BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors.
Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: Shah, Sohrab

eRA COMMONS USER NAME (credential, e.g., agency login): s_shah

POSITION TITLE: Associate Professor, Department of Pathology & Laboratory Medicine, University of British Columbia; Scientist, Molecular Oncology, BC Cancer Agency

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Queen's University, Kingston ON, Canada	B.Sc.	05/1996	Biology
University of British Columbia, Vancouver BC, Canada	B.Sc.	05/2001	Computer Science
University of British Columbia, Vancouver BC, Canada	M.Sc.	05/2005	Computer Science (Bioinformatics)
University of British Columbia, Vancouver BC, Canada	Ph.D.	11/2008	Computer Science (Bioinformatics)
University of British Columbia, Vancouver BC, Canada	PDF	10/2010	

A. Personal Statement

Dr. Shah received a PhD in computer science from UBC in 2008 and was appointed as a Principal Investigator to The BC Cancer Agency and the University of British Columbia in 2010. He holds the Canada Research Chair in Computational Cancer Genomics, and is the recipient of both a Michael Smith Foundation for Health Research Career Investigator Award and a Terry Fox Research Institute New Investigator Award. His research focuses on understanding how tumours evolve over time through integrative approaches involving genomics and computational modeling. He has made seminal contributions to understanding of clonal evolution in ovarian cancer[1,2] and discovered that specific mutational patterns in the genomes of ovarian cancers are prognostic in terms of treatment outcomes[3]. Dr. Shah has also pioneered computational methods for inference of mutations in cancer genomes as well as deciphering patterns of cancer evolution. He has led development of novel Bayesian statistical models, algorithms, and computational approaches to analyze large, high dimensional genomics and transcriptomic data sets, from both patient tumours and model systems. This includes advancing molecular profiling of cancer cells at single cell resolution[4]. Dr. Shah has been at the forefront of studying tumor evolution in breast, ovary and lymphoid malignancies. His work has been published in Nature[5], Nature Genetics, Nature Methods[6], NEJM, Genome Research, Genome Biology, amongst others. Dr. Shah oversees an annual budget of >$1M in competitively awarded funding from philanthropic, government and international bodies.

1. Bashashati A, Ha G, Tone A, Ding J, Prentice LM, Roth A, Rosner J, Shumansky K, Kalloger S, Senz J, Yang W, McConechy M, Melnyk N, Anglesio M, Luk MT, Tse K, Zeng T, Moore R, Zhao Y, Marra MA, Gilks B, Yip S, Huntsman DG, McAlpine JN, **Shah SP**. Distinct evolutionary trajectories of primary high-grade serous ovarian cancers revealed through spatial mutational profiling. *J Pathol*. 2013 Sep;231(1):21-34. doi: 10.1002/path.4230. PubMed PMID: 23780408
2. McPherson A, Roth A, Laks E, Masud T, Bashashati A, Zhang AW, Ha G, Biele J, Yap D, Wan A, Prentice L, Khattra J, Mullaly SC, Kalloger S, Karnezis A, Shumansky K, Siu C, Rosner J, Chan HL, Ho J, Melnyk N, Senz J, Yang W, Moore R, Mungall A, Marra MA, Bouchard-Cote A, Gilks CB, Huntsman DG, McAlpine J, Aparicio S, **Shah SP**. Divergent Modes of Clonal Spread and Intraperitoneal Mixing in High-Grade Serous Ovarian Cancer. *Nat Genetics*. 2016; 48(7):758-67. doi:10.1038/ ng.3573
3. Wang YK, Bashashati A, Anglesio MS, Cochrane DR, Grewal D, Ha G, McPherson A, Horlings HM, Senz J, Prentice LM, Karnezis, Anthony N, Lai D, Aniba MR, Zhang AW, Shumansky K, Siu C, Wan A,

McConechy MK, Li-Chang H, Tone A, Provencher D, de Ladurantaye M, Fleury H, Okamoto A, Yanagida S, Yanaihara N, Saito M, Mungall AJ, Moore R, Marra MA, Gilks CB, Mes-Masson A, McAlpine JN, Aparicio S, Huntsman DG and **Shah SP**. Genomic consequences of aberrant DNA repair mechanisms stratify ovarian cancer histotypes. *Nature Genetics*. 2017 Jun;49(6):856-865. doi: 10.1038/ng.3849

4. Zahn H, Steif A, Laks E, Eirew P, VanInsberghe M, **Shah SP**, Aparicio S, Hansen CL. Scalable whole-genome single-cell library preparation without preamplification. *Nature Methods*. 2017:14(2):167–73. doi:10.1038/nmeth.4140
5. Eirew P, Steif A, Khattra J*, Ha G, Yap D, Farahani H, Gelmon K, Chia S, Mar C, Wan A, Laks E, Biele J, Shumansky K, Rosner J, McPherson A, Nielsen C, Roth AJL, Lefebvre C, Bashashati A, de Souza C, Siu C, Aniba R, Brimhall J, Oloumi A, Osako T, Bruna A, Sandoval J, Algara T, Greenwood W, Leung K, Cheng H, Xue H, Wang Y, Lin D, Mungall A, Moore R, Zhao Y, Lorette J, Nguyen L, Huntsman D, Eaves CJ, Hansen C, Marra MA, Caldas C, **Shah SP**, Aparicio S. Dynamics of genomic clones in breast cancer patient xenografts at single-cell resolution. *Nature.* 2015 Feb 19;518(7539):422-6. doi: 10.1038/nature13952.
6. Roth A, McPherson A, Laks E, Biele J, Yap D, Wan A, McAlpine JN, Aparicio S, Bouchard-Cote A, **Shah SP**. Clonal genotype and population structure inference from single-cell tumor sequencing. *Nature Methods.* 2016;13(7):573-576. doi:10.1038/nmeth.3867

B. Positions and Honors

Positions and Employment

2000-2002	Bioinformatics software developer, CMMT, UBC, Vancouver, BC
2002-2004	Chief, High throughput bioinformatics, UBC
2002-	Instructor, Canadian Bioinformatics Workshops Series
2005-2008	Research Assistant, UBC Department of Computer Science
2006-2009	Instructor, Interprofessional Health and Human Services, UBC
2008-2010	Postdoctoral Research Fellow, BC Cancer Agency
2010-2014	Assistant Professor, Department of Pathology and Laboratory Medicine, UBC
2010-	Scientist, Molecular Oncology and Breast Cancer Research Program, BC Cancer Agency
2010-	Associate Member, UBC Dept of Computer Science
2013-	Faculty Member, Genome Science and Technology Graduate Program
2013-	Associate Member, Genome Sciences Centre
2013- 2019	Adjunct Professor, SFU School of Computing Science
2015-	Associate Professor, UBC Dept of Pathology and Laboratory Medicine

Honors

2006-2008	Senior Graduate Trainee Award; Michael Smith Foundation For Health Research
2006-2009	University Graduate Fellowship (declined); UBC, Canada; $48,000
2007	International Society for Computational Biology Travel Fellowship to ISMB 2007
2008	Student Service Award; Department of Computer Science, UBC
2008-2011	Postdoctoral Fellowship; Michael Smith Foundation For Health Research, $120,000/3yrs
2008-2011	Canadian Breast Cancer Foundation Bioinformatics Fellowship; part of $500,000 over 5yrs to Dr. Sam Aparicio
2009-2011	Research Fellowship; Eli Lilly, $130,000 over 2yrs
2009	International Society for Computational Biology Travel Fellowship to ISMB 2009
2010	Lap-Chee Tsui Publication Award; from the Canadian Institutes for Health Research Institute of Genetics in recognition of outstanding published health research carried out by trainees, for the discovery of the mutation in FOXL2 in granulosa cell tumors of the ovary (published in NEJM);
2011-2019	MSFHR Career Investigator Award; $635,000 (over 8 years)
2012	Associate member of the Peter Wall Institute of Advanced Studies
2012-2015	Terry Fox New Investigator Award (TFRI); Are genomic instability and clonal diversity prognostic indicators of high grade serous ovarian cancer?; $449,503
2013	Distinguished Achievement Award for Overall Excellence – Early Career. Fac. of Med UBC
2013-2018	Canada Research Chair (Tier 2) in Computational Cancer Genomics
2015	Award for Early Career Excellence in Research and Discovery. UBC Dept. of Pathology
2016	UBC Killam Research Prize. Applied Science, Junior Category

C. Contributions to Science (*corresponding author, #first author)

1. Cancer Genomics My research Program has driven discovery and computational model development in cancer genomics and tumour evolution with significant progress in breast, ovary and lymphoid cancers. This has led to recognition locally, nationally and internationally. My program of research focuses on evolutionary dynamics of cancers using a combination of genomics and statistical modeling of tumour progression. Since 2010, I have raised more than $8.4M (my portion) in competitive grant funding to support this work, and my papers have been cited 7469 times (Google Scholar, h-index: 35, i-index: 52). My work has produced 7 first/senior/corresponding author contributions in NEJM, Nature, Nat Methods.

2. Clonal Evolution in Solid Cancers My research as resulted in several world firsts including the determination of tumour evolution demonstrated at nucleotide resolution in a lobular breast cancer (Shah et al, Nature 2009#), the first description of the mutational landscape and clonal evolution in a population of triple negative breast cancers[a], establishing reproducible patterns of clonal dynamics in patient derived xenografts[b] and quantifying the degree of clonal diversity in primary untreated HGS ovarian cancers[c]**.** My lab led the data analysis of the METABRIC project, leading to the most precise characterization of prognostically significant molecular subtypes of breast cancer, establishing a new standard in the field of breast cancer patient stratification[d]. Studying evolution in cancer has exploded in recent years in the field. The lobular breast cancer paper has been cited 718 times since 2009 and the triple negative breast cancer work has been cited 655 times since 2012.
    a. **Shah SP***, et al, Caldas C*, Marra MA*, Aparicio S*. The clonal and mutational evolution spectrum of primary triple-negative breast cancers. *Nature* 2012 Apr 4;486(7403):395-9. (*co-corresponding authors)
    b. Eirew P*, Steif A*, Khattra J*, et al, **Shah SP****, Aparicio S**. Dynamics of genomic clones in breast cancer patient xenografts at single-cell resolution. *Nature*. 2015 Feb 19;518(7539):422-6. doi: 10.1038/nature13952. ** - corresponding author; * denotes equal contribution
    c. Curtis C*, **Shah SP***, et al, Caldas C, Aparicio S. The genomic and transcriptomic architecture of 2,000 breast tumours reveals novel subgroups. *Nature* 2012 Apr 18;486(7403):346-52. (* equal contribution)
    d. McPherson A, Roth A, Laks E, Masud T, Bashashati A, Zhang AW, Ha G, Biele J, Yap D, Wan A, Prentice L, Khattra J, Mullaly SC, Kalloger S, Karnezis A, Shumansky K, Siu C, Rosner J, Chan HL, Ho J, Melnyk N, Senz J, Yang W, Moore R, Mungall A, Marra MA, Bouchard-Cote A, Gilks CB, Huntsman DG, McAlpine J, Aparicio S, **Shah SP**. Divergent Modes of Clonal Spread and Intraperitoneal Mixing in High-Grade Serous Ovarian Cancer. *Nat Genetics.* 2016; 48(7):758-67. doi:10.1038/ ng.3573

3. Discovery of New Cancer Genes My work has identified 3 new cancer genes: FOXL2[a], ARID1A[b] and CIITA[c]**.** This series of papers describes discoveries of novel, somatic, recurrent alterations in ovarian cancers and lymphomas. These studies represent single gene discoveries associated with cancer subtypes that had not previously been implicated in disease progression. FOXL2 has led to new class of diagnostics for granulosa cells of the ovary, while ARID1A has opened up the study of chromatin remodeling as a disrupted process in cancer biology. Additional collaborative efforts with Drs. Marra, Gascoyne, Jones have led to the discovery of EZH2 mutations in follicular and diffuse large B cell lymphomas, and PTPN1 mutations in B cell lymphomas.
    a. **Shah SP**, Köbel M, Senz J, Morin RD, Clarke BA, Wiegand KC, Leung G, Zayed A, Mehl E, Kalloger SE, Sun M, Giuliany R, Yorida E, Jones S, Varhol R, Swenerton KD, Miller D, Clement PB, Crane C, Madore J, Provencher D, Leung P, DeFazio A, Khattra J, Turashvili G, Zhao Y, Zeng T, Glover JN, Vanderhyden B, Zhao C, Parkinson CA, Jimenez-Linan M, Bowtell DD, Mes-Masson AM, Brenton JD, Aparicio SA, Boyd N, Hirst M, Gilks CB, Marra M, Huntsman DG. Mutation of FOXL2 in granulosa-cell tumors of the ovary. N Engl J Med. 2009 Jun 25;360(26):2719-29.
    b. Wiegand KC, **Shah SP**, Al-Agha OM, Zhao Y, Tse K, Zeng T, Senz J, McConechy MK, Anglesio MS, Kalloger SE, Yang W, Heravi-Moussavi A, Giuliany R, Chow C, Fee J, Zayed A, Prentice L, Melnyk N, Turashvili G, Delaney AD, Madore J, Yip S, McPherson AW, Ha G, Bell L, Fereday S, Tam A, Galletta L, Tonin PN, Provencher D, Miller D, Jones SJ, Moore RA, Morin GB, Oloumi A, Boyd N, Aparicio SA, Shih IeM, Mes-Masson AM, Bowtell DD, Hirst M, Gilks B, Marra MA, Huntsman DG. ARID1A mutations in endometriosis-associated ovarian carcinomas. N Engl J Med. 2010 Oct 14;363(16):1532-43.
    c. Steidl C*, **Shah SP***, Woolcock BW, Rui L, Kawahara M, Farinha P, Johnson NA, Zhao Y, Telenius A, Neriah SB, McPherson A, Meissner B, Okoye UC, Diepstra A, van den Berg A, Sun M, Leung G,

Jones SJ, Connors JM, Huntsman DG, Savage KJ, Rimsza LM, Horsman DE, Staudt LM, Steidl U, Marra MA, Gascoyne RD. MHC class II transactivator CIITA is a recurrent gene fusion partner in lymphoid cancers. Nature 2011 Mar 17;471(7338):377-81. *Equal contribution.

4. Computational methods for cancer genome interpretation My lab has developed several leading edge statistical and computational approaches for analysis and interpretation of cancer genomes. These include ReMixT[a] for clone-specific genomic structure estimation in cancer, E-Scape[b] for interactive visualization of single-cell phylogenetics and cancer evolution, PyClone[c] for inference of clonal population structures in tumours, TITAN[d] for identification of clonal diversity in the genome architecture of tumours, defuse[e] for identification of gene fusions from RNASeq and mutationSeq[f]. These methods have been in continual application to NGS datasets in my and collaborator labs as described above, driving discovery. I have released numerous software tools that have been downloaded >4000 times and are in use in laboratories worldwide.
    a. McPherson A, Roth A, Ha G, Chauve C, Steif A, de Souza CPE, Eirew P, Bouchard-Côté A, Aparicio S, Sahinalp SC, **Shah SP**. ReMixT: clone-specific genomic structure estimation in cancer. Genome Biology. 2017 Jul 27;18(1):140. doi: 10.1186/s13059-017-1267-2.
    b. Smith MA, Nielsen CB, Chan FC, McPherson A, Roth A, Farahani H, Machev D, Steif A, **Shah SP**. E-scape: interactive visualization of single-cell phylogenetics and cancer evolution. Nature Methods. 2017 May 30;14(6):549-550. doi:10.1038/nmeth.4303.
    c. Roth A, Khattra J, Yap D, Wan A, Laks E, Biele J, Ha G, Aparicio S, Bouchard-Cote A, **Shah SP**. PyClone: statistical inference of clonal population structure in cancer. Nature Methods 2014 Apr;11(4):396-8. doi: 10.1038/nmeth.2883.
    d. Ha G, Roth A, Khattra J, Yap D, Melnyk N, McPherson A, Prentice L, Bashashati A, Laks E, Biele J, Ding J, Le A, Rosner J, Shumansky K, Marra M, Gilks CB, Huntsman DG, McAlpine JN, Aparicio S, **Shah SP**. TITAN: Inferring copy number architectures of clonal cell populations from tumour whole genome sequencing data. Genome Research. 2014 Nov;24(11):1881-93. doi: 10.1101/gr.180281.114.
    e. McPherson A, Hormozdiari F, Zayed A, Giuliany R, Ha G, Sun MGF, Griffith M, Moussavi AH, Senz J, Melnyk N, Pacheco M, Marra MA, Hirst M, Nielsen TO, Sahinalp SC, Huntsman D, **Shah SP**. deFuse: an algorithm for gene fusion discovery in tumor RNA-Seq data. PLoS Comput Biol. 2011 May: 7(5):e1001138.
    f. Ding J, Bashashati A, Roth A, Oloumi A, Tse K, Zeng T, Haffari G, Hirst M,Marra MA, Condon A, Aparicio S, **Shah SP**. Feature based classifiers for somatic mutation detection in tumour-normal paired sequencing data. Bioinformatics. 2012 Jan 15;28(2):167-75.

Complete List of Published Work in MyBibliography: http://1.usa.gov/1GoSVB6

D. Research Support

Ongoing Research Support

TFRI #N/A Connors, Marra, Steidl, Shah, Scott, Weng, Morin, Mungall, Slack (PI) 07/01/16-06/30/21
The Terry Fox New Frontiers Program Project Grant, Overcoming treatment failure in lymphoid cancers
Goal: Precisely determine the nature of clonal evolution and the dynamics of the immune response during the course of follicular lymphoma as it transits through differing clinical trajectories.

CIHR Foundation # N/A Shah (PI) 07/01/15-06/30/20
The clonal dynamics of ovarian cancers: phylogenetic models of chemosensitivity and resistance
Goal: Support for research program.

CCSRI Impact # N/A Liu G (PI) 02/01/2015-01/31/20
REAL-PDX: Resistance modeling in EGFR and ALK Lung cancer Patient-derived xenografts for personalized post-progression therapy
Goal: To utilize serial biopsies and Patient-derived Xenograft models (PAXM) as an innovative strategy to improve clinical management of EGFR/ALK-related (EAR) NSCLC patients.
Role: Co-applicant

Canada Research Chair #N/A Shah (PI) 04/01/13-03/31/18
Canada Research Chair in Computational Cancer Genomics
Goal: Salary support for research program.

TFF1021 Huntsman (PI) 07/01/13-06/30/18
The genomics of forme fruste tumours: New Vistas on Cancer Biology and Treatment
Goal: To study all aspects of less common (forme fruste) tumours, including the identification of driver mutations, the investigation of clonal architecture, functional characterization, and analysis of mutations within the circulation of patients.

Role: Co-applicant; Lead, data analysis core.

CIHR #N/A Aparicio (PI) 04/01/13-03/31/18
Linking clonal genomes to tumour evolution and therapeutics
Goal: To extend current analyses of genetic mutations in aggressive breast cancer tumours.
Role: Co-applicant, Bioinformatics lead

CCSRI #N/A Aparicio (PI) 02/01/13-01/31/18
Defining the role of clonal genomes in the evolution and treatment of cancers
Goal: Systematic characterization of how breast cancer cells mutate / evolve and become drug resistant.
Role: Co-applicant, bioinformatics lead

CCSRI #70160 Huntsman, Shah (PI) 02/01/13-01/31/18
Contextual Genomics: The foundation for subtype specific approaches to ovarian cancer control
Goal: to use contextual genomics, an integrated approach to interpreting cancer genomes, to identify oncogenic driver mutations in clear cell and endometrioid carcinomas of the ovary and use them to define treatment opportunities for targeted therapies.

Completed Research Support

Genome Canada # N/A Shah (PI) 07/01/13-06/30/16
Computational interpretation of cancer genomes: Defining mutational landscapes for translational genomics
Goal: to deliver user-interface based open source software solutions for interpretation of cancer genomes.

CCSRI #N/A Shah (PI) 02/01/14-01/31/16
Building a Bridge from the Cancer Genome to the Cancer Clinic with Visual Analytics
Goal: To design/develop and apply an interactive data analysis and visualization system empowering clinical researchers to engage in data interpretation.

CFI Leaders Opportunity Fund / BC Knowledge Development Funds (matching CFI funds) / Other eligible partners Shah (PI) 04/01/13- 03/01/16
Computational infrastructure for defining genomic landscapes and resolving the clinical impact of somatic mutations in cancer
Goal: Infrastructure project.

CIHR # MOP115170 Shah (PI) 10/01/11-09/30/15
Genomic disruption in high-grade serous ovarian carcinomas: Steady State or Continuous Drift?
Goal: to investigate chromosomal rearrangements in HGSOC and their precursor lesions.

Genome Canada # N/A Shah (PI) 07/01/13-06/30/15
Measuring and modeling tumour evolution from next generation sequencing data: Enabling clinical study of clonal diversity in cancer patients
Goal: to develop a novel and innovative set of statistical models and software to make inferences about evolutionary dynamics of tumours.

TFRI # N/A Shah (PI) 11/01/12-10/31/15
Are genomic instability and clonal diversity prognostic indicators of HGSOC?
Goal: to establish the role of genomic characteristics in predicting clinical outcome in high grade serous ovarian cancer.

CBCRA #N/A Aparicio (PI) 11/01/11-10/31/15
Genome heterogeneity in predictive models of drug action in triple negative breast cancers.
Goal: To apply next-generation sequencing techniques to an assessment of how xenografting methods and drug selection affect the mutational and clonal evolution of transplanted breast tumours.
Role: Co-applicant, bioinformatics lead

DoD #N/A Pike (PI) 01/01/13-12/31/14
Multi-disciplinary Ovarian Cancer Outcomes Group. (PI: Malcolm Pike). Department of Defense, 2012 Ovarian Cancer Research Program Outcomes Consortium Development Award.
Goal: To identify factors responsible for the small proportion of long-term survivors diagnosed with HGSC.
Role: Co-applicant

CCSRI # N/A Shah (PI) 04/01/12-03/31/14
Finding driver mutations in cancer through integrative profiling of mutational landscapes and transcriptional networks
Goal: To investigate the impact of somatic mutations on transcriptional networks in cancer.

CIHR # N/A Huntsman (PI) 10/01/10-09/30/14
Mutations in SWI/SNF chromatin remodelling complex: alt. mechanism for ovarian carcinogenesis
Goal: To investigate the involvement of ARID1A and other SWI/SNF genes in clear cell cancers of the ovary and other ovarian carcinomas, and their precursor lesions.