCTGGAGGGACAGAGATGA	456
GTAGGAGGTGCTGGTGCAGGGC	457
GCATCAAATCATCCATTGTTGGG	458
ACCCAGGTCCAGATGAAGGTCCC	459
AAGGCCAGGCCACCACCCC	460
GCTTCCAAATTGGCCTTGTCGC	461
AAAAAATTATCCAGAACTCAAC	462
AGCTGCAGTCTCCACAAACC	463
CAATTTCCTCAAGTGGTCTGG	464
GATGTGAACTTTTAAAGGGA	465
CGTCATGTTCTCATCAGGGG	466
AGCTCGGCCGTCAGCAC	467
TTTCGTCTCCCTGGACAACCCGG	468
GGCTGCCTCCAGGGTGGACTGA	469
CCTGCCCTGCAGGCCCTG	470
GCAACTGGCGTGGGGCGGGCTGT	471
TGACCGCCCTGCAGGGTGG	472
GCGGGCTCTGCTTGCACCAACGG	473
TCATGCCCGGGAGGCAACGGGC	474
GCTGATGCGTGGACGTCGTCCTCGC	475
GCAGGTGGCTGCTATCGGGGGCG	476
GCCACCCGACAGCGAGATGGCA	477
TCCCCATCTGCCAGGCAATCC	478
	7578411
	7578360
	7578487
	7579258
	7579319
	7579436
	7579518
	7579822
	58740447
	58740327
	58740654
	58740529
	58740853
	58740751
	74732953
	42531864
	13054605
	13054500
	33792258
	33792359
	33792748
	33792966
	33793061
	33793200
	31021073
	31021264
	TP53_010_Myeloid_Panel
	TP53_011_Myeloid_Panel
	TP53_012_Myeloid_Panel
	TP53_013_Myeloid_Panel
	TP53_014_Myeloid_Panel
	TP53_015_Myeloid_Panel
	TP53_016_Myeloid_Panel
	TP53_017_Myeloid_Panel
	PPMLD_001_Myeloid_Panel
	PPMLD_002_Myeloid_Panel
	PPMLD_003_Myeloid_Panel
	PPMLD_004_Myeloid_Panel
	PPMLD_005_Myeloid_Panel
	PPMLD_006_Myeloid_Panel
	SRSR2_001_Myeloid_Panel
	SETBP1_001_Myeloid_Panel
	CALR_001_Myeloid_Panel
	CALR_002_Myeloid_Panel
	CEBPA_001_Myeloid_Panel
	CEBPA_002_Myeloid_Panel
	CEBPA_003_Myeloid_Panel
	CEBPA_004_Myeloid_Panel
	CEBPA_005_Myeloid_Panel
	CEBPA_006_Myeloid_Panel
	ASXL1_001_Myeloid_Panel
	ASXL1_002_Myeloid_Panel

TABLE A-continued

	SmmIP_Probe_List
CCTGGGACACACAAGCCACT	479
GAGCAGGGGGCCTCTGCATCCTT	480
GCCCTGCTGGTCAGTCCTAG	481
CACAGCCCACTAAAGAGGAGCCA	482
CGGGGTGGAAGTGGCGCAGGA	483
GTGGTGATGGTGGTGAGGCCCTGCG	484
GGTGGGGATGATCGGGGCATAT	485
TGCCAGGGCTTGCCCCCTACTGTC	486
GTACACTTTCAGGGGTGCTCGGG	487
GGATCCTGTAAATGTGACCCCC	488
GCAAGGCTGGCATGGCTGGT	489
GGTACTGAAACAGCCAAACCA	490
GCTTGGCAGTTCTTTCTCT	491
GGAGACTCTGAAGCACTGAGTCCT	492
CGATGGGATGGPATCCATGCA	493
GTTGACAGTAACCTCCATTGCTT	494
GGTAGACCTTCAAAGTCAGGGCTG	495
GTAGCTTGCCTTAGAGAAGGT	496
GTGGGGCACATTGTTCAATTGG	497
GCAACTGCATCAAGTGGTTAG	498
CCCTCCATTCAGTGACAAATCCCA	499
GCAGTTCTTCCTTGTGTG	500
GCGAGGCCATGGCTGGCTTTTG	501
CCTGGTTCTCATCCTCAAATGTG	502
AACCCCTTCAAGGCCAGGC	503
	31021171
	31021457
	31021383
	31021554
	31022205
	31022405
	31022316
	31022664
	31022579
	31022903
	31022803
	31023107
	31023005
	31023348
	31022225
	31023445
	31023541
	31023730
	31023643
	31023850
	31024024
	31024088
	31023955
	31024203
	31024325
	ASXL1_003_Myeloid_Panel
	ASXL1_004_Myeloid_Panel
	ASXL1_005_Myeloid_Panel
	ASXL1_006_Myeloid_Panel
	ASXL1_007_Myeloid_Panel
	ASXL1_008_Myeloid_Panel
	ASXL1_009_Myeloid_Panel
	ASXL1_010_Myeloid_Panel
	ASXL1_011_Myeloid_Panel
	ASXL1_012_Myeloid_Panel
	ASXL1_013_Myeloid_Panel
	ASXL1_014_Myeloid_Panel
	ASXL1_015_Myeloid_Panel
	ASXL1_016_Myeloid_Panel
	ASXL1_017_Myeloid_Panel
	ASXL1_018_Myeloid_Panel
	ASXL1_019_Myeloid_Panel
	ASXL1_020_Myeloid_Panel
	ASXL1_021_Myeloid_Panel
	ASXL1_022_Myeloid_Panel
	ASXL1_023_Myeloid_Panel
	ASXL1_024_Myeloid_Panel
	ASXL1_025_Myeloid_Panel
	ASXL1_026_Myeloid_Panel
	ASXL1_027_Myeloid_Panel

TABLE A-continued

SmmIP Probe List	
GTGGGGTACAGACTCCAAAGGAAG	504 ASXL1_028_Myeloid_Panel
GCCAGAAACAGGAAAGCTACTGGG	505 31024429
GAAGGGGTCACTGAGCTCTGGG	506 31024533
CCTCTAGTCCTCCACCTTTC	507 31024643
GCAGCACGGTGAAGCATCTCG	508 31024759
GCTCTGTATTTGCCCCCTGTGGT	509 31024876
GAGGTCAACTGATCTACCAAAAGCA	510 31024985
GGTGTAGGGGGGAGCTGGCTT	511 57484392
GCGGGCAGGTAGGTGTGTGTAG	512 36164550
GGTACCGGGCTGGGAGTAGGT	513 36164640
GCGGGGTGGAGATGGAGGG	514 36164725
GCGGAAGTGAGTAGGGTTGCCGA	515 36164740
GTCCAGGAGCTAGGGTCATG	516 36164821
ACGCCATTTCACCTGGACGTG	517 36171551
GAGGACAGGGTTGGCGTG	518 36171668
CGGGCTGGTCTGATCATCTAGT	519 36206645
GCGGCGCACAGCCATGAGGGT	520 36206751
GGGCTGGTACACCCCTCCAGCT	521 36206820
CATCATGCCAGGATCACAG	522 362231754
GCTGAGCTGAGAATGCTACCGC	523 36252824
GCAGAGGAAGTGGGTCTGGCTCA	524 36252939
GGCCAGCACCTCCACCATGCT	525 36259181
GCCAGTGAGTGACTGAGGACA	526 44514751
CATGGAATAATGTCAGCAGCATGAC	527 445244436
GCATGCGTGTGGAGGGACTG	528 15833892
GGCCAATATGTTGAAAATTAATCTCAC	529 15833769

TABLE A-continued

	SmmIP_Probe_List
AAATTCAGGAAAAAGAACCCAGCC	530
TTTCCTCAATTGTTCCACTGCG	531
GCTTCCAGGTCTTGGAGAAAGAG	532
GTAATAATGAAAGTGGCCCAAC	533
GTAAGGAGCTGTTAGATCTGGTGG	534
CGTTCTAACAGCATTGTCAGAG	535
CTTATGGTGTGACCCCCACC	536
TGCCCAAGTCCAATGCCCTTG	537
CATGTGGTAGCTGGAGCATC	538
CAGCAGGGAGGTCTATGGCCCG	539
CAGGGTTCTTCTCCCCCTGGGCGCTGAG	540
GCTGGAAGCTTCTAAATGATG	541
GGTGTGAGGACACAGAGGAGA	542
GCAGCTCTGCCTTTCGTTTTC	543
GCATGCTGCTGTTGCTTACTTTC	544
GCCTTCAGGTCACTGGCCCA	545
CCAGTACTGAGCCTGTCAG	546
GACAGGGGATTGCAACAGCAT	547
CCTAACCTCAGGTAGTCAAG	548
GCCGCAATGCCCTGGGCCA	549
GCTTTGGAGGTGGCTAGGG	550
GGTOAGGCCAGTTCAGGG	551
GGCTATTGTTGACCAACTGGTC	552
GGTCAAACATTAATCTAACAGACACA	553
GCAAGTTGCAATTGTTGGGT	554
ZRSR2_003_Myeloid_Panel	15836680
ZRSR2_004_Myeloid_Panel	15838326
BCOR_001_Myeloid_Panel	39911360
BCOR_002_Myeloid_Panel	39911563
BCOR_003_Myeloid_Panel	39911472
BCOR_004_Myeloid_Panel	39914615
BCOR_005_Myeloid_Panel	39914711
BCOR_006_Myeloid_Panel	39932867
BCOR_007_Myeloid_Panel	39933099
BCOR_008_Myeloid_Panel	39932988
GATA1_001_Myeloid_Panel	48649480
GATA1_002_Myeloid_Panel	48649716
GATA1_003_Myeloid_Panel	48649600
SMCIA_001_Myeloid_Panel	53431919
SMCIA_002_Myeloid_Panel	53432033
SMCIA_003_Myeloid_Panel	53432127
SMCIA_004_Myeloid_Panel	53432252
SMCIA_005_Myeloid_Panel	53432356
SMCIA_006_Myeloid_Panel	53432571
SMCIA_007_Myeloid_Panel	53432460
SMCIA_008_Myeloid_Panel	53432798
SMCIA_009_Myeloid_Panel	53432684
STAG2_001_Myeloid_Panel	123181254
STAG2_002_Myeloid_Panel	123181181
STAG2_003_Myeloid_Panel	123182853

TABLE A-continued

		SmmIP_Probe_List		SEQ_ID
AAGATGGCCCTCAGACTGCTT	555	123184027	STAG2_004_Myeloid_Panel	
CCAGTCGGTCAAGGTAGTTATA	556	123184910	STAG2_005_Myeloid_Panel	
GTTGCTATGACCCCTGACAAG	557	123185048	STAG2_006_Myeloid_Panel	
GCATATTGCACTAATGTCAGAT	558	123185136	STAG2_007_Myeloid_Panel	
GAAATAAGGAGTAACAGGGCTT	559	123189974	STAG2_008_Myeloid_Panel	
ACCATGTCAGTCATTAGTGAATC	560	123220383	STAG2_009_Myeloid_Panel	
CCACCGGTAGCAAAGAATTTCGG	561	123220499	STAG2_010_Myeloid_Panel	
CCGGGAGAACAGAGACCTTGAAA	562	133511669	PHF6_001_Myeloid_Panel	
GCCACATTAAAGTCATCAAAGAATGC	563	133511625	PHF6_002_Myeloid_Panel	
GCATTTCATCATCATCAAAGGG	564	133527622	PHF6_003_Myeloid_Panel	
GTATGTAAGTTCTAAGGGTGTAT	565	133527501	PHF6_004_Myeloid_Panel	
CCACGTTGAGGCCACTTTTCAG	566	133527920	PHF6_005_Myeloid_Panel	
GGGAGGAGAAAAATGAAGCACGA	567	133547793	PHF6_006_Myeloid_Panel	
GCTTGGTGTCACTAGGGCTGC	568	133547896	PHF6_007_Myeloid_Panel	
ATGAGAAAATTAAACATTCAAGATCC	569	133549033	PHF6_008_Myeloid_Panel	
GACTGCAAAGGTACATTTCTG	570	133551218	PHF6_009_Myeloid_Panel	
scan_target_sequence				
CGGGGGGGTACCTGTAGTGTGAGGA				571
AAAGGG				
GCCTTCGGCTCTCATGTTATGGCAGTGTACTCTCTGTCAGCTATCCAGTATGTCAAACAAACAGGTTCAACCCTATAACCACCTTGTGTAAGAAC				572
CTGGGG				
AAATGACATGAGTACAAACTGTTGAGGCTAGGTTGGAGCAGGACTGACAAATCCAGCTAATCCAGAACCACATTGTAGATGAATATGATCCACATAGAGGTGAGGC				573
CCACTG				
CCTTACACACAGGAAAATACTCTTCAACGGAGGAGGCTGGGGATGACTGGCCGGCTCATGACCCGGCCAGCAGTGTGCTCGCTCGCCAAGGGCTCATGTGGAGACGTGAGTA				574
TAGTGG				
TTCTCCCCAGGGTATTGTTTCCCAGTCCACTATACTGACGTCTCAACATGAGCCGTTGGCGAGGACTGCTGGCCAGTCATGGAGCCACCTCTT				575
CGCTCC				

TABLE A-continued

TABLE A-continued

SmmIP	Probe List	
CTTCAGGCCCCTGGCCATAAGGGCACCAAGGTAATCAGGGACCCAGTGGCTGGGACCTGGCTGGGACATGCCAGGCAGATCCACACAGGGCTGGGAAGCCATGCCATTAGG GAG	595	
ACATGGGTGCTTGTGACGTGGCTGGTGGAACGGACTGCGAAACGGACTCAGGCCATCAGCTTCTCAACACACACCTGGGGACAAGCCAGCTTGTTGCCAGGGCTTACACT TGCAG	596	
CCGTGAGCTGTTGGAGTGGCTCACCAGCCAAGCAGCCATGTACCGCAAAGTACCGCAAAGCAGCCATCTACGAGGTGGCTGCAGGTGGCTCCCTGCTGGAGCTGGAGGAG CCCTAGA	597	
ACCACTGAGAAATTGCCGCTCCGAAACCAACATGACCCAGGGGTGGCTTCAAGGTGGCTCGGCGCGTCAAGTGGCTCATCCACCAAGACACAATGGGGCTGGCCACCCGGCAGT 598		
CCTCTGTGACCACTGTGTAATGATTCTGCTGTTGGGCTTGGGCTGGGATTGGGAGCTGGGGGGTTTGGGAGCTGGTGTGGGGAAACTGGGGGCTTCTCTGGTGGCAGGGCGCAT 599		
GGCATTCCTGGCCCCAGCATGGAACCCCACGGGCTCAGGGCTGGTAGGACCCAGGGCTCCAGGAACGGGGCTTGGGAGCTGGGGATCAGTGGGGTCACTGGGGCTCAGCTGGAGACTC CC	600	
CCATAAGGAAATAAGATAACCCAAATAGCCCTCAAGAACGGCCAAACCCATTTTAAATAAATATAATGTAATTAGTTAGATTATGCTGCCTTAAGTTATGAAAGATA ATCAGA	601	
ATGCAAGAATATGCCAACACTACTAGAGAAGTGTATGTTAACCTTATTGAGAATTCTGAGGAAATTGAAAAAAATGAGGAAATTGAGGAAATTGAGGAAATTGAGGAAATTGTTAA TGTTAA	602	
TAAAACCTGTGTTGGTTGTAGGCTCTGTGATGAGCAGGAAAGTTCGGACCATCAGNGCTTGGCCATTGGGCTGGCTGGGCTGGCTGGGAGCAACTCCTTATGGTATCGAATCTTT GATTCCT	603	
AGGGCAGAGGCTAACAGCCAAAGCTCTAGCTGTGTTACGGACATACTCATCCTCATGTTATATCAGGTCTCATGGTCAAGATCATAGTAGCAGACCCAGCAGCTAAATGTA AACAAA	604	
TTTGGCTGTAGGCCTCTGCCCTGGGATCTCTTATTGGCCCTTCTTAAAAGCTGTGCAAAAGCAAGAAGTCTGGCAAGCCGAGACACTGGTATAAAGATTGTACAACAGATA GCTATT	605	
ACTACTGTATCCCATTAAAGCATGACGACCTATGATGATGTTACCCATCCACTACACAGCCGGGATATTITGCAGATAATGGTTCTCTGAAAGACCGTGCACCCAGATAATT TCGTAT	606	
CTAAGTTAACGGGCACCTGACCATGAAAGGAGGGATCGAACACTCGAACGGAAAGATGTCACAAAGTCAAGAACGGAAAGTGGCTGGGACTGCTTCAGGAGCTGTCAAAGTGA CA	607	
CACAGGGCTGTGAGACAGGGTCCCGTGGCTTTCGGCCATAAGGTGGCTGTGCTGACATTGGACACA	608	
CAGAGGGGGAGTGTCAACTGTGGGGCAACCTGTCACCCCTCTCAGCACCCGCAACCGGCACACTACCTGTGCAATGCCATGCTGGGCTCTACACAAAGATGATGGCAAGAC GAC	609	
TGACATAGGCCATTTCCTGTAGCAAAACCAAGAAATCCTGTACTACGACAGGTGGCTGGGAGATCCTGAGTGGCTGGGATTCAGGAGGATTCAGGAGGATTCAGGAGGAT ATTTT	610	
ATGGGTACTCAGGTTCTCTTAAACCACATAATTAGAATCATCTTGATGTTCTGGCTAGCAAAATCACAATCTTGATGTCATGCCAGGAGGATTCAGGAGGATTCAGGAGGAT GTCTCT	611	

TABLE A-continued

SmmIP Probe List
AGACTAAGTCATTCCTGATAACCATCACCTCCATTGCCAGACAACTCTGGCTACAAGCTCCAGAAATGGAA 612
ACTCTTCAAAAGTTATATGGATAACCTGTATGAAGGGAAAGCCAGATACTGCTGAGTCCTGACTTACACAGAAA 613
TATTCATATAACTTTGAAAGTAGTGCCTACTTGTCTCCATTACTTCGGATGAGCTCTCTCAGCGTAGGGCTTCATTCTGGAGCTTGTAGGCCAGAG 614
AAATTGAAACAAGCCAAAGGCTTAATGGAAAGACCTAACCTCGGGTAAGCCANGAAAAGAACGAGTGAACCAAATGCTCCGATTGAGTAAAGAAATCT 615
GTTGAGTCTGTTCAATTCTGATCTGAGGAGCCAGAGAGAAAGGGTCAACTAACTGTGGTTTATTCCCAATTGGAAACACTTGGAATACCCCTACTTCTGTAAAGTCAGGA 616
CTTCACA  AATGAGCAGGAGGGAAAAGTGTAAATTACCATGACAGAAACATTGTTATTACTTAAAAACAGGCTGTTAACTCTGATTAACTGCACTACAGATTCTTC 617
GGAGA  TCAGAATCTGAAAGCTCTGGATTTCAGGCCACTGCACTTGAGCTTATGGTGAATCTTAACTGCACTACAGGTTACAGATTCTGGCTACAGATTCTTC 618
GCAGTG  AATGCGATTAACAGTCAGCTACTAATGAGTTGTCCTTGAGATCACUTCAGGCAGATCAATTCAGGCACAGACCTCTAACACTGAGCTGCCTCTTC 619
ACTGTA  TTAATGGCATTATATGTGAGATGTGGTTTCTGCACTGGAAATGGAAACAAACTGGATAATATTGAGAACAGTGTGTTTCAGGAGTTACCATGTT 620
CAACTACACACAAAAACTGAGATTGGATATGCCATCTCTGCAAAATAACCTCCAGGGAAACACACAAGCTAGCTGGCTCTGGAGAATCTGTTGAGTT 621
CATATCTCAAAACTGATTGGTTGTTGTTGAGCTAGTTACTGGCATATTAGCATATCAGCATCATCACAGGCCTGACTC 622
ACCCAT  TTTCTGCCACTACCACCAACCAATTGCTCTTCTCCCCCTCTCTCCAGCTCAGGTTCTCAGAAGGAAAGACTCTGATGGTAGTTTA 623
GAAGAA  GGTAGTGGCAGAAAAGGAAATCCTTAGIGAAACACTGAGGTTGGTGAAGTAAGCCATTCAATTGTTAAATAACGGTCAAGGTGCCACAGGAGCTTGC 624
GGAAAC  CCATCTCACATGTATGCAGGCCCTTCGATGCTTGTGAAAGGCCCTCAGATAATTTGTAAGCTGAACTGAGTCAATGACTGTTCCATGTGTTCTGAGAAA 625
ACARGA  AGATGGATAGGACTCTGGAAAGGTGGCTCAGGTTACCCCTCTATTTCACCTCCCTAAAGTGTGTTACTTGGTTGGGTAGTGGCTGTTCTAAACTCCACCACT 626
CAAGGT  GAGATTCTGAAGGGTCAAGACAGGAAACACGAGATCTTGCCCTGAGTGTCTCATCAACTGCTGGCAGTGTCCACTGCTGAGATGGTGTGTTGAGTT 627
CTAAAA  GCCCTTCAGAAATCTGCTTGTGTTCTCATCAACTGCTGGCAGTGTCCACTGCTGAGATGGTGTGTTGAGTTGCTGAGATGGTGTGTTGAGTT 628
TCAGA  GGGTCCC2AGGC2AGCCTACACCAAGGAAACACACAGCTGGAGCACAGCTGGAAACAGTACAGTGGACCAAGTACAGTGGACCAACATCTCCAGTTC 629
CAAAAA

TABLE A-continued

SmmIP Probe List
AAGCTTGGCCAGCCCCAGCACTGGAAATTCCAGTGTATTGTCAGGAGATTCAGTGGCTCATTTGATGGAGAATTGATGGCAGTGGCTCATTTACGTT TTAGAT
ACTAAAAAAACTTATGCCCAGTGTGAACACGACTTGAACTGAATCAAACAGGCTTCAAGAGCTGAGCCATTTCAGAGCTAACTCACACCTTGCACATAAACAGGAGCACAAACA CAACCA
ACATAAAGTTTTCAGTTGGGAATCTGGCTCTTGTGAAAATGAAATCTAGTGCACAGCAGTGCACATGAGCTTGTGGTAATATGGCTGTGTTGGAGAAGTGCACCTGGTGTGAGG GTTTTT
GATGATTCTGGCCAGACTAAAGGAGAAATGTTCATGGTGAATCAGTATTAAATCAAGCGAGTTCGAGACTCATATAATGCCAAATGGGACTGGAGGAGTACAGAAATATAAA ATCGTA
GATCCTTCCTTGGCTGATCATGGCTGGGGTAGTTGCAGCTGGGAAACGCTGGGATTTGCTGACTTCTTATTGTAATTTCGTTGCTGCTGTTGGGGAGATGTGAACTC TGGGAT
TAGTTTCAGAAATAAGGAGACAGRACTAACATCTGAACACTTTGCAGGGAAACAGACCAAAACTTGATCACATGCCAATATTTCGAAATAATGTGATCCAAAGCAAGATCTTCAGTTC ACAGGT
ATCTCTGAAACTAGGTGTGTATTTGTTGAAACAGAACCTGTATTGTCATGCACTTGATTGTCATGGCTGACTATAAGGGAAATTCTACGATTATAATTCTGTACTTCCTCCAGTCC CATTTG
ATACATAACCAGGAAATGTTTCCTGCTGCACTGGGAGGAAGTCACACTCAAGCCCCCTCCAGAAGGACACTAAAGCAGTGTGCTCAAGGGCATCTTACAGAAAGCAA GAAAG
TGGTTATGTATCAAGTACCTTGTGAGCAAGTTGCGAGCTGTTGAGCAGACATATCTGGTTCTATTATCCCTGTAGAACCTGAAGCTTGTGACTTCTGCTCCTGTTCT TGAAAGCAGCT
CAGATGCAAGGGCAATTAGGTGCGAACCTGGATGCAAGGCCACATGCCATGCCCCACAGGACACCACAGAAGAAAAAAACATGGAAAAAGGTAAACTAAGCAAGAGAATCACCTGCAAGCT GTGTAT
ATACAGGCATGTGGCTTCAGGTTGCATCCACCTTAATTGGCCTGTGCATCTGACTATGGCAAGACTCOAGTTGGGTGCTGTTGCTGCTGCTCTGCTTGTAAAGAGATGCCAC CTTAGA
AAATCACAGAGCAAGTAAAGTGAATAATGTCAGGCGCAGTCAGTTGACTAGAACAAACACTGCAAGGAAACTGTAGGCCACACCCAGCTTAGCCAAACAA ACATTTCAACTTTTACTTGCTTCTGTGATTGAGTAAAGGCTTATGGTCAAATAAGCACTTGGGCTGAAACTGTGCTCAAGATGCTCCTTGTGCA CATTT
AGATACTCTTAAATTTATGGTAAACCTGTCAAGACTCAATGATTGTCAGTTCAGTTCCCATCTGCAAGTGTAGGTAGTGCAGAAATGACTGAGACACATGGGTTATCCAGAATT AGCAAAATTAT
AATAAATTTTATAGGAGTATCTGTTATTGGAAGGTGACTCTATAAAATTATGGAAAGAACAGAACGGCTGTTCTGCTGAGAAGTGTGTTGCTGCTCTAA ATAATAATCTTCTTATTCAGAGCAAAATTATGGAAAGATGAGGTCTTCTTAATCCCATCTAGGAGCAGGTCCATTAGGAAATGCAAGGAAAGGTA ATTAAC
GGGTTCTTAAGTTGGACAGAAGGGTAAGCTTATAGGATTGAAGAGTCATCTPACTCTGTAAGTGGCTCATTGCTAAGTGGTAAGTGTGACTT GATAAA

TABLE A-continued

SmmIP Probe List
CTGGCCACACCTGTGAGGCTGCAGTGTGATTCTCATCCTGGTGGAAAGGAATCCCCCTGTCTCTGGCTGACA CGTCGA 647
GGATGAGAATCACACATCACTGCAGCCTACAGGTGGCCAGTCGCTCCGGACCAAACACAGTAGCTTCTTCACT CAAACA 648
CAACCAAAGATGGGCTTTCCTATCACTGGGCCAAAAGGGGGAGAGGCCCTGGGCTTCACTTACTCTCATTCATT CGTAA 649
ATAGGAATGAATTGGTTGTTGAGGAAACTTGCGCCTGTCAGGGCTGGATCCAGAAACTCTGGCTCATGGATT TGTAAG 650
TAACAAACACTCTTTGGTCACTCCCAGCAGCTTAACACTCCTGGATCTGGCTCTGGCAAACCTACATCCATT ACAGGT 651
AGGAGAGAAACTGGAGTCAATTGCAAAACCTGTCCACTCTTATGGCACCAACATAAGAACCTGACCTGATGC ATAATAATCATTTAAGTTAAACTCATGGTAAGTTAAATAATCATTT 652
GAGHGCCGGTGGTCTGAGGAGGGCCCTCAATTCTCAGGGGTCATGCACTGGACTCTGGTGTCTCATGGC TGGGCT 653
AGTACCCCTGAGAATGGACGGCCTCTCTCAGACCCAGCGGCACTCTGGTGCTCTGTGTCAATTCAATCT TACACC 654
CCTTATAGAAAGTCTCTGAGCTGAGTTGGAGTGTGGAAAGCTCAGGGAGAAAAACGGAGTGGTGC GAGCCA 655
CCACACTCCAAACTCATCCACGTCAAGACATTGTATAAGGCAGAAGCTGTCTCATCCTCAGGTTTC AGGGAA 656
TGAAAGCTTCCCTCGAGAACAGCTAAATAAAATGAAAGGAAAGTCAGGCCCATCAGTA TGTAAA 657
ACTTTCTTTTCAATTGAGCTGTTCTCAGGTGAGCTTCTAGTTCTGGCTTCTGACTGGCTCTGCT CTTTTC 658
ACAGAACCTTGGGACTTTCAGGCCAGTCAGCCAGTCCAGCAGGCCCTACAGAACGCCACACGCC GCTGCT 659
GGCCAAATCCAGTTAGTCCATTCAAAACTCTTCACACACTCAGATACTATGGAAACCA CTAATC 660
AGTTGGATAAGGACTACTGGATTGGCGCTCATGAGCTTCTGAGACTCTGTCAGAGCT GCTGCT 661
TTACCA 662
GAACCCAGATATGGGAGCAGTGTCCACTGATAGGTTCCATTGATGATGATGATG TATGAA 663

TABLE A-continued

SmmIP Probe List
AGACCAAAATGTACATCATGTTAGGGAAAATTGCCCTTATCCCACTCATGAGATGGATGCCACTTCATGGAGGCCACCTCTAGATTACACCCAAATCTGAGCAATCCAACATGGACTAT AAAAT 664
TCCCTACATGATGTACATTGGCTTAATGGTACAACITCGTGAACCATCTCCCTGCATATTGGTTCCATAACCTAAGTATTAGTAAAGTAAACTCTGGCTATTTCACAAACCTTGCT GGTAA 665
AACATGGACTATAAAATGGTAAACATCACCTCAGATANCCATAACTAACATGAGCTCAGGCTCGGGCATGTTAACAGCTCTCTCATGCCATCTCAAAACAGAGAA TGACAT 666
ATGCCCTGCACTTCACAAAGGAAATGACATGCTTCCACACAGCTAATGGTTATAAGATGCTTAAACCATGATAGAACTGTGTGTCAGGGAGGCTTACACA AATTA 667
CGAGCAGGCTTCTGGATCCTGACATGGGGAGTGGCCGCGTGGCTCCAACTCATGGTCAATTCTCATTGGCTGAGCTGAGCTGAGCTGAGCTGAGCCACATG TAGAA 668
CGCTGCTGTCGACCAAGCACCTCATGTTGTCCTCTGGACCCAGAACCCGCAACGGCTAGTGCCTAATGGTGTGCTTTCCTGACCATTAGATCACTTAATTGGTAAGGCCTCCTTGG CACAA 669
AAGCCAAAATGGCTGAAAAAGCCGTGAGAAAGAGAGTGTGAAAAAGTATGGCCCAAGACTATGCTCCTCAGAAATCCATGGCAAAAGTGAACGGAGCCTGCTGAGCCACATG AAACTT 670
CAGCCATTGGCTTCCAAAGGCCAACCCATGTTGGCTCATTCTGCTCTTATGGTAAAGACGAGGGAGATCCCTGGTGGTGGTGGTGGTGGTGGTGGTGG TGGCAT 671
ATATATCTGTTGTAAGGCCCTGTGACCCGAGTCAAGGCATATGGAGATGTAGTTACTCTGGAGTCTGTTGCTACGGACATGGTCCCTTCGGCAAGAGACTCTGAGGTGATCTGAG GGCTCT 672
ACAGAAATGAAATAGACGGAAAATTTTAACAAATTGTTAACCTTAAAGAGACTCTTAAAGAGACTCTCCACTGCCAGAGACTCTGAGTGGCTGGAAAAAAAAGAAATGTTGG AAGAA 673
AGAACCTGTTCAAACACTGATGGACCCACTCCATCGAGAATTCACTGTAGTAGCTAGACCAAAATCACCTTACTGTAGGTCTCTCATGAGAAATATACTCTGAGGTGATGAA GGAAA 674
TGTCAGGGATTTCATTCCTCTGGCGACATACTTCAGGGCTCATCTGGGTGATCTGAAACACAGGCCATCCAGACTGGCAGAGATGTCGGCTGGGATGGCT ACTTAA 675
CTTGGCAATTATGATGGTAACGGTGTACAGGATAGTATTTCAGATTTCAGATGAGCTGTTGTTGATACAGGTGGTAAAGTACATTCTAGCATGAT CTCTAA 676
ATTTACCGAATGATTGCAAAACGAATTGGTACCCCTGGGGTGGATCCACCAAAATCTAAAGAAAAAA TTCAAGATGAGCTGACAAAGGGAAAGTGTATGATAAATACATGTCAGGTTCTGTCAACTTGACACAAATGGTATGTT TTCAGA 677
TGATGTGATTGGTTTATCTAGCATCTTCTAGCATCTATTGCTGGCACCATCTGACGTGGCAGGCTGGGGATTTTATCAAGATCCTGTGAGAAATAATGAATTCATCTGAGAATACTGTGGAG AGGTAA 679
TCCACAAAGTAAGACAGGGTCAGGGTCAACACTCTGGGACGGCTAGGTTGACTCTGGCTGGTGTGACTGTGCTTGCAGGGACTCAGGGCATCCGGAAAGGGTTGGACCTTCAGAGAG AGGGTT 680

TABLE A-continued

SmmIP	Probe List	
CCCTGACCTCTGTCTTAACTTGTGGAGGCCGCTGaccATGGACAGTAAATAATGTGTCCTGCAGAAGAACTGCAGTTCAGC GG GGTCCAAAAGGTGAGCACAAGTCACCTCTGGAAAGA	681	
ATCACACCCTGTGATCATCCACGGCAGCCCTTGACAGTTGTCCTTGATGAGACAAAATTITGTGAAAGTTGTCATGTAGTTCAAGGTGTAAGTTGCTTGTGAT	682	
TCCCGAACAAATTGGTTAATTTCCTGTGTTTCAGGTTGTGGCTGACACTGCAAGAAGATAACGCTGAAAAGGGTAGCATCTTCATCCTCTCATTATTAGCTAACAA	683	
ATATCT		
TATTTTGAGCTTTCTATGCAACACCAACACTTATAAGCGGAAGAACACAGCTCTAGACAAACACCTTGGAACCAAGCTGTTACCCAGTTGGTAAGGACTTAGTGCCCTA	684	
ATTATT		
TCTATGTTGGGGTACATCAGGGGAAGTGGCCCTGGCTGNTCGGGTAGTTCTATGACATAACTGACATAACTGAAAGAAAAATTAACTGAAACAAATAACTGAACTTTTG	685	
AAAACA		
CCACATAGATGGACCAAATGCTAAATCTGTCAGAGGAGCAAAAGCTTACACTCCTTCATAAGCTTTCTGTAGGGGATGTTTAAATAATGACTGCTTCTCATCGTAAGTGCAATT	686	
ATTGTA		
ATGAAACTTTTACATAAACATTCTTATATGGGAGATGAAGTTTACGATGGTACTCTCATGGAAACTTAATAATGATGGAAAGGTACACGGGATAAGGT	687	
GACCTTAGAAAAGGGAAAGGGAGGAGGAGGAGATAATTGGATGAATTGGCTCAAAGAAATTGAAATCCAGGGTTCTAGAGGGACGAAAGCAGGACATGAGCAGCGTGTGTT	688	
ATCGGT		
TATATGCTTTACACGTGCTTACACGGCTGTACAGAGACCTTACAGAGAACCTTACAGAGAACGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAGG	689	
CCTAGA		
ATATTACCTTCAGTAGTCTGTTATTCCACAAAGGCTGAGCAGGTTAAAGAAAACAGTTTCTACTCCCTCTGTCTTCCACATCATCAATTCTGGTGGGGAGATCCAAG	690	
TAGTAACAAATCT		
TATATTCCAGTTAAGAACAAAAGCCAGGGAAAGCTTAATTTGTGACAGTGTCAAGAGCTTACGCAAACTTAGGCTTAACTTAGGCCAACTTAGGATTATTCAGATATGTTAC	691	
TACTTT		
GGGGGGCTGTAGTCCCTGATTCACTGGATCCCCGTGAAACCAATGCCAACATGCAAACTGTTCCAAATGAGGAAAGGATTGCAATTGGGAGCTATTGATAAACT	692	
GGTAAGCATATGAA		
TGAGTATCTAATGACTTAAATCATTCATTCATGTTGAAACACCATTTGTTCAATGAGTAGGTCAATGGCTTAAATGTGGCTCATGAGTATTGTAATGAAATACTTGTGAT	693	
TTCTGAA		
TTTCCTCACAAAGCATTGGTTAAATTATGGAGTATGTTGGAGACGAGAGTAAAGTAAAACACTACAGGCTTTCTATGCTTCTCAGGGCATCTGTTTTGTTTATATGAAATACT	694	
CAGTT		
AGGCACATTAAATGGAAATAGACAGCAAAACAAAGTGTAGCAACCATTCGGCTGAAAGGTAAACCTGAGTCAAAATGGCTTACATGTTATTGTAATGAAATACTTGTGAT	695	
AACCAAG		
TCTAAAATGCTAAATCAAGGAAAGCTTAAACCTGTTCCAGGAGCTGACTTCACGGCATGTTAGAAAGGTATTCAATTCAAAAGTATTCAATACATGGATAGGCCATT	696	
GAAAT		
TCTTACTCTGTATATTAGTTTATTCACATGTTGATTCAAGTCAAGCAGGAGATTAAATGGAGTTTAATAAAATGAAATCTCTGGAGAGGTTACTTTCTGCCTCT	697	
TAACAA		

TABLE A-continued

SmMIP Probe List	
ACCAAAATTCTATTTAGGATGCTATTCTATGATCAGCAAACGTGAGGTACAATCCAGATTGACAAGCTTCAAAACATGTTGAAAGACTCTTACTTGCTAGCATGGAAAGTT	699
TCAACC	
TTAAATGATTGTTAGAATTATACTGTTTAAGCTAAGAATTAGTATTACAAACCTCCAAGTAAAGTAAACAGTCATAGTGAAGCAGGGCCAGCTGGGTGAAACTTCCATGCTAGGAC	700
AAATAA	
TGTTTATAGGTGACCAAGTCAGCCATGGGTGCTTAACCTGGGTATTATGACAAAGGAAAGTCTGACTTGAATTGAAAAGATGTTAGAAAAGCAGAAGAAGACTAGGTGAA	701
CTTGA	
AGTTACGCACTGTGTTACCTGTATGAGTCTCTGGGTGTTCAAGGGTGTGGTCAAGGGAAACTTCTGCAAACTTACCTGGAATGGTTCACCTAAATGGACAGAGAA	702
GGTCTA	
CCCCAAAGGTGAGAACCATACCAAGTGTGACTTCAGGGACTGTGAAAGGACTGTAAGGACTCAAGGTGAACTGGGTTCTGTCAAGCCAGGCTCAAAAGCACCCAAAGGACATACAGGTTGAGGTTCACTTCTCATTTG	703
CTGGCA	
CCTTTTCACTGGCTCAGATGCCACCGTACAGAGTGGGCTACTCCAGGCACACGTGACATCTGAGGCACAGAGTAAGCAGGGGAGCCTTAAGCCACATGGAACATTC	704
ACCTAG	
AGACCACTGAGAACGCCCTCTCATGTGTCTACCCAGGTGCTTAAGAGATAATTAAAGAGATTTAAGCTGTCCCACTTACAGTGCACAGCAGGAAGCAGACACTGGTAAGTGTGCCCGTGTCCAG	705
TCTTGG	
ACTCTGAATGCTCTGTGAAAGAACCCGTGCTGTGATTCTGTATGGGTCTGGCTGAGGATGGGGTTATCGCTCTGTGACCTGTGCTGTGCAAAACAAAGAAGGAAAA	706
TATTTATTCACTAATAGCTTTAATTTTAATCAAGGAACAATATGATTATACTGTGAGATGGCTCCACATTCCAACATGTAAAATATGTGCTGAAAATGTAGGTGTA	707
AAAGATT	
TTACATAGCTGAAAAAAGTGCCTTAGAAGCAGGATGTAGATGCCAGGATCTGGTACATGGGTGCACTGGGTCTCAATCTTACATCCTTACATTTCAGGACATATT	708
TACATA	
TTTACATCTTGTGTTCTCTGAGGAATCAGAGGTAGGGACTTACAGGACTTACAGGAACTAGGAAAGTTATGGAAATCTTACATCAGGAAAGCAGGTAAGTAACTGAA	709
CCCTGT	
AAATAAAATGTGATTGCTCTAGAACAGTACAGAACACAAAAGGCTCAGGACTTACGGAAAGTATGGAAAGTTATGGAAACATCAGCAAAGAACAGGTAAGTAACTGAA	710
ATAAA	
TGTTTCTCCCTCTCAGGATTCCCTACAGGAAAGCAACTGTTGAGGAACTAGTGAATTGAGGAAACCTGTGCTCTGGATATTCTGCAACAGGGACTACAGTCATGGGACCGTA	711
CACAG	
CTGAATAATTAACCTGTGTTAGTGTGCTGAGCTGGGTAGGAAAGGTGCTGCTGAGCTTAATTCAGTAACTTGTGACGAAATATGATCCTTACAGGAAACAAATAGAGGTAATCTGTT	712
TAATA	
GTTGATGTTCCATGTGAAATTACTGGCAAAACTCAGGCAACTGGCAAAATGTTCTCCCTCATAGTAACTCAGGTATGATGTTCTGAAATCTGATGTTGGGTGACAGGTCATTCTCT	713
AAATAA	
TTCTTCCAGACACTACAAACAAACAGGAGTGCACACTTCTCTAGGCCAAACTCTCTAGGCCAAAGGAGGTAACTCTCTGAAACATCCCTGCTGTAAGTATAAT	714

TABLE A-continued

SmmIP	Probe List	
AAAAACATGGAAAAGCTTACCATGATGATATTGTCAATTGTGATTGTCATTGGATCACCATTGGTAGGACAACCCCTGGTATGATAACTAGAGAAAAAGA GACAC	715	
TGTCGCTCTTGCCCCACAGATGACCCACATGGTCAATTGTGATGTCATTGTGATGTCATTCAATGAACGTCCCTGTCGGCCATTCCAGGACTGCGGAGAACAAAGC AG	716	
TGACTGGATATTGACGTCCAAAACCATCCAGATGGTGC GGTCCTAGAGGTCAAGGATGGTCCAGAGAGCAAGTACCTGAGTATTATGCGGTCAGCATTATATGAAAC ACTACA	717	
ATAAGTAGGAAATAGCAGCCTCACATTGCCCTGACACACATAGTTGGAAATCACTCACTGATGATACTCAGGCAATCCAAAGTCACATATTCACCACTTCCCGTGGTGA CAGAACCCGACGTTACAAATTCTGTGGCTTCCAGCUGGGTCATCATCTGAGTTCTGAGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCTGCT CCTGGC AAAAAA	718	
TTTGCAGGGAAAGGTACTAGGTCAAGGTCTTTGGAAAAGTGTGAACGCCAACAGCTTATGGAATTAGGAAACAGGACTCAATCCAGGTTGCCGTC TA	719	
CTAAATTCTCTGGAAACTCCATTGAGATCATATTCTGAAATCAACGTAAGGTTACTCAATTCTGAGGACTCTAACCTGAGGGCCGGTACACTGAGCTGCT TAATT	720	
ACAGGTGACGGGTCTCAGATAATGAGTACTCTACGGTATTGATTGAGAAATATGAAATGATCTCAAAATGGAGTTTCCAAGAGAAAATTAGAGTTGGTAAGAATGGAA ATGTT	721	
TTTACCTTGCCTTACCTTTGACTGTGACAATTAGCAGGTTAAACGCAATGAGAGGAAACACCAATTGTCATAGATGAGATGTTGGATCTGGATGAAAGGGAG GGGCT	722	
AATATCACAGAACAACTGTGTACCTGGAGTTAAAGGATCGTCTCACAAAGATGCCAAGGAAATGTTATGCACAGCACTGACCCCTTTATG AGAGTA	723	
ATGTTAGGTACTGCTCGACACCCACTGTGTTCTGTTAGCCTTTCTATCCAGACTCCTCTGTGATCTCTGTCAGCTGAGTGGTTCCCTATAGA AGGTGA	724	
TTATTTGGAGACTTGTGAAACACTTCTCCAGGTCAAGATGGTATGGGTATCCATTGGGCTACTTGGCAGGACTTGCGAGGACTCTGGTTTC AAAGAA	725	
AGCTCCAATGGGGGTGCCCAAGTCAGTGGATCCCTCTCCACCCCTGGCTACCTGGCCTACCTGGCTGCCATTGGGCTTGTCAGGACTAGGC GTITTT	726	
CCAGGGACTAGGCCTGGATTTGGAGATGGATGGCTCCGGAAAGACAGTCCGGATAGTTCCATTGGGACTTTCACATCTGGGACTCTGGTGA AGGA AGGA	727	
GGGGGGCTGTCAAGTGGGAAACAAAGTCAGTGGAGATGTGAGTCAGTGGTGAACATGAGTTTTATGGGGGGGTAGACTGACCC GTAGGA	728	
TCTTTTAACTCAGGTACTGTGTATATCTTACTTCTCCCTCTCTGCTGCTGCAAGTCCGGCTTGAGATGTTGAGCTGAGGCTTGG GCCAG	729	
CTCTTTCTAGCACTGCCAACACCAAGCTCCTCCAGCCAAAAGAAGAACCACTGGTACTAAGTCAGGTACCTTCAAGTGGAAAG TTCCA	730	
	731	

TABLE A-continued

SmmIP Probe List	
CTCCAGGACAGGACAACACGCACCTCAAGCTTCCAGTATTACCACTACTCAGGATAGGAAAGAGGCAAGGGCAATAAGGAATCAGGTCTTACCTGTCCCATTTAAAAA	732
CCCTGCCTGGAGAGACCGGCCACAGGGAGAAATCTCGCAAGAAAGAGGAACTCAGGAGCTCACACAGCTGCCAGGGAGCACTAAGCAGGTAAAGCAAGGACAAGAGGGGG	733
GCACAGCAGGCCAGTGTGCAAGGGCTCTGAACCTGGAGTCAGTGTGATGTTAGGATGGTCACTGGCTCCGGTCATGCCCATGAGGAACACTGTTAACATGTAGT	734
CCCTGCCTGGCTGATCCAAAGGCACTGGCCTGATCTGGCTGTGTTATCTCCACTGACTGTACCTGACTTCACTACAACTACATGTGTAACACGTTCCCTGGATG	735
GGGCACCAACACACTATGTGAAAAGTGTTCTGTATCCAAACTTCCACTGGATAAGATGCTGAGGAGGGCCAGACCTAAAGGAAATACTGTGAGGAAT	736
GAGTATTGCGATGACAGAAACATTTGACATAGTGTGGTGGCCCTATGAGCCGCTGAGGTCTCGTCACTGGGTCTCTGGAGGAGGGGTIAAGGGTGGTGTCACTGGCC	737
CAAAACCTCGTATGTGCTGACTGTTGATGTGCAATGGCATGGGCGGGGGTGTGGAATCAACCCACAGCTGCAACAGGCAGGGCTTGGCCAGTTGGCAAAG	738
GTCACAGGACATGACGGAGGTTGTGAGGGCTGCCCAACATGAGGCTGCTCAGATGGGATGGTGAAGCTG	739
TTCACCTGTGCCCTGACTTCAACTCTGTCCTCTCCCTCTCCCTCTCCCTCTCCCTCAACAAAGATGTTGGCAACTGGCCAAGGACTGCTGTCAGGTGTTGA	740
GGGATACGGCCAGGCATTGAAAGTCTCATGGAAAGCCAGGCCCTAGGGCAACTGACCGCTGCAAGTCAAGACTGGCTGTCCAGAATGCAAGAAAGGCCAGAGGAACCTGTA	741
GTACAGAGACTGGGTGTCAGAATGCAAGAAAGCCAGGGAAACCGTAGCTGCCCTGGTAGTTCTGGAAAGGGACAAAGATGACAAGGGGAGGGCTGTTGCAAGGGCC	742
GGCCCCGGTGTAGGCTGTTGAGCTGGCAGGGGACAGGGGGGACAGGGGAGCTCTGGAGCTTCATCTGGCATTCTGGGACTCTGGGTCTTCACTGGAAACCATGTTAAATATGTGCCGGGACA	743
GGCTGGGGGGCTAGGACCTCTGGCTCTGACTCTCTTACCCATCTACAGTCTCCCTGCACTCTGGCTCCAAAGCAATGATGATTGTTGTTGTCCCGGACATATGAAZATGGTTCA	744
CITGCAGGGAGCCAGACTGCCTCGGGTCACTGCCATGGGAGGCCAGTCAGATCCTAGGCTCGAGCCCCTCTGAGTCAGGAAACATTTCAGACCTATGGAAACTGTGAGTGGATC	745
AAAGTTCACTGTGAGATACTCGAGAAATGTCAGGAGTCATGTCAGAACACGGCAGGTATGGTCCTAGAATTCAACCTGGCCATGGATCCTCCTCAGTGA	746
AAACCTCTAAAAAAATTCTGAGAAGGCATTGCTAGAACACGGCAGGTATGGTCCTAGAATTCAACCTGGCCATGGATCCTCCTCAGTGA	747
AAATGAAAGCCAAAGAAATTGAAAGACCCCTCAACAAACTTAAAGGACATTAGAGAGTCACATTGCAAAACTTAAAGGAGTAAAGAACAA	748
TGGCAGGGAGGTGACATCTTCAATTGTTGGTCCATGCAAGTGTGTTGATTAGTGGACACAGGCCATTGTCAGTGTGTTGTTGAAAGTCAAGTGTGTTGAGTGTGTC	749

TABLE A-continued

TABLE A-continued

TABLE A-continued

SmmIP Probe List	
GATTCAAAGAGGAGTTCTTCTTAAAGGTGAAAGATCAGAAGGAAGTCGGTATGTCACAGGACAGTAATTCAAAATGCTGCCTCAGGAAAGGCCAGGAGATCTTACTACCTCG AGAAACA	787
AACACCTGTTCTCATCTCCAAATGTGATCTCCTTGGCCAGGAGAACAGTGCGGACAGGGCCATGGCTCTGCTGATCAGAGAAATGTTACAGGCAAGGAAAGGCTTGGGATGT GGCTGC	788
TTGGCTCTGGAAATGTGGTGGCACACCTTCAGGGCCCAAGGGATGGCTCTGCTGATCAGAGATGGATCCCTCAGTTTTCAGTGGGAAGTGGACAGGAAAGCACAATCTCA TGTCCTG	789
CCAAGCAAAACTCCATGTGTTGGGTACAGACTCCAAAGGGAAAGACTGGGTCACATGCCCTTGTGGCAGGTCAGAATGAGAAAGACATTGTGGGGTCTCTTAAG GCAAT	790
TCTCTTAAGGCAAATGCCGAGAACAGGACTAGTCCCCTGGATAGTCCCCTGGCAACTGGCTACTGGGATGCCCCTTGTGATGGACTGCCCCCTCTGGAAATTACCCCGAGA GCCAGG	791
GAGGCCAGGGAAAGGGCTCAGTGAGCCTCTGGAGCCTTCTTCTCCCAACTCAGGATCAAGCAGGATTITATGGGAAGGCTTAAACTCAACTGAGTTCCACCAAGGTTA ATIATT	792
TTAAATTTCCTCTAGCTCTCCACCTTCCAAAGGGCTTGTGGAAAGTGTGGCAGCTGAGCCAAAGGAAACTTGGTGCAGCTGCACTCCTTCCTGCAAATGTTCA CTGACA	793
GCAAAATGTTCACTGACAGGACGGACGGTGGAAAGGATCTCGCTCAGTGTGCTCAGGTGCGCTGAGGCTGAGCCAAAGGCTGATCATGTCACAGATGACTGTTGAAATGTTCA CTCTAA	794
GTATATAAAAAGGTAACAGTTGGCTTAAGGTGAAACTTGTGCTCCTGAAACTTGTCTCCTGAAAGATTCCAGAAGTCAGGACACGGCAGGAGGAGGTCTGCTGAAAACAAAATT CTGACA	795
AGCAGGGCGAGGGCGGTGGAGGGCGCTGGTAGGGGGGAGGATGGGGGGGGAGGCTGG CTGACA	796
CCGGCGGAGGGCGCGTAGGTGAGGTGAGGTGAGGG CTGACA	797
TGTGGTAGGGCTGGCCAGGCCATGGCGCATGGCGTAGGG CTGACA	798
CGCTGGTAGTGTGATGGGGGGGTGGAGGGAG CTGACA	799
CACCCAGAACGCCATTTCACCTGGACAGGGCATGCAACCCCTCTGGAGAAACTTTCAGTGAAGTAAGGCCACTTGAAGTCAAGTCAAGTCAAGTCAAGTCAAGTCAAGTCA TGGAG	800
TTTACATATAATTGACCTTCTGATTCAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATAAAGGGAGATA CCAGCA	801
CCAGTTGGTGGTGGCCAGGTGAGGAGGG CTGACA	802
TTCAGGGAGGCCAGGGTGG CTGACA	803
CCCATCCCTCCCTCCCTGCTCCCAATAAGACATGGCAAGAAACTAGATG CTGACA	804
ACAGGGAAAGCTTCACCTGACCATCACTGTCAGGCTTCAAAACCCACCCCAAGTGCCACTACCAAGGAGGACCTGGAGGAGGAGGAGGAGGAGGAGGAGGAGGAG CTGACA	805
	806

TABLE A-continued

SmmIP Probe List	
TTCAAGGATACTGGACAGATAACGTAACCTCTTCCACTTCGACCGACAACCTGAGGTCAATTAAATCTGCAACCTGGTCTTCTCATGGCTGGTAGCATTTCAGCTCAGCCGAGT AGTTT	807
AAGGTATGATACATCCCTGATGTCGATTGTCCTTTGACTGGTGTAGGTGGCCTAGGGATGTTCCAGATGGCACTCTGGTCACTGTGATGGCTGGCAATGATGAAAC TACTCG	808
CTCTCGGCCAGTACCTTGAAAGCGAATGGCGAGGGCTTGTGCGAGCGCTGGCAAGCGCTGGCGACCAGCTGCCGGGTGTC TAGGCAGGAGGAAAGTGGGCTGCGTGGTCAAGCGACTTCAGAGAACCTGGCTGCGCTGAGTGGGTGAGTGA GGAGTG	809
AAAAGGTGTGATGACTTGAAATAACCGTGGTTAATGACAGCCGATCCAGGCCGAGCTGTCAACCGTGAAGCTGAGTGGGTGAGTGA GGAGTG	810
TCGTTTATTGTGGAACCGAGGACCTGTCATGACGACATGCTCCAATTGAAATAAATGAAAGACTGTGACTCTGTAAGGAAATGAGAGTGTATTATTGCTGGAAAGATAT CAAACA	812
ATGACTATGACCCCTGACGCCAGCTGGAGTACAGCGAGGAAAGAACCTACCAACAGTCTAGACTCTATGAGGATGGATGTTGGAAATTATGTTAACGGTAAACATCTGCGTATGAAAGAAAAGCTTAAT TCACTA	813
TGTCACAAATCAGGAAACATCCACAGAGATACTTACGACTGGTACTGACATATAACATTCAGCTGAACTTCCAAATTGCACTGAGCTGACCTAGCGCAGCATGAAAGATGCTAT CATAAA	815
AAAGGAAGAAGATGCAAGCAGCCCTTCTGTTAACGGACGATGGTATGCAAGGACAGACAGCTGCAAGTGTGAATTCTGCCCCGTGACCCGGAAATGGCATTGGTAAA GACRAAGTGTATT	816
GCTTACCACTAGTGTCTGAGGCCAGAICACTGGGTGAGGCCACTCTACAGGGCCAGAGTCTGAAATTCTCCACAGCTTAACAGCTCCCTACTTCTCAGGG TTGAG	817
AATTCCACGTTGGAAATTGCAAGGAAATATGCGGGAGGACATTCAATTCTTAAGGACATTCAGTGGCCAGTGGCTCACAAACAGAAAGAAAATGCTTTGAG TTTCCA	818
GCATATTGCTGCAATTTCACCGTGGAAATTGCAACATTGCAAGGGAGAAATTATGCAAGGCTTCTGCAAGTCTTCTGCTCCAAAGACCTGGAGCCCTTCACCC CTGAAA	819
TCATACCTGTTAAAGAACATTTCACATGTTCACTGTGGTCATTTCATGATEGGTCACTCTGAGTACTGAGTCAAGGGGTCAACCCATAAGGGAGAAGTAGTCGGACAATTTC AGTGTAT	820
AAAGGAGAACAACTGCTTATAAGCAAGTGTGGCTTGGCTTGCATGAGCATAATTCTATTCGGCCTCTCTCAGGAGTGTGAGAACGATCACTTGGAAATTGTC TTCTCT	821
CATTGGCAATTGGGGGGGTGATCGGGAGGCTGGGGCTGAGACTGGACACTGACACTGACCTGAAACGTTAGTGTGACAGCATGGTGGCCCATGGTAACCTCGGTGCT GTGTTA	822
TTGGATCTATAGATAGAACCAATTCTGGAGGAATACTGTTCTGGAGGACTAATTCTGGCTGTTGACCCACTAAGCCACTTCCAGGAGGACTAATTCTGGCTG CTTTTT	823

TABLE A-continued

SmmIP Probe List
ATCTATAAGATCTGAAATCATCAGFACTGCTCCCTCATCTGGTGGCTGCCAGTCCTAACGAAAGAACATGGCAAGGAAACATGGCTGCGTGAACAAAGGCATGGACTGGCG ATACCA 824
CCCGCTCTGTCCTGCAAGGTTAACCCAGGGCTCCATGGAGTTCCCTGGCTGGCTGGGACCTAGAGCCCTCCCTGGCTGAGTGGCTGGATCTGGATCTGGCTCTGGTGTCTCCACACC AGAAAT 825
AGGCTACAGAACACTCCCAGGTAACCTCATGGATGGCTGCTTGGCTGAGTGGCTGGGTGCAATGGAGATCCTGGCTAGGGTCAAGAATACCACTGTGGGATACTICA GAAATG 826
CTGTAGGCTCAGGTCCTGTAGTAGGCCAGTGCGGAGCTGAGGGCAGTGGCTGGGTGAGGAAAGTGTGCATCCAGGCCCTCACGGCCAGAGGGAAAAACCCCT GATTCT 827
AACAGGGCTGAAGCCAGGCCAACCTGCAAGATCAGGGCTAGATGICGCTGGGAGTACTCTGGGCTCATCTGGCTCCTGAGTGGCTGGGTGACCTAGGCTTAGGACTCCACTGCTA CCTGAC 828
ACTGGACCTGACGGAGCTGCCCCCTCTGCTCCTGAGTGGCTGCTGGCTCCTCTGCTGAGGAGACAAAGAAGGGCTAGGGTAAAGGTGTGGTGAACCTAGGCTTAGGACTCCACTGCTA AAAACA 829
ACCTAGGGCTTAGGACTCTCCACTGCTAAACAGCAGCTGCTGGCTTACTTTCAGCTCCTCTGCTGCTGAGGCTCCTCTTCAACTGTGTACTGCTTCTCATCCAGGCCGT GCCITG 830
GCCCTAGGTCACTGGCCACCAAGAGATCACTCCTGACTCTGGGATAGGGTTCCATCCAGTGCCTACACACAGCAGGGGAAAGAGTGAACAAAT GAATCT 831
GAGAGCTGAAACAAATGAAATCTCCAGTACTGAGCCTGGCAAGGGAAATCCACACTTGTGGCTGAGTGGCTGGCCTCTGAGTGGGGCTGGCTGGCAATCTCCACGTT GTCAACA 832
CCAGGTCCGGAGTTCTCATCTGTGGCTTACCTCTGTGGGAGAACGGCTCAGTGGCGAGACACAAACAGGGAGTACTAGAGGGGGCCCTGTGAACACTGGCTGACCCAAATCCCCA ACAAG 833
AACCTGGGAGCTGAAGGCCCCAGCTAGTGTATTGCTATGAGCCACCTCATCATCAAAGGCCCTGAGTATGCTGGCAATGCCCTGTGACAACCTGCTGACAACTGCGAAG ATGCC 834
TAATGGCATCCATTTCTGCCCCAAACCTTGGTTACAGCAATCTGATACTCTTGTGGCTGCATAGGTCAATGAGGGCGCTGACTGAGTAACACTGGAGGAAAAACTGAAG TATCAA 835
TGGATGCCATTATGTGAACTCGGAGAACAGCCGGGACTGTTATCCAGGAGCAGCTGGGAGCCCTGGAGCTTGTGACTACTCTGGCTCTTGAACATGAGTGGCTTGTG GGATT 836
AATAATGGATAATACAAAGACAAATATGAGGAAACGGAAATAAATGATGGAAAACGCCAACATGAGGGCTAGAACTCTGGCTACAAAGGGAAAGGGTAACCTTTATATGAA TATTTA 837
CCAATCATTATTCGTTCAATTGTCTTGTATTATCCATATAATGTAAGATTAGTGCACATTACAGCTTGTGCAACTCATAGCTATTAAAGAGTAA AAGPAT 838
AGCTTCAGGAAAATCAAGATGAAATAGAAATATGATAATGCAATTGCTACAGTAACTGGGTAAAGTGTGACAGTTTTCATAATAGCATTATGTAAATTTC TACTCA 839
CCCAATTCACTGATGCCATTGCTGAAATTGAGGTATTGCAATTGAGGATATTGCAATTGAGTGGATTGATGCTTCTTAATGACAGTTATTAAATATGTGGTGGAC TATGAT 840

TABLE A-continued

SmmIP Probe List
TTTAATGGATTGCTCATCTTGTCAAGGGCTTTAGCAAGGGAAGTAAAGACTCAAATGCTTACTGCTCATCAAGGGCTTTATTATAACAAAGAGCTTATTCCAACACTGGAAC
TTTTA 841
ACTTTACCGTGGTCAGGTAGTATTACTTAAAGAATTACATGGTCATTGCCATTGACAAGAACACTTCTTGCCTTAAATATTAAATTGTCCTTAGGAT
AGATT 842
AAAAAATTTTAAATTGCTTACGGATGAAATTGTCATGTCATTGACAAGAAATATGATGTTGAGTACAAAGGAAATAAAATTACTCACTCTGTTTACAGTAATGATGTA
TTTGT 843
ATATATAATTACTTTGTAGAAAATTCTCAGCTGCTACTGCTACTGGCGGTAGCTGAATAAACAGATGATAAGACATTTCACAAATCTCTGAGAAACTCTCACTAC
TCCTAA 844
GATTTCTTCAGGTAGTTACTGGAAAGITCATGACCTTCAAGATGTCACTCCGAAAGAGGATGTTGCTTACCTGAGTCTTACCGAAATTCTTGCTAGCTGGTGTGAT
GATGAC 845
TTACTGAATGAAAGCTGATGCCCTCAACCACCTTCCCCTTCTGATGGTTGATTTTACTCCGTACTGTGATGGTGTGATTCCACTTAATGACTGACATGGTGTCA
TCATCA 846
AAAAAGGGCCTACAGACAGGCCAAAGTGGCTTGTAACTCAAAATAGAGACAAGGAATGTCAGTTACTAATATGTAAGGGAGCTTACGTAAGTGCATGGTA
AGTATA 847
CAGATATTAGTAACTGTGCCACATTCCTGCTCTATTGACTTACAAAGGCCACATTGCGCTGTCTGAGGCCCTTTCTGTTGCTCAACTGAGCTTGACATGATTAAATTGCCCT
TACAT 848
ATAAGCTCAATACGAGAAACCTTACAAGGAATTACATGTAATTATTAACTCTTTAACATAATACCTCTTGGGGTTTGTAAAAAATTTCCT
TTCAAA 849
TTTATCATGCAATGCACTGGTAGTGGTAGTGTCTGTGACATGTTCACATCACACCAATTGGCTCAGGAATATGGCACAAAGAACATCTACAGCAAACGAAAAATAATA
TTATA 850
ATTCTTCATTTCATTAGGGCTTATGCCAAAAACAGAAACTCACAATCAACTCGAAGGTACATCATTAG
AATACCGATAGCATATTTCATGATTTCAGTTAACATTGAGAGATAGGTCTTACATTGAGAGATACTGCTCAGAGGAGCTTACAGAACATCTACAGCAAACGAAAAATAATA
CATATA 851
TTGGCTTAAAGAACCCATGCTTACCATGCACTTATGGGAGCTGCCCTCTGGGATTAAATATGCACTTCTGCTTCAATTCTCTCCCTACATGGCAAATCCAC
ATTTAG 852
GACCATTCCTTCCTGTTAAATCTCTGAGTACAGTTAAATTAAGTCAAGTCTCMAAATTGCTCMAAATCTGCTTGTGAGCTGGACTGTGCCAGAGAAACACTAGAGAGAA
A 853
TGTTTCCTACTGTAAATTCCCTGTCAGACATATTTCATGTTAGCTTACCTCAAGGTTTATTCAACACAGGTTTATTCACTCAAAATAGTAGCAC
CAGGCT 854

TABLE A-continued

	SmMIP Probe List	feature_start_id	feature_stop_id	probe strand	failure_flags
miP_sequence	seq	feature_start_position	feature_stop_position		
TCAGACTTGCCCCACCCNNNNCTCAGGTTCCCGATAATCCGA CGGTAGTGTNNNNCTGTCGCCACCGCAGGTCTCCCTGCCTGG	856	43814931	43815035	-	0
GTTGGAGGGTAAGGGGGAGGGNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNATGGCAAATAACAGAGGAA	857	115256486	115256577	+	0
GTAGCCGGTAGCTGTAGTCTGTNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNCAACAGGTTCTGCTGGTGTG	858	115258743	115258748	-	0
ACTGGAAAACAAATAACCCGGNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNATACCTAGTTGCCCCCATGTC	859	25457148	25457289	+	0
GCTGAAGGGTAGATTGGCTGTGTTGGATTTCACTCGGATAATCCGA CGGTAGTGTNNNNNTACCCGCCCTCTGCGCT	860	25457144	25457294	-	0
CCGGGTGTGGCATCTGGTGTGTTGGATTTCACTCGGATAATCCGA CGGTAGTGTNNNNNTCCCTCTGCGCT	861	25458573	25458698	-	0
GCAGGGAAAGGAAGGGAGGAAGGATNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNATACCAAGGTTCTGTTGTT	862	25459792	25459882	-	0
GCTCTGGCCTGGGGGTGTNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNCTGCTGTTCTGCTCCCTTGG	863	25461992	25462092	-	0
GCGGATCATGCGAGGGGGTAGANNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNAGGTAGAACGCCATTAGTGAG	864	25463166	25463483	+	0
GCGTAGTGACAAGGGACATCTNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGCCCAAGCTGATGGCTTCT	865	25463166	25463483	-	0
GCTGTCAGGGACAGGGAGA CANNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGGAGGGACAGGATGGTA	866	25463503	25463605	+	0
TTGGAGGCCATCTCCCTGGGACCCCTNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNCTCACACCTCCGGGCC	867	25464533	25464580	+	0
GTCCATGCTGTGGGGCGAGAGGGAGAAGGGGAGCTGAGGACTGGGATTCAGGT	868	25464429	25464508	-	0
GTGAGGGTGCAGGCCAACAGAGGTNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGTGGGGAGCTGGGAC	869	25466760	25466845	-	0
CTTCCTTAATGGCTGCCCTGGCAAGNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNCAGACTACAATTCCT	870	25467088	25467139	+	0
GCCCTGGGGCTGGCTCGAGCTNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNAAGGTACTAGGGCTGCTGC	871	25467018	25467212	-	0
CCCTGGAAACTGCTACATGTGCNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGCTCCCTGCTGCTACTGGCT	872	25467018	25467212	-	0
GCTGTTGTTGGCTCCAGTGTNNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGGTTCTGACCCCTCCGGCTG	873	25467407	25467525	-	0
GGTAGTACACCGAAGGGCCTCGAGCTNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNTCTGGTGGGGTGTCTCCCT	874	25468119	25468204	+	0
TGCCGTGAGGGCGCCCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNCATCCCTCCCTGCTTCCAG	875	25468119	25468204	-	0
CCGGCCCTGCTCCCTCGGATGGNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNCTCCTAAGTGCCTCTGCTACTCT	876	25468379	25468940	+	0
CACATGTCGGTGTACACTCTCTGNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNTCTGGTGGCCACCCCTCTCCA	877	25469025	25469183	+	0
TTCCCCCACCCCTCCCTAACAGNNNNCTCAGCTTCCCGATAATCCGA CGGTAGTGTNNNNNGGTTCTGCTGGAGGTGG	878	25469025	25469183	+	0
GTGACACGCCAGGGTGGGGTTGAGGCTAGTGTNNNNNTAGGCCAGAAGGGCTGGAG	879	25469487	25469650	+	0

TABLE A-continued

SmmIP Probe List
GGCTGCCAAGGCCCTCACAGAGNNNNCTTCAGCTTCCCGATATCCGACGGTAGTGTNNNNNTGATTGAATGGGCCCTGGGG
CACCAACCCATGCCCTTGAAAGTGHNNNCTTCAGCTTCCCGATATCCGACGGTAGTGTNNNNNGACTCTCGTAGATGGCTTGCGGT
GCACTAGGAGGCCCTGGAAAGTGHNNNCTTCAGCTTCCCGATATCCGACGGTAGTGTNNNNNGTGTGTTGAGAGTGTATG
TTCCCCCAGACCCTCCCAANNNNCTTCAGCTTCCCGATATCCGACGGTAGTGTNNNNNTACTGCACAAACCCACAACCTT
GTGTCTTGGGATGACGGCNINNCTTCAGCTTCCCGATATCCGACGGTAGTGTNNNNNATGGGGGATCAGGGTGGCAGGG
CGGGCCCTGGTTTCTTNNNNCTCAAGTCTCCGATATCCGACGGTAGTGTNNNNCTGGCTCGTCAATCGCCTGCTTGTGTTGGT
AGGTAATTTGGGATTACCTTCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTAGTGGCATATTCGAT
CTGGATAATGTTTCAATGGTTCTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGGTATCTTATCCTCTTATGG
GTGTTAAAGCCTTATGAAAGGTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTAGTAAATGTTGGCATATTCGAT
GAAGGGAACTCATGAGTTGGTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGGCAATAAGAAGGAATGCC
CTTATGGCTGTGCATCTTGCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGTAAACAAACAGCTAGAGCT
GCTGCCATTTGGCATATTTCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCAAAATCACATTATTCGCAACATG
TGCAAGGAAGTCAATCCCCTTCACTTCCGATATCCGACGGTAGTGTNNNNCTGAAAACACTGGTTGCCT
GGTGCCTCTGGCTCTGGGGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNICATGTGCAGCTGTAGTAGAGGC
CACTCATZAGCCAAAGCGAACAGCAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGCTCTCCCTGTCCTCCTG
GTCCAGGAACATGGAGGAGTGNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGTGTCTGGTTTCCAGCACTC
GTGRATAACATTAATTAGTTGGAGGAGTGNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGCAGACTGTCAAGCAGAGA
GCCCACTGCTGAGAGCTCATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACAAACATGTTGAGGGCAC
GTAGAGGTATTCAAGGTTTGCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNAAATGGAGAACCAAAGTGGC
GTTCGTGTGCAAAATGGAGGTGNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGGTTCCCTTCATAAGGG
TCTCTAGCCAAGAAAATGAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACTCTGGGCTCCTTCAGATCAAG
CGACTATCTGGCTTCCCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGTTCTCAGTTCAGCTTGTG
TGGZACACACATGGTAACTCTGGTAACTCTGGTCACTTCGGATATCGTCCCGATATCGACGGTAGTGTNNNNCAAGGCTTCAGATCTG
CATTGGTGAATGACTCTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACTTCACT
GTGAGTGGCCAGGGCTGTGATGATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGAAACCAAGATCTCACATA

TABLE A-continued

SmmIP	Probe List					
GCACCATAGGCAATTAGGACTGCNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNACTCATAGTAGGCCCTGACTG	905	10615044	106158550	-	0	
CCAGCAGGAATTGCAAAGCNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNACTCGACGGTAGTGNNNNCTAGAAACCGAAA	906	10615091	106156165	+	0	
GCAGCTGGTTGGAGGGAGCTNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNCTATTCGAGGGATGGGG	907	10615044	106158550	-	0	
CACCAACCCTAACCCAAANNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNCTAGTGTCACTAAGGATTCC	908	10615044	106158550	+	0	
TGAAAGAGAATTCTCACCAANNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNCAATTGTGATGGTGGTGGTGTGT	909	106156165	106156274	-	0	
CCAATGTCAGAAACACCTTAAGCINNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNCAACCTTCCAGAGTCCTAAT	910	10615044	106158550	+	0	
GCTTTTCTCTGAAGGAAGCTGNNNNNTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGAAGGGCTGCCATACTGTGT	911	10615044	106158550	-	0	
CGTAATGGCATGACTGCCATCANNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNTGTAGAAAGAACAGGCAA	912	10615044	106158550	+	0	
CCAAATGGAAACAGTCATTGTCCNNNNNTTCAGCTTCCGATATCCCACGGTAGTGNNNNNCGTGTTGCTCTTGTCTCG	913	10615044	106158550	-	0	
CCCCACACAGGGCACCTCINNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNCTGAAATTCACATGCCCTGGGG	914	10615044	106158550	+	0	
GGGATTCCGCCTGGTGAAGAACGANNNNCTTCAGCTTCCCGATATCCCACGGTAGTGNNNNNGCTGTGTGTTTCTGGTGT	915	10615044	106158550	-	0	
TCCCGAGAGTTCACATCCTCTCAGTTCAGTCCCGATATCCCACGGTAGTGNNNNCAACAAAGGGAGATCCTCAA	916	10615044	106158550	+	0	
GGAACTGGAGATGGTGGTCACACTGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGCTGTGTCAACACTGGGG	917	10615044	106158550	-	0	
GAATACTCCCTTATAGTCAGACCATGNNNNCTTCAGCTTCCCGATATCCCACGGTAGTGNNNNNATGTCAGCAAAGGAAG	918	106157293	106157510	+	0	
GGTTGTGTTGTGCTGTGTGTTATGNNNNCTTCAGCTTCCCGATATCCCACGGTAGTGNNNNNTAGTGTGCTGGCAAAGAAT	919	106157294	106157418	-	0	
GCTTCAAGAACAGGAGGAGAAGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNCTTGTCAAAACAATACACACC	920	10615044	106158550	+	0	
GACATTATGAGTCGAACACTGCTNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGATGTGTTGTTCTT	921	10615044	106158550	-	0	
CAGAAAACAGGACCCAAACNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNCTTGTCAGCAAAGGTACTTGT	922	10615044	106158550	+	0	
GTGAGAGAATCTGCTTGGNNNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNAGGACAGAAAACATTGCA	923	106157742	106157861	-	0	
AATGTCAGCAAGAACGACCAACNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGACCATAGGTCTTGCCTAGT	924	106158077	106158150	+	0	
GCAGCATGCTTGGTAGTTCGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGTCAAACGTGACTGGCCCTG	925	10615044	106158550	-	0	
CTTCTTCAGAAAAGACACCAACNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGACCATAGGTCTTACTCTC	926	106158273	106158480	+	0	
CACAGCTTCAGGGTAGTTCGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGAGTGTGACAGGTGTATCC	927	10615044	106158550	-	0	
CTTCAGATATGGGATTTCCTTCTNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGACTCACCTTCAAATACT	928	106158273	106158480	+	0	
GCTGGGTTGGCTATCAAGTCTNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNGAGTGTGACAGGTGTATCC	929	106158273	106158480	-	0	
GCAAGGGACAGGCAAGATAACGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGNNNNNTAGTATTAATGGGTCATAA	930	106162468	106162605	+	0	

TABLE A-continued

SmmIP Probe List
GCCTTGGCTTAATCTGGGNNNNCCTCAGCTCCGATATCCGACGGTAGTGTNNNNNTGTATGTGTGTCTGT
CCAATCGGGTGTGCCATTGAATNNNNCTCAGCTCCGATATCCGACGGTAGTGTGTNNNNNTGTATGTGTGTCTGT
CCCCAACCCAAACAAAANNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNCGGATTCCTTCCCACACCA
GCTCGAGTAGAGTTCTAGCCNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNACGGTAGACTCTCTCTTT
TTCAGAAGAGATCCCNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGCACAGCTATAATATGCTATCC
TTCGGATCCAGCCCTGACAGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNAGGGATATACATCAGGAAG
GGCAGCAATGTAACAACUTACTAGACACNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNAGAATATTCACITATAC
GAGGACAGCTTAGGAGCTGTGAGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNATAATGAAACAGAGCACCA
GAAAACCTACTAGTATTAGACACNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNAGCACAGAGTCCAAACATGC
GTCAGAGCTTGCCGACAAAGGAAAGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGGATGAGGAGCTTCAGTCTCG
GTAAGACATTACAGCCTAAACTACNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNTTCTCTCTGAGCTT
GCAATTGAGATAAATGCTGTGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNAGGCAAAAGGTCAGCAG
GCCGAAAAAAACTCAGTACCTGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNGTGTTGAGCTGATGGGCTG
CCCCAGCAGCAGGCCACACNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNTTCTGTCTCTTACCCGTCC
CCATGAAACCTAACCTGGCTTNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNCCACCATACATGAGAC
GCTGGGGTGTGGTGGCTCCTTNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGGCTGAGGTGTGTGAAG
GCCZAGGGTTGGAAATAGCAGAGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNCAATGAAATGAAACCTATC
CCTCGAGCTTGAGATGGGTGGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGGCTGAGGTGGGAAATAG
GGTAAACATCATCACCTTCACNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGGCTGAGGTGGTACATT
GTTGATGGATGGTGGTAGACTGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNNGGCTGAGGTGGGCAATT
GCTTTCCZACAGCTAATGGGTNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNACACCCAAATGTGAAATCC
GTGATGCTTAATGGTCAGGAAAGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNCATGTCAACAGCTCTTC
TCACCCACAGGATCTCCNNNNCTTAAAGCTTCCGATATCCGACGGTAGTGTNNNNCAACATGGCTGGCTGGACAG
GCAGTTCTATCATGGTAAAGAGCTGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNACAGTGGCTGGCTGG
CAGZGCCZACCTAACCTGGCTTCAAGGNNNNCTCAGCTCCGATATCCGACGGTAGTGTNNNNACATGGCTGGCTGG
931 106163988 106164088 + 0
932 106164823 106164875 + 0
933 106164725 106164940 - 0
934 106164725 106164940 - 0
935 106180773 106180933 + 0
936 106180773 106180933 - 0
937 106182914 106183008 + 0
938 106190761 106190911 + 0
939 106190761 106190911 - 0
940 106193714 106194080 + 0
941 106193714 106194080 - 0
942 106193714 106194080 + 0
943 106193918 106193967 - 0
944 106196203 106196292 + 0
945 106196203 106197683 + 0
946 106196203 106197683 - 0
947 106196203 106197683 + 0
948 106196203 106197683 - 0
949 106196203 106197683 + 0
950 106196203 106197683 - 10
951 106196203 106197683 + 0
952 106196203 106197683 + 0
953 106196203 106197683 + 0
954 106197125 106197218 - 0
955 106196203 106197683 + 0

TABLE A-continued

SmmIP	Probe List				
GCAGCTCACGGCTTGACACACNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTTCAGCTTCCGATACGGGTTTT	956	106196203	106197683	-	0
GAAGTTCATGTGGCTCAGCGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACAAAGGGGTGATATCAT	957	106196203	106197683	-	0
CCAAACACTCATAGAACATCATTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACAGCAATGATCAACTGTT	958	170837531	170837568	-	0
CAGTAGATCATTTCCATAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACATCACAAAATGATCC	959	140453092	140453191	+	0
CACACAAAGCCCTGCTGAAGATAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGGGGGAGGGTAGCAGA	960	148504736	148504801	+	10
GGGTTTTCTACTGGATTGTGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTACTGACACCAGTGTCT	961	148506160	148506251	-	0
GTAAGCACAGCCCAGTGAAATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTACTTGTGATAGCAGTTGG	962	148506400	148506485	+	0
GCTGGGAGGCACTGAGTTCCTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTAGGGTTGATACCTTTATCC	963	148507415	148507487	-	0
GGCACTGATAACCTGTTACGTTAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTTCAACCCTCCCTTTTGTGA	964	148508716	148508816	-	0
GGAGGTTCTCACTCATACCCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTACTGTCCAAATGGTCAAGGGC	965	148511048	148511235	+	0
GTAGTTAGCTATTAGTGTGATGCAANNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGGCTGTCCGGAGAGTGTGA	966	148511048	148511235	-	0
GCATGAGAACTAAATAGGCTTTCAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTCAACCATGTTACAACCT	967	148511999	148512138	-	0
GCTTTGTCTTCAATTGTGTTAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGTCTGTGGATTGTGAGCT	968	148512570	148512669	-	0
GCAGAGGGTACTTGAGGGACTTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTTAAAGATCTTGTGTCAT	969	148516685	148516783	-	0
GTTTCTAAAGGTTCCATGTGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNCAGATTAGCATTGGCTCA	970	148523544	148523730	+	0
CGTTTCAATTTCATCATTGTGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNACTTCCTCTGAATGTACCC	971	148523544	148523730	-	0
GAGCCATATGCTCTCTCTGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNTTTCTCTTGTGGAAG	972	148526828	148526931	-	0
TGTTCTCTGTGGATAATGTTCCGATATCCGACGGTAGTGTNNNNNTTACCGCTTGTACAGAA	973	117864785	117864951	-	0
GAGGACCAACAGCAGGATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNGAAGTAATAATTCTGCAACT	974	117864785	117864951	-	0
GAATAATCAGTAAGTTGGCTCTNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGGAAACT	975	117866482	117866595	+	0
GGATCTGGACCGCCACAGCAGGATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNAGCAAGTATGAGCAAGC	976	117866604	117866713	-	0
CCTTTAGATTACAGCATNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNTTTACAGTGT	977	117868403	117868530	-	0
AGACTAGAGGGTTGATTATCAGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNAAGGACAAAAAGAGCAAA	978	5069950	5070055	-	0
CAGGATCACAGCTAGGTGTCAGTCAGTNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGCAAGTATGAGCAAGC	979	5073739	5073781	+	0
CTTTCTACACATGGGTGGAAAGTCAGTNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNTTCACTTCTGACAACTTAC	980	112350168	112350333	+	0
GCTGGTTATTCCCTTTGAGCAGGNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTAAGCTTATTCTCCCTCT	981	112350168	112350333	-	0

TABLE A-continued

SmmIP	Probe List
GTTAGATGTCAGGGATAAGCCNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGTACCAATAAAGATTG	982 112350747 112350893 + 0
AGTAACCTCTCCAGGAAGATTCAATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGTACCAATAAAGATTG	983 112350747 112350893 - 0
CAGCTGGCCGCGTGTTCAGTCAATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGTACCAATAAAGATTG	984 112352828 112352984 + 0
GAGCTTCAAAAGACATTTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGTACCAATAAAGATTG	985 112352828 112352984 - 0
GCAAAGCTCAATGAAAACCTGCCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNACAGA OCTTACATATGTT	986 112356245 + 0
GCCTGGCCCTAACATGTGGCANNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNINGAAAAATAATGTAAGAAA	987 32413516 32413615 + 0
GCTGTGTTCCCTGGCTAGGGTTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTCAATAGAATATGTCCTT	988 32414197 32414308 - 0
GTCTTGAGGGAGAGTGAACACTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGCACACATGAAGGGG	989 32417797 32417956 + 0
GCAAACATGGTCAAGAGTCCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGCACACATGAAGGGG	990 32417797 32417956 - 0
AGGCTCAGTGGCTCACAGTCGCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGGGCCTGCTGTGCTC	991 32421491 32421591 + 0
GAGCCCTGTGAGCACCTCATGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGTTAACATTATAATGCACT	992 119148874 119149011 + 0
GTTGCAATGTGGACCCCCATCTCAACNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNACGTTAACATTTCAGA	993 119148874 119149011 - 0
GAGGAAGGAGGAGGGAGGCTCENNINNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGTATTTCAGATGCACTG	994 119149218 119149335 + 0
CACGATCTGTTCTGAAATCENNINNCTCAGCTTCCGATATCCGACGGTAGTGTNNNINGTACCTATGTCCTAGTAGG	995 25378562 25378647 - 0
GACTGGGAGGGTTCTTGTNNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGCAGTAAATACTCAGAC	996 25380275 25380285 - 0
GCATATTATGGTGCAGGACCATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNATAAGCCCTGTAATGAAATGA	997 25398211 25398286 - 0
GTCCATTGAAAGGGAGGCAANNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCCATCTCTTAAATGCCC	998 1123888139 1123888229 - 0
TCCGCTCACTAATAGTCACTCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGAGTAAATAATTGACTTTC	999 112910747 112910847 + 0
GGTACATAGTCCTGGACTGTCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGCTAGAAATGTATGTCAG	1000 112915440 112915540 - 10
GGAAACAGAAATATTCACTGGGAGGCAANNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCAACTAAAAAGAAC	1001 112926228 112926328 - 0
GCGAGGATTGAAAGAGCAGGCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGTGTCTCTGTAGGT	1002 112926848 112926919 + 0
GGCAGGCTCTGTGAAACACTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNACAAATAAGCCGTATAAAA	1003 28592612 28592705 + 0
AAGGAGCAATTAAATGTAATGTAACCTCAAGTNNNNNCTCAGTNNNNNCTCAGTNNNNNCTCAGTNNNNNCTGAGGTGG	1004 28602314 28602426 + 0
GTGGAAGG3CAGG2AACAGATGNNNNCTCAGTNNNNNCTCAGTNNNNNCTCAGTNNNNNCTGAGTACCTACCATTTGTC	1005 28608022 28608130 - 0
GCTTCAGGAGATGAAATGATGAGTCAGTNNNNNCTCAGTNNNNNCTCAGTNNNNNCTGAGTACCTACCATTTACAAACT	1006 28608200 28608360 + 0

TABLE A-continued

SmmIP	Probe List				
TCTGAGGATTCTTCCATTGGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNGAAGCAGTACAGATGGT	1.007	28608200	28608360	-	0
GCAAAAGAGTGTCACTCAGCTTCCGATATCCCACGGTAGTGTINNNNGAAGAAGATAATGAATT	1.008	28608437	28608546	+	0
CTGCTGAAACCCACTGTCCAANNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNGGGAAATTCTGATGGTGG	1.009	28609629	28609815	+	0
GCTGTCATAGATGGAAAGTTAGGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNACCCCTTATGGCTCACTC	1.010	28609629	28609815	+	0
CGITGTAAATAAGCTCATGGCTGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNAAGGCATCAATGCTTAA	1.011	28610070	28610185	+	0
GCAGATGATGGTCCGGAAAGACNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNAAGAGGATGGCTAGGCAGG	1.012	90631835	90631946	+	0
GAGATAATAAGTGGTCCCAACTGCAAGNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNGGTATGGCTTGGTCCAG	1.013	90631835	90631946	+	0
GACAGAAGCAGGGAGGAGGAGATGAGATGAGATGAGATGGGGAGGAGATGGGGT	1.014	7572925	7573012	+	0
GCTGGAAAGGCCAGGGGGANNNNNCTTCAGCTTCCGGATATCCGACGGTAGTGTINNNCAAACAAATGTAACITGAACCA	1.015	7573973	7574036	-	0
GTCIAACACTCAAATGGGNNNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNCTCACTTTATCACCTTCTTGTGC	1.016	7576850	7576934	-	0
ACCAAGGCTCATCTACTCCNNNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNCTCTCTCTGTGCGCCGGCT	1.017	7577014	7577158	+	0
CCAAGGGTGCAGTATGGCTCAAGNNNNNCTTCAGCTTCCGATATCCCACGGTAGTGTINNNNGCTTGAAGTGCTGTTGTGT	1.018	7577014	7577158	-	0
GTAGTGGATGGTGGTACAGTCAGANNNNNCTCACTCAGCTTCCGATATCCCACGGTAGTGTINNNNAGGCCAAGGAGGGCTGGG	1.019	7577495	7577613	+	0
GCGGCATGAACCGGAGGCCATNNNNCTTCAGCTTCCGGATATCCGACGGTAGTGTINNNNAAAAAAAAGGCCTCC	1.020	7577495	7577613	-	0
CCTGGGACCTGGCAACCAACNNNNNCTCACTCAGCTTCCGGATATCCGACGGTAGTGTINNNNACCAAGACCTCAGGGCTCATA	1.021	7578168	7578295	+	0
GTGAGGAGTAGGGGGCTTTCNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNAGTGGAGGAATTGGTGTGTG	1.022	7578115	7578211	-	0
GTTGAGGGCAGGGAGTACTGTAGGANNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNATGGGGCAGCGCCCT	1.023	7578364	7578560	+	0
GGGCTGGAGAGACAGACGGCTTNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNCACTGCCATCTAACAGCA	1.024	7578364	7578560	-	0
TTCCACACCCCCGGGNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNCTGCCCTCTCAGTTGCTTTATCTG	1.025	7578364	7578560	-	0
TTTCGGAAAGGGACAGAAGATGAGNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNCAAAACAAAAGAAATCAGGG	1.026	7579308	7579600	+	0
GTAGGAGGCTGCTGGTGCAGGGCCTCCNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNTAGGGACCTGGAGGGTGGG	1.027	7579308	7579600	+	0
GCATCAAATCATCCATTCGCTGGCTTGGGNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNAGAGGGGGCTGGTCAAGGG	1.028	7579443	7579523	+	0
ACCCAGGTCAGATGAAAGTCCNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNTGGGGACCTGGAGGGTGGG	1.029	7579308	7579600	-	0
AAGGGCAGGCCACACCCNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNTAGCTGGATCCCCACCTTTCT	1.030	7579812	7579915	-	0
GCCTTCCAATTGGGCTTGTGCGCCNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNGCTTCTCAGAGAATTTTAG	1.031	58740352	58740920	+	0
AAAAAATTAATCCAGAGACTCAACNNNNNCTCACTTCCGGATATCCGACGGTAGTGTINNNNCTCGAGCTATCTAGCTG	1.032	58740352	58740920	-	0

TABLE A-continued

SmmIP Probe List					
AGCTTGCAAGTCCTCCACAAACNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNNGAAGATGTCAAACCTGTGCC	1.033	58740352	58740920	+	0
CAATTTCCTCAAGTGGTCTGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNCAATTCTGGTTTCATT	1.034	58740352	58740920	-	0
GATGTTGAACCTTTAAGGGANNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNATGCAGCAGACTTGGGG	1.035	58740352	58740920	+	0
CGCTTATGTTCTCATGAGGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNGTTCCTGGTTGATGAACT	1.036	58740352	58740920	-	0
AGCTGCGCCGTCAGAACNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNGGTCCCGGGGTGGTGTGAG	1.037	74732956	74732961	+	0
TTCCTGCTCCCTGGACAACCCGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNCTCCATAAGGAAATACGCT	1.038	42531868	42531969	+	0
GGCTGCTCCTCCAGGGTGAACTGANNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNNAAGAGAACGAAA	1.039	13054525	13054730	+	0
CTTGGCCCTGCCCCGGCTGTGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNATCTTGTCTCATCATCTCCT	1.040	13054525	13054730	-	0
GCAACTGGCGTGGGGCGGGCTGTGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNCCAGGTAGTGTGAGCTG	1.041	33792300	33792469	-	0
TGACCGCTCTGGCAAAGGGGGGAGGAGGAGTGTGG	1.042	33792244	33793326	-	0
GCGGGCTCTGCTTGTATCACCGGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNCCAGGGTGGGTGG	1.043	33792674	33792865	+	0
TCAATGCCCGGGGAGCCGACGGGNNNNCTCAGCTTCCGATAATCCACCGTAGTGTNNNNNGGGTGGGTGG	1.044	33792970	3379310	-	0
GCTATGTGATGGACGCTCGTGTGNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNCTTGGCCCTTCTCTGC	1.045	33793025	33793090	+	0
GCAAGTGGCTCATCGGGGCCGNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNGTGGGGGAGCCT	1.046	33793243	33793300	+	0
GCCACCCGACAGGAGTGGGAGGAGGAGTGTGG	1.047	31021087	31021127	+	0
TCCCCATCTGCCAGGCCATCCNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNAGATCTGAAACGCCAG	1.048	31021087	31021127	+	0
CCTGGACACACAGGCCACTNNNNCTCAGCTTCCGATAATCGACGGTAGTGTNNNNTTGATCTTAGAACCCCTGCT	1.049	31021087	31021127	-	0
GAGAGGGCGCCTGCACTTNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNCCGAATTCAGGTCAGT	1.050	31021087	31021127	+	0
GCCCCGCTGGGTAGGCTTGANNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNAGGTAGGAACTGTGATCAG	1.051	31021087	31021127	-	0
CACAGCCACACTAAGGGAGCCANNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNAGGTAGGAACTGTGATCAG	1.052	31021087	31021127	+	0
CGGGGTTGAACTGGCCGCAAGGAGNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNAGGTAGGAACTGTGATCAG	1.053	31022233	31025152	+	0
GTGTGATAGTGGTAGGCGCTGTGNNNNCTCAGCTTCCGATAATCCACGGTAGTGTNNNNAGGGCGAGGTCA	1.054	31022435	31022452	+	0

TABLE A-continued

SmmIP Probe List					
GTTGGGGATCGGGGCATATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTCCGATGGCAGTGTGGGCC	1055	31022322	31022412	-	0
TGCCAGGGCTTGCCCCCTACTGTCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTCCGATGGCAGAGCT	1056	31022233	31025152	+	0
GTACACTTCAGGGGTGCTGGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTCCGATGGCAGCTGTAGTAGG	1057	31022233	31025152	-	0
GGATCCTGTAATGTGACCCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTCCGATGGCAGCACTTCTG	1058	31022233	31025152	+	0
GCAAGGCTGGCATGGCTGGTNNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNACATTGTGCGAGGAACGGTGG	1059	31022233	31025152	-	0
GTTAGTGAACAGGCCAACCAACCAGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGAGAAAGGCAATTGTGATGA	1060	31022233	31025152	+	0
GCTTGGCAGTTCTTCTCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTAATCACCTCCCTCATGGAGG	1061	31022233	31025152	-	0
GGAGACTCTGAAAGGACTATCCAAATGCAANNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGCAATGCTGGGGATTG	1062	31022233	31025152	+	0
CGATGGATGGTATCCAAATGCAANNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNAGGATCTAGACCCCTCTCAGC	1063	31022233	31025152	-	0
GTGACAGTAATGCCATTGGCTCTTCTCTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNCTTGTCACTGCACTGTCTC	1064	31022233	31025152	-	0
GGTACACTTCAAAGTCAGGGCTGGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNATGTCCCTGTAAACAGAC	1065	31022233	31025152	-	0
GTACCTTGCCCCCTAGAGAACGGTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGGTCTCGAGCTATGTGCCG	1066	31022233	31025152	+	0
GTGGGGCAAGATTGGTTCAAATGGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGGTCTGGCTGGTACTCAG	1067	31022233	31025152	-	0
GCAACTGCATCACAAAGTGGTTAGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNGCACTGTTTTCCAAGAC	1068	31022233	31025152	-	0
CCCTCCTCATCCAGTGCATAAATCCANNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTGGAGCAGCCCCAGTCTT	1069	31022233	31025152	+	10
GCAGTTCTTCCCTTTAGTTGTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGGCACTGGTGGCTCAAATCTGG	1070	31022233	31025152	+	0
GCGGGCCATGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGGCTCTGG	1071	31022233	31025152	-	0
CCTGTTTTCATCTCCAAATGTCNNNNNCTTCAGCTTCCGATATCCGACGGTAGTGTNNNNCTGGTGGCTCAAATCTGG	1072	31022233	31025152	+	0
AACCCCTTCAGGCCCCAGGCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNCCAGGAACTCTACTACCTCGAG	1073	31022233	31025152	+	0
GTGGGGTAAGACTCCAGGGAAAGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGGCAAGGAAAGGAGCTT	1074	31022233	31025152	+	0
GCCAGAAAGGAAAGGCTACTGGNNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNNTCCAGGAAAGTGGGA	1075	31022233	31025152	+	0
GAAGGGGCTCAGTAGGCCTCTGGANNNNNCTCAGCTTCCGATATCCGACGGTAGTGTNNNNAGAAAGACITTTGTGGGG	1076	31022233	31025152	+	0

TABLE A-continued

SmmIP Probe List				
CCTCTAGGCTCTCCGACCTTCTNNNNCTTCAGCTTCCGGATATCGGACGGTAGTGTNNNNCTTGCCCTCTGGAAATTACCCC	1077	31022233	31025152	+
GCAAGCACGGTGGAAAGCATCTCENNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTCAACTGAGTCCACAGCT	1078	31022233	31025152	+
GCTCTGTGTATTGTGCCGTGTGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTCAACTGAGTCCACAGCT	1079	31022233	31025152	+
GAGGTCATGGATCTCACAAAGCANNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTCAACTGAGTCCACAGCT	1080	57484402	57484481	-
GTTGGTAGAGGGGGAGCTGGCTTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTTGCGGAGGCTGGGTG	1081	36164474	36164925	+
GCGGGCCAGGCTAGGTGGTAGTGTGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNACATGGAGACTGGTAGGAG	1082	36164474	36164925	+
GTCGACCCGGCTGGGGAGTAGGTGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTTGCGAAGGCCGGTAGG	1083	36164474	36164925	+
GCGGGGGTGGAGATGGGGGGAGTAGGTGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNGGGTAGGGGGGGAGTAGG	1084	36164474	36164925	+
GCGGAAGCTGAGTAGGGGGTTGGGGAGTAGGTGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTGGGGAGTAGGTGGAGG	1085	36164474	36164925	+
GTCCAGGGAGACTAGGGTGCATGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTCATGGCTCTCCCTCTGTG	1086	36171591	36171765	-
ACGCCATTCTACCTGGAGCTGGGCTGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCATTTTAATCCACCCAC	1087	36171591	36171765	-
GAGGCAACAGGGTTCGGGCTGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNGGGTAGGGTGTGCACTGGGG	1088	36206704	36206900	+
CGGGCTTGCTGTATCATCTAGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNGGGTAAAGGAGTGGAGTGG	1089	36206704	36206900	+
GCGGCGCACAGCCATGAGGGTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTTCCCTCTCCCTCCC	1090	36206704	36206900	-
GGGCTGGTACACCTCCAGGCTTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTTCTCTCTATCGTGTCCCC	1091	36231767	36231880	-
CATCATTCGCAGCCATCACAGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNGGTTCTGCCATGAAACGFTG	1092	36252844	36253026	+
GCTGAGCTGAGAAATGCTAACCGCTCCAGGCTTNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNATCACTACACAAATGCCCTAA	1093	36252844	36253026	-
GCAGAGGAAGTTGGGGCTGTGGTGGCANNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTGTCCTCCACACCAC	1094	36255157	36259187	+
GGCAGGCCACTCCACCATGCTGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTGTCCTGTCAGGCCAGTGCG	1095	36255192	36259400	+
GCGAGTGAAGTGAATGAGACAGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTGTCCTGTCAGGCCAGTGCG	1096	44514777	44514876	-
CATGAAATAATGTCAGGAGCATGACNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCAAAACACTGGCTAAACG	1097	44524444	44524480	+
GCATGCGTGTGGAGGGAGACTGNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNATGGAGCACTGGAGAGGG	1098	15833798	15834016	+
GGCCAATAGTTGAAAATTAATCTACNNNNCTCAGCTTCCGGATATCCGGCTGTGGTNNNNCTGCGTCAAGGTCAATAGT	1099	15833798	15834016	-

TABLE A-continued

SmmIP Probe List					
AAATTCAGGAAAAAGAACCGCCNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1100	15836703	15836772	-	0
TTCCTCAATTGTCACACTGCMNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1101	15838328	15838442	+	0
GCTTCAGGTCTTGGAAAGAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1102	39911360	39911656	+	0
GTAATAATGAAAGTGGCCCAACNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1103	39911360	39911656	+	0
GTAAGGAGCTGTTAGATCTGGTGGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1104	39911360	39911656	-	0
CGTTCTCAACAGCATGGCAGAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1105	39914617	39914770	+	0
CTTATGGTGTGACCCCCACNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1106	39914617	39914770	-	0
TGCCCCAGTCCAATGCCATTGCTTGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1107	39931589	39934460	+	0
CATGTGGTAGCTGGAAAGCATCAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1108	39931589	39934460	+	0
CAGCAGGGAGGTCATATGCCCTGGCCCTGAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1109	39931589	39934460	-	0
CAGGGTTTCTCCTGGCCCTGAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1110	48649515	48649604	+	0
CAGTGAAGCTTCAATTGCAATGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1111	48649516	48649738	+	0
GCTGTTGAGGACACCAGGAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1112	48649516	48649738	-	0
GCAGCTCTGCCTTTCCGGTTGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1113	53431940	53432902	+	0
GCAGTGCCTGTCGCTTACTTTCNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1114	53431940	53432902	+	0
GCCTTCAGGTCACTGGCCCAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1115	53431940	53432902	+	0
CCAGTACTGAGCTGTGTCAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1116	53431940	53432902	+	0
GACAGGGATTGGCACAGCATANNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1117	53431940	53432902	+	0
CCTAACCTCAGGTAGTCAAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1118	53431940	53432902	+	0
GCCGCAATTGCGCTGGGCCAGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1119	53431940	53432902	-	0
GCTTTTGAGGCTGGCTAGGNNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1120	53431940	53432902	+	0
GGTCAGGGCAGTGTCAAGGGNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1121	53431940	53432902	-	0
GGCTATTGTGTGACCAACTTGGTGNNNNNCTCAGCTTCCCGATAATCGACGGTAGTGTNNNNACAGAACAGAACAAAC	1122	123181202	123181359	+	0

TABLE A-continued

SmmIP Probe List					
GGTGAACAACTAATCTAACAGACACAGACACAGATTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGCCTCATGGCTCGTTT	1123	123181202	123181359	-	0
GCAAGTTGCATATTTCGGGTGTTGTTGATTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGAATGATGGTTTTTAC	1124	123182853	123182930	+	0
AAGATGTGCCCTICAGACTGCTTCCGATATCCGACGGTAGTGTTNNNNNTATGGATCGTTTTCCTTCC	1125	123184036	123184161	+	0
CCAGTCGGTCAGGGTTAGTATTANNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGAATGAAATAATAGAG	1126	123184969	123185250	+	0
GTGCTATGACCCCTTGACAAGGNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNAGAGCTTAATTCCAAGCTGGA	1127	123184969	123185250	+	0
GCATATTGCACTAATGTTCAAGATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNCTTCTGCTTCTCTT	1128	123184969	123185250	+	0
GAAATAGGAGTAAACAGGGCTTNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNGCCTTAAAGGAAATGAGTAACAG	1129	123189975	123190088	-	0
ACCAGTGTAGTCATTAGTGGAAATGGCTTAAAGGAGACTTCCGATATCCGACGGTAGTGTTNNNNGTAAAGCTTAACAGTTTC	1130	123220395	123220624	+	0
CCACAGGTAGCAAAAGAATTGGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNAAAGGAAATAATTATATCC	1131	123220395	123220624	-	0
CCGGCAGAACAGAGACCTTGAANNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNTGTCAAGCTCAGTGAACAG	1132	133511647	133511790	+	0
GCCACTTTAAGTCTCAAGAAATGCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGCTGCACCTTCTGGTTT	1133	133511647	133511790	-	0
GCATTTCATCATCATTAAGGCTGTATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNCTACACTGTGCCATTCATG	1134	133527529	133527670	+	0
GTATGTGACTTTCAAGGCTGTATNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGTTCTCTGTATTGAGC	1135	133527529	133527670	-	0
CCACGTTAGCCCACTTTCAGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNTAGTTGCTACTAATTGTTG	1136	133527932	133527989	+	0
GGGGAGGAGAAAATGAGGACAGANNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNGAATGTTAAAGCTTGA	1137	133547847	133548010	+	0
GCTCTGGTGTCACTAGGGCTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNAAACAAAACAAAAACAAAA	1138	133547847	133548010	-	0
ATGCAGGAAATAAACATTCAGAAATCCNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNNGTTAGGAAATAGACACTGT	1139	133549044	133549153	-	0
GACTGCAAAGTGTACATTTCTGNNNNCTCAGCTTCCGATATCCGACGGTAGTGTTNNNNITAGGAAATAGACACTGT	1140	133551219	133551319	-	0

## REFERENCE LIST

- [0137] 1. Diepen S Van, Katz J N, Albert N M, Henry T D, Jacobs A K, Kapur N K, Kilic A, Menon V, Ohman E M, Sweitzer N K, Thiele H, Washam J B, Cohen M G. Contemporary Management of Cardiogenic Shock: A Scientific Statement from the American Heart Association. *Circulation*.
- [0138] 2. Helgestad O K L, Josiassen J, Hassager C, Jensen L O, Holmvang L, Sørensen A, Frydland M, Lassen A T, Udesen N L J, Schmidt H, Ravn H B, Møller J E. Temporal trends in incidence and patient characteristics in cardiogenic shock following acute myocardial infarction from 2010 to 2017: a Danish cohort study. *Eur J Heart Fail* 2019; 21; (11):1370-1378.
- [0139] 3. Jentzer J C, Lawler P R, Diepen S Van, Henry T D, Menon V, Baran D A, Džavík V, Barsness G W, Holmes D R, Kashani K B. Systemic Inflammatory Response Syndrome Is Associated With Increased Mortality Across the Spectrum of Shock Severity in Cardiac Intensive Care Patients. *Circ Cardiovasc Qual Outcomes* 2020; 13; (12):1033-1045.
- [0140] 4. Andrié R P, Becher U M, Frommold R, Tiyerili V, Schrickel J W, Nickenig G, Schwab J O. Interleukin-6 is the strongest predictor of 30-day mortality in patients with cardiogenic shock due to myocardial infarction. *Crit Care* 2012; 16; (4).
- [0141] 5. Jaiswal S, Fontanillas P, Flannick J, Manning A, Grauman P V, Mar B G, Lindsley R C, Mermel C H, Burt N, Chavez A, Higgins J M, Moltchanov V, Kuo F C, Kluk M J, Henderson B, Kinnunen L, Koistinen H A, Ladenvall C, Getz G, Correa A, Banahan B F, Gabriel S, Kathiresan S, Stringham H M, McCarthy M I, Boehnke M, Tuomilehto J, Haiman C, Groop L, Atzmon G, Wilson J G, Neuberg D, Altshuler D, Ebert B L. Age-related clonal hematopoiesis associated with adverse outcomes. *N Engl J Med* 2014; 371; (26):2488-2498.
- [0142] 6. Acuna-Hidalgo R, Sengul H, Steehouwer M, Vorst M van de, Vermeulen S H, Kiemeney L A L M, Veltman J A, Gilissen C, Hoischen A. Ultra-sensitive sequencing identifies high prevalence of clonal hematopoiesis-associated mutations throughout adult life. *Am J Hum Genet* 2017; 101; (1):50-64.
- [0143] 7. Young A L, Challen G A, Birnbaum B M, Druley T E. Clonal haematopoiesis harbouring AML-associated mutations is ubiquitous in healthy adults. *Nat Commun* 2016; 7:12484.
- [0144] 8. Genovese G, Kähler A K, Handsaker R E, Lindberg J, Rose S A, Bakhoum S F, Chambert K, Mick E, Neale B M, Fromer M, Purcell S M, Svantesson O, Landen M, Hoglund M, Lehmann S, Gabriel S B, Moran J L, Lander E S, Sullivan P F, Sklar P, Grönberg H, Hultman C M, McCarron S A. Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence. *N Engl J Med* 2014; 371; (26):2477-2487.
- [0145] 9. Dorsheimer L, Assmus B, Rasper T, Ortmann C A, Ecke A, Abou-El-Ardat K, Schmid T, Brune B, Wagner S, Serve H, Hoffmann J, Seeger F, Dimmeler S, Zeiher A M, Rieger M A. Association of mutations contributing to clonal hematopoiesis with prognosis in chronic ischemic heart failure. *JAMA Cardiol* 2019; 4; (1):25-33.
- [0146] 10. Jaiswal S, Natarajan P, Silver A J, Gibson C J, Bick A G, Shvartz E, McConkey M, Gupta N, Gabriel S, Ardissino D, Baber U, Mehran R, Fuster V, Danesh J, Frossard P, Saleheen D, Melander O, Sukhova G K, Neuberg D, Libby P, Kathiresan S, Ebert B L. Clonal hematopoiesis and risk of atherosclerotic cardiovascular disease. *N Engl J Med* 2017; 377; (2):111-121.
- [0147] 11. Jaiswal S, Libby P. Clonal haematopoiesis: connecting ageing and inflammation in cardiovascular disease. *Nature Reviews Cardiology*.
- [0148] 12. Yu B, Roberts M B, Raffield L M, Zekavat S M, Nguyen NQH, Biggs M L, Brown M R, Griffin G, Desai P, Correa A, Morrison A C, Shah A M, Niroula A, Uddin M M, Honigberg M C, Ebert B L, Psaty B M, Whitsel E A, Manson JAE, Kooperberg C, Bick A G, Ballantyne C M, Reiner A P, Natarajan P, Eaton C B. Supplemental association of clonal hematopoiesis with incident heart failure. *J Am Coll Cardiol* 2021; 78; (1):42-52.
- [0149] 13. Sano S, Oshima K, Wang Y, Katanasaka Y, Sano M, Walsh K. CRISPR-mediated gene editing to assess the roles of TET2 and DNMT3A in clonal hematopoiesis and cardiovascular disease. *Circ Res* 2018; 123; (3):335-341.
- [0150] 14. Baran D A, Grines C L, Bailey S, Burkhoff D, Hall S A, Henry T D, Hollenberg S M, Kapur N K, O'Neill W, Ornato J P, Stelling K, Thiele H, Diepen S, Naidu S S. SCAI clinical expert consensus statement on the classification of cardiogenic shock. *Catheter Cardiovasc Interv* 2019; 94; (1):29-37.
- [0151] 15. Medeiros J J F, Capo-Chichi J-M, Shlush L I, Dick J E, Arruda A, Minden M D, Abelson S. SmMIP-tools: a computational toolset for processing and analysis of single-molecule molecular inversion probes derived data 2. *bioRxiv* 2021:2021.06.03.446993.
- [0152] 16. Pascual-Figal D A, Bayes-Genis A, Diez-Diez M, Hernández-Vicente Á, Vázquez-Andrés D, la Barrera J de, Vázquez E, Quintas A, Zuriaga M A, Asensio-López M C, Dopazo A, Sánchez-Cabo F, Fuster J J. Clonal hematopoiesis and risk of progression of heart failure with reduced left ventricular ejection fraction. *J Am Coll Cardiol* 2021; 77; (14):1747-1759.
- [0153] 17. Watson C J, Papula A L, Poon GYP, Wong W H, Young A L, Druley T E, Fisher D S, Blundell J R. The evolutionary dynamics and fitness landscape of clonal hematopoiesis. *Science* (80-) 2020; 367; (6485):1449-1454.
- [0154] 18. Abdel-Wahab O, Adli M, LaFave L M, Gao J, Hricik T, Shih A H, Pandey S, Patel J P, Chung Y R, Koche R, Perna F, Zhao X, Taylor J E, Park C Y, Carroll M, Melnick A, Nimer S D, Jaffe J D, Aifantis I, Bernstein B E, Levine R L. ASXL1 mutations promote myeloid transformation through loss of PRC2-mediated gene repression. *Cancer Cell* 2012; 22; (2):180-193.
- [0155] 19. Assmus B, Cremer S, Kirschbaum K, Culmann D, Kiefer K, Dorsheimer L, Rasper T, Abou-El-Ardat K, Herrmann E, Berkowitsch A, Hoffmann J, Seeger F, Mas-Peiro S, Rieger M A, Dimmeler S, Zeiher A M. Clonal haematopoiesis in chronic ischaemic heart failure: prognostic role of clone size for DNMT3A- and TET2-driver gene mutations. *Eur Heart J* 2021; 42; (3):257-265.
- [0156] 20. Geppert A, Dorninger A, Delle-Karth G, Zorn G, Heinz G, Huber K. Plasma concentrations of interleukin-6, organ failure, vasopressor support, and successful coronary revascularization in predicting 30-day mortality of patients with cardiogenic shock complicating acute myocardial infarction. *Crit Care Med* 2006; 34; (8):2035-2042.

- [0157] 21. Heeschen C, Dimmeler S, Hamm C W, Brand M J van den, Boersma E, Zeiher A M, Simoons M L. Soluble CD40 ligand in acute coronary syndromes. *N Engl J Med* 2003; 348; (12):1104-1111.
- [0158] 22. Shami A, Edsfeldt A, Bengtsson E, Nilsson J, Shore A C, Natali A, Khan F, Lutgens E, Gonçalves I. Soluble CD40 levels in plasma are associated with cardiovascular disease and in carotid plaques with a vulnerable phenotype. *J Stroke* 2021; 23; (3):367-376.
- [0159] 23. Milner J D, Orekov T, Ward J M, Cheng L, Torres-Velez F, Juntila I, Sun G, Buller M, Morris S C, Finkelman F D, Paul W E. Sustained IL-4 exposure leads to a novel pathway for hemophagocytosis, inflammation, and tissue macrophage accumulation. *Blood* 2010; 116; (14):2476-2483.
- [0160] 24. Qin Y, Zhang C. The regulatory role of IFN- $\gamma$  on the proliferation and differentiation of hematopoietic stem and progenitor cells. *Stem cell Rev reports* 2017; 13; (6):705-712.
- [0161] 25. Baldridge M T, King K Y, Boles N C, Weksberg D C, Goodell M A. Quiescent haematopoietic stem cells are activated by IFN-gamma in response to chronic infection. *Nature* 2010; 465; (7299):793-797.
- [0162] 26. Agarwal P, Li H, Choi K, Hueneman K, He J, Welner R S, Starczynowski D T, Bhatia R. TNF- $\alpha$ -induced alterations in stromal progenitors enhance leukemic stem cell growth via CXCR2 signaling. *Cell Rep* 2021; 36; (2):109386.
- [0163] 27. Abegunde S O, Buckstein R, Wells R A, Rauh M J. An inflammatory environment containing TNF $\alpha$  favors Tet2-mutant clonal hematopoiesis. *Exp Hematol* 2018; 59:60-65.
- [0164] 28. Broek I Vande, Asosingh K, Vanderkerken K, Straetmans N, Camp B Van, Riet I Van. Chemokine receptor CCR2 is expressed by human multiple myeloma cells and mediates migration to bone marrow stromal cell-produced monocyte chemotactic proteins MCP-1, -2 and -3. *Br J Cancer* 2003; 88; (6):855-862.
- [0165] 29. Bick A G, Pirruccello J P, Griffin G K, Gupta N, Gabriel S, Saleheen D, Libby P, Kathiresan S, Natarajan P. Genetic interleukin 6 signaling deficiency attenuates cardiovascular risk in clonal hematopoiesis. *Circulation* 2020; 141; (2):124-131.
- [0166] s1. Mehra M R, Canter C E, Hannan M M, et al. The 2016 International Society for Heart Lung Transplantation listing criteria for heart transplantation: A 10-year update. *J Heart Lung Transplant*. 2016; 35(1):1-23. doi: 10.1016/j.healun.2015.10.023
- [0167] s2. Organ Transplant|US Organ Donation System|UNOS. Accessed Jan. 27, 2022. <https://unos.org/transplant/>
- [0168] s3. Khush K K, Cherikh W S, Chambers D C, et al. The International Thoracic Organ Transplant Registry of the International Society for Heart and Lung Transplantation: Thirty-sixth adult heart transplantation report—2019; focus theme: Donor and recipient size match. *J Heart Lung Transplant*. 2019; 38(10):1056-1066. doi: 10.1016/j.healun.2019.08.004
- [0169] s4. Costanzo M R, Force T, Rosa M, et al. The International Society of Heart and Lung Transplantation Guidelines for the care of heart transplant recipients. *J Heart Lung Transplant*. 2010; 29(8):914-956. doi: 10.1016/j.healun.2010.05.034
- [0170] s5. Kittleson M M, Kobashigawa J A. Long-term care of the heart transplant recipient. *Curr Opin Organ Transplant*. 2014; 19(5):515-524. doi:10.1097/MOT.0000000000000117
- [0171] s6. Giarraputo A, Barison I, Fedrigo M, et al. A changing paradigm in heart transplantation: An integrative approach for invasive and non-invasive allograft rejection monitoring. *Biomolecules*. 2021; 11(2):1-17. doi:10.3390/biom11020201
- [0172] s7. Jaiswal S, Fontanillas P, Flannick J, et al. Age-related clonal hematopoiesis associated with adverse outcomes. *N Engl J Med*. 2014; 371(26):2488-2498. doi:10.1056/NEJMoa1408617
- [0173] s8. Jaiswal S, Natarajan P, Silver A J, et al. Clonal hematopoiesis and risk of atherosclerotic cardiovascular disease. *N Engl J Med*. 2017; 377(2):111-121. doi:10.1056/NEJMoa1701719
- [0174] s9. Bhattacharya R, Zekavat S M, Haessler J, et al. Clonal hematopoiesis is associated with higher risk of stroke. *Stroke*. 2020; 53(3):788-797. doi:10.1161/strokeaha.121.037388
- [0175] s10. Dorsheimer L, Assmus B, Rasper T, et al. Association of mutations contributing to clonal hematopoiesis with prognosis in chronic ischemic heart failure. *JAMA Cardiol*. 2019; 4(1):25-33. doi:10.1001/jamacardio.2018.3965
- [0176] s11. Bolton K L, Koh Y, Foote M B, et al. Clonal hematopoiesis is associated with risk of severe Covid-19. *Nat Commun*. 2021; 12(1):5975. doi:10.1038/s41467-021-26138-6
- [0177] s12. Genovese G, Kähler A K, Handsaker R E, et al. Clonal hematopoiesis and blood-cancer risk inferred from blood DNA sequence. *N Engl J Med*. 2014; 371 (26):2477-2487. doi:10.1056/NEJMoa1409405
- [0178] s13. Dawoud A A Z, Gilbert R D, Tapper W J, Cross N C P. Clonal myelopoiesis promotes adverse outcomes in chronic kidney disease. *Leukemia*. 2022; 36(2):507-515. doi:10.1038/s41375-021-01382-3
- [0179] s14. Pascual-Figal D A, Bayes-Genis A, Diez-Diez M, et al. Clonal hematopoiesis and risk of progression of heart failure with reduced left ventricular ejection fraction. *J Am Coll Cardiol*. 2021; 77(14):1747-1759. doi:10.1016/j.jacc.2021.02.028
- [0180] s15. Sano S, Oshima K, Wang Y, Katanasaka Y, Sano M, Walsh K. CRISPR-mediated gene editing to assess the roles of TET2 and DNMT3A in clonal hematopoiesis and cardiovascular disease. *Circ Res*. 2018; 123(3):335-341. doi:10.1161/CIRCRESAHA.118.313225
- [0181] s16. Medeiros J J F, Capo-Chichi J-M, Shlush L I, et al. SmMIP-tools: a computational toolset for processing and analysis of single-molecule molecular inversion probes-derived data. *Bioinformatics*. 2022; 38(8):2088-2095. doi:10.1093/bioinformatics/btac081
- [0182] s17. Jaiswal S, Libby P. Clonal haematopoiesis: connecting ageing and inflammation in cardiovascular disease. *Nat Rev Cardiol*. 2020; 17(3):137-144. doi:10.1038/s41569-019-0247-5
- [0183] s18. Sano S, Oshima K, Wang Y, et al. TET2-mediated clonal hematopoiesis accelerates heart failure through a mechanism involving the IL-1 $\beta$ /NLRP3 inflammasome. *J Am Coll Cardiol*. 2018; 71(8):875-886. doi: 10.1016/j.jacc.2017.12.037

- [0184] s19. Sano S, Wang Y, Yura Y, et al. JAK2-V617F-Mediated clonal hematopoiesis accelerates pathological remodeling in murine heart failure. *JACC Basic Transl Sci.* 2019; 4(6):684-697. doi: 10.1016/j.jactbs.2019.05.013
- [0185] s20. Sano S, Wang Y, Ogawa H, et al. TP53-mediated therapy-related clonal hematopoiesis contributes to doxorubicin-induced cardiomyopathy by augmenting a neutrophil-mediated cytotoxic response. *JCI Insight.* 2021; 6 (13): e146076. doi: 10.1172/jci.insight.146076
- [0186] s21. Yura Y, Miura-Yura E, Katanasaka Y, et al. The Cancer Therapy-Related Clonal Hematopoiesis Driver Gene Ppm1d Promotes Inflammation and Non-Ischemic Heart Failure in Mice. *Circ Res.* 2021; 129(6):684-698. doi: 10.1161/CIRCRESAHA.121.319314
- [0187] s22. Fuster J J, MacLauchlan S, Zuriaga M A, et al. Clonal hematopoiesis associated with TET2 deficiency accelerates atherosclerosis development in mice. *Science.* 2017; 355(6327): 842-847. doi: 10.1126/science.aag1381
- [0188] s23. Nikolova A P, Kobashigawa J A. Cardiac Allograft Vasculopathy: The enduring enemy of cardiac transplantation. *Transplantation.* 2019; 103(7): 1338-1348. doi: 10.1097/TP.00000000000002704
- [0189] s24. Chih S, Chong A Y, Mielniczuk L M, Bhatt D L, Beanlands R S B. Allograft vasculopathy: the achilles' heel of heart transplantation. *J Am Coll Cardiol.* 2016; 68 (1):80-91. doi:10.1016/J.JACC.2016.04.033
- [0190] s25. Lee F, Nair V, Chih S. Cardiac allograft vasculopathy: Insights on pathogenesis and therapy. *Clin Transplant.* 2020; 34(3):e13794. doi:10.1111/ctr.13794
- [0191] s26. Fahmy N M, Yamani M H, Starling R C, et al. Chemokine and chemokine receptor gene expression indicates acute rejection of human cardiac transplants. *Transplantation.* 2003; 75(1):72-78. doi:10.1097/00007890-200301150-00013
- [0192] s27. Tarazon E, Corbacho-Alonso N, G. Barderas M, et al. Plasma CD5L and non-invasive diagnosis of acute heart rejection. *J Heart Lung Transplant.* 2020; 39(3):257-266. doi:10.1016/J.HEALUN.2019.11.004
- [0193] s28. Jones I K A, Orloff S, Burg J M, et al. Blocking the IL-1 receptor reduces cardiac transplant ischemia and reperfusion injury and mitigates CMV-accelerated chronic rejection. *Am J Transplant.* 2021; 21(1):44-59. doi:10.1111/ajt.16149
- [0194] s29. Alyaydin E, Welp H, Reinecke H, Tuleta I. Predisposing factors for late mortality in heart transplant patients. *Cardiol J.* 2021; 28(5):746-757. doi:10.5603/CJ.A2020.0011
- [0195] s30. Newell L F, Dunlap J, Gatter K, et al. Graft-versus-host disease after liver transplantation is associated with bone marrow failure, hemophagocytosis, and DNMT3A mutations. *Am J Transplant.* 2021; 21(12): 3894-3906.
1. A method of predicting the risk of a disease condition of a solid organ in a patient, the method comprising:
- receiving a sample from the patient containing hematopoietic stem cells;
  - sequencing the sample to detect a degree of clonal hematopoiesis;
  - comparing the degree of clonal hematopoiesis in the patient to a control degree; and
  - determining the patient is at an elevated risk of the disease condition if the degree of clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner.
2. The method of claim 1, wherein the degree of clonal hematopoiesis is measured using a variant allele frequency of mutations determined to be associated with clonal hematopoiesis.
3. The method of claim 2, wherein the variant allele frequency (VAF) is  $\geq 2\%$ .
4. The method of claim 3 wherein the VAF is  $\geq 5\%$ .
5. The method of claim 1, wherein the following genes are sequenced in the sample: TET2, DNMT3A, and ASXL1, and optionally one or more of, but preferably all of, BCOR, BRAF, CALR, CBL, CEBPA, EZH2, FLT3A, GATA1, GATA2, GNAS, IDH1, IDH2, JAK2, KIT, KRAS, MPL, NRAS, PHF6, PPM1D, PTPN11, RAD21, RUNX1, SETBP1, SF3B1, SMC1A, SMC3, SRSF2, STAG2, TP53, U2AF1, WT1, and ZRSR2.
6. The method of claim 1, wherein the sequencing is performed using single-molecule molecular inversion probes (smMIPs).
7. The method of claim 2, wherein the mutations associated with clonal hematopoiesis are detectable by the probes listed in Table A.
8. The method of claim 2, wherein the mutations associated with clonal hematopoiesis are detected using a library comprising at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.
9. (canceled)
10. (canceled)
11. (canceled)
12. The method of claim 1, wherein the solid organ is a heart.
13. The method of claim 12, wherein the disease condition is cardiogenic shock.
14. The method of claim 13, wherein an elevated risk of cardiogenic shock is associated with an elevated risk of death.
15. The method of claim 13, further comprising treating or preventatively treating the patient for cardiogenic shock.
16. The method of claim 12, wherein the disease condition is an adverse outcome after orthotopic heart transplant (OHT).
17. The method of claim 16, wherein the adverse outcome is an elevated risk of mortality and/or elevated risk of cardiac allograft vasculopathy.
18. The method of claim 17, further comprising treating or preventatively treating the patient for cardiac allograft vasculopathy.
19. The method of claim 12, wherein the disease condition is hypertrophic cardiomyopathy.
20. The method of claim 19, further comprising treating or preventatively treating the patient for hypertrophic cardiomyopathy.
21. The method of claim 1, wherein the solid organ is a lung.
22. The method of claim 21, wherein the disease condition is an adverse outcome, including death, after lung transplant.
23. The method of claim 22, further comprising treating or preventatively treating the patient for the adverse outcome after lung transplant.

**24.** A kit comprising a library of probes library comprising at least 50%, 60%, 70%, 80%, 90%, 95%, 98% or 99% of the probes listed in Table A.

**25.** (canceled)

**26.** (canceled)

**27.** (canceled)

**28.** A method of predicting the benefit of immunotherapy in a patient with melanoma, the method comprising:

- a) receiving a sample from the patient containing hematopoietic stem cells;
- b) sequencing the sample to detect a degree of clonal hematopoiesis in TET2;
- c) comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and
- d) determining the patient would benefit from immunotherapy if the degree of TET2 clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner.

**29.** The method of claim **28**, further comprising treating the patient with immunotherapy.

**30.** A method of predicting metastatic risk in a patient with a non-hematological cancer, the method comprising:

- a) receiving a sample from the patient containing hematopoietic stem cells;
- b) sequencing the sample to detect a degree of clonal hematopoiesis in TET2;
- c) comparing the degree of TET2 clonal hematopoiesis in the patient to a control degree; and
- d) determining the patient is at a lower risk of metastasis if the degree of TET2 clonal hematopoiesis in the patient is higher than the control degree in a statistically significant manner.

**31.** The method of claim **30**, further comprising treating the patient with a treatment and monitoring regimen reflective of a low risk of metastasis.

\* \* \* \* \*