



GENETICURE

HYPERTENSION INTEGRATED COMPUTATIONAL GENOMIC MEDICINE

NEXT GENERATION CARE TO IMPROVE OUTCOMES, EFFICIENCY AND ECONOMICS

GENETICURE & MAYO CLINIC FOUNDING TEAM

SCOTT SNYDER, CEO

Ran \$10B of category volume & OTC pharmacy, for Target Corporation

RYAN SPRISLER PHD, CSO

Founding member of the Center for Applied Genetics and Genomic Medicine at University of Arizona
Genetics Core facility

ERIC SNYDER PHD, COO

Pre-doc and post-doc fellow in CV Diseases at Mayo Clinic. Second post-doctoral fellowship in
Nephrology and Hypertension

TIM CURRY, MD PHD, MEDICAL DIRECTOR

Mayo Clinic Center for Individualized Medicine. Integrative physiologist with special expertise in
cardiopulmonary and neural physiology.

DAVID HERBERT, EVP STRATEGY

Chief Admin. Officer Mayo Medical Laboratories; Chair Mayo Clinic Global Business; and Dir. at Mayo
Medical Ventures

SCOTT DYLLA, PHD, BOARD OF ADVISORS

Geneticure Investor and Advisor. Former Chief Scientific Officer, Stemcentrx, \$6B Exit to Abbvie

RAMSEY KILANI, MD, BOARD OF DIRECTORS

Founder, Managing Partner Western Skies Partners. Principal and Founder, Gliavent Group. Seasoned
Lab and Diagnostics Executive

BRAD WILSON, BOARD OF ADVISORS

CEO Emeritus of BlueCross BlueShield of NC

MARION SNYDER PHD, LAB DIRECTOR

Seasoned private commercial lab director overseeing \$500M+ in revenue over the past decade, startup
veteran, Harvard trained PhD

JORDAN LIPTON, MD, BOARD OF ADVISORS

Concierge Physician and Partner at Signature Healthcare. Member, International Physician Advisory
Board at Private Physicians Alliance

JOSEPH FALSONE, MD, BOARD OF ADVISORS

UNC Health Physician, Cardiology.

HYPERTENSION: THE LEADING PREVENTIBLE CAUSE OF DEATH IN THE WORLD

- TREATED WITH TRIAL-AND-ERROR (MULTIPLE VISITS, LAYERING MEDICATIONS)
- 45% PREVALENCE, 76% UNCONTROLLED
- \$200B+ ANNUAL COST
- 60% OF PATIENTS ON THE INCORRECT MEDICATION BASED ON GENETICS

RESPONSE TO THERAPY IS NOT UNIFORM (OR ALWAYS DOWN)

Ex. Hydrochlorothiazide Mono-therapy:

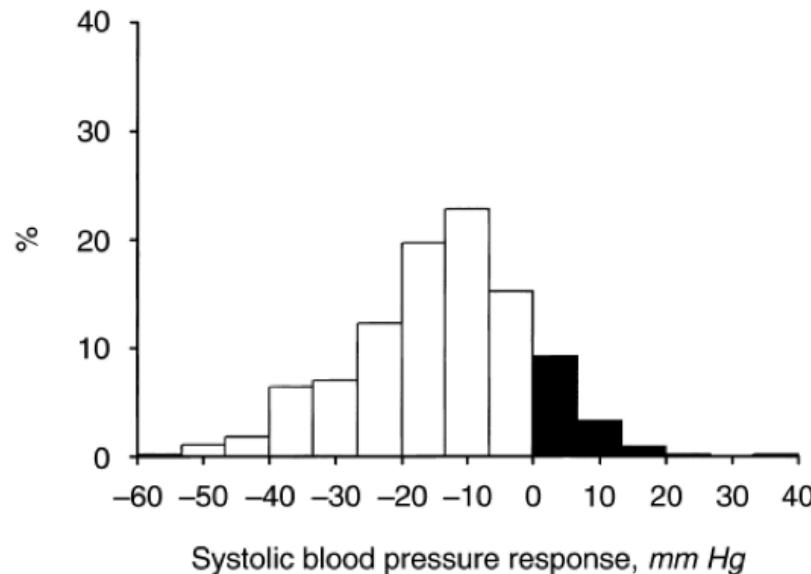


Fig. 1. Frequency distribution histogram of systolic blood pressure (BP) responses to four weeks of hydrochlorothiazide, 25 mg per day, in the combined sample of 225 African Americans and 280 Caucasians. Symbols are: (□) decreases in BP; (■) increases in BP. Data are mean = -14.4, SD = 13.4, N = 505.

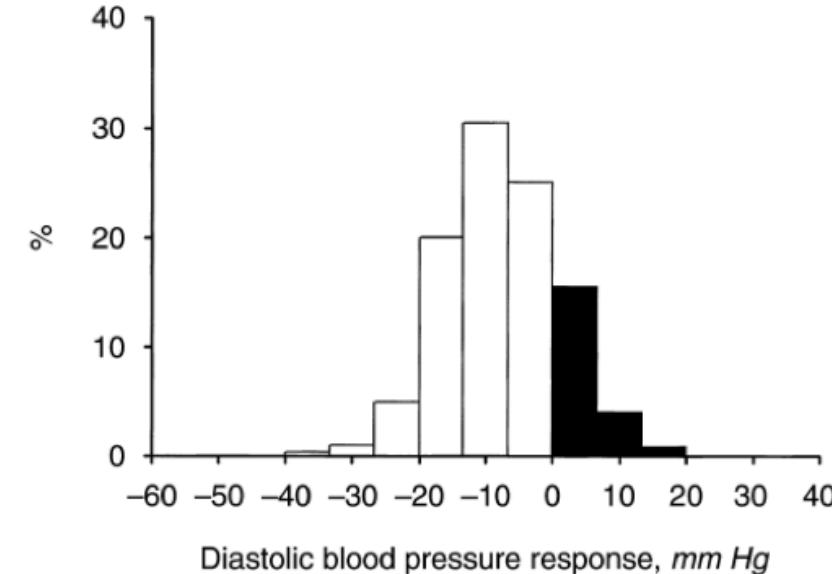


Fig. 2. Frequency distribution histogram of diastolic blood pressure (DBP) response to four weeks of hydrochlorothiazide, 25 mg per day, in the combined sample of 225 African Americans and 280 Caucasians. Symbols are: (□) decreases in BP; (■) increases in BP. Data are mean = -7.8, SD = 8.4, N = 505.

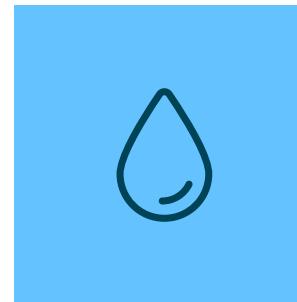
HYPERTENSION IS GENETIC

GENES CAUSE:



**HOW HARD THE
HEART BEATS AND
HEART RATE**

~15 Cardiac Medication Options



**SODIUM
REABSORPTION IN
THE KIDNEYS**

~15 Renal Medication Options



**BLOOD VESSEL
CONSTRICKTION**

~10 Vascular Medication
Options

GENETICURE FOR HYPERTENSION



ID	rs10	rs10	rs11	rs12	rs15	rs18	rs19	rs21	rs22	rs22	rs38	rs49	rs50	rs51	rs69	rs70
HG00110	GA	GC	G	G	C	A	CG	C	TC	CT	T	T	C	C	T	G
HG00112	A	C	GC	G	G	AG	C	CT	TC	T	TC	T	C	A	T	GT
HG00127	G	GC	GC	AG	G	AG	CG	C	TC	CT	TC	GT	CT	CA	CT	GT
HG00179	G	G	C	G	GC	A	CG	T	C	T	C	G	CT	A	CT	GT
HG00183	G	GC	GC	AG	GC	A	G	CT	TC	T	C	GT	CT	A	CT	G
HG00189	A	C	G	G	C	A	G	C	T	CT	C	G	C	CA	T	GT
HG00235	G	G	G	G	AG	CG	C	TC	CT	T	G	C	C	T	T	T
HG00252	G	GC	G	AG	G	AG	CG	C	TC	T	C	GT	C	CA	T	G
HG00269	GA	GC	GC	G	G	AG	C	CT	TC	CT	C	GT	CT	CA	CT	GT
HG00274	GA	GC	G	AG	G	A	C	C	TC	T	C	G	CT	A	CT	GT
HG00339	GA	GC	GC	G	G	A	G	CT	TC	T	C	GT	CT	A	CT	G
HG00346	G	C	G	AG	G	G	C	C	TC	CT	C	G	C	A	T	GT
HG00707	GA	C	G	A	G	A	C	C	C	T	C	T	T	CA	C	G
HG01107	GA	C	G	A	G	G	C	C	TC	T	C	G	T	A	C	G
HG01131	G	GC	G	AG	G	A	C	C	C	C	TC	G	T	CA	C	G
HG01447	GA	C	GC	AG	G	AG	C	T	C	T	C	G	C	CA	T	T
HG01583	GA	C	C	G	G	AG	C	T	C	T	TC	GT	C	A	T	T
HG01605	GA	C	GC	G	G	A	CG	CT	TC	CT	TC	G	CT	A	CT	G
HG01775	GA	C	G	G	G	A	C	C	C	C	TC	G	C	CA	T	GT
HG02787	G	G	G	AG	G	A	C	C	T	T	C	G	T	A	C	G

CHEEK SWAB COLLECTION

Home or Office

No charge for Kit / Shipping Included

PATENTED ALGORITHM
APPLIED TO 17 HIGHLY
SPECIFIC SITES FOR HTN

The digital tablet screen displays the "GENETICURE Hypertension Pharmacogenomic Panel Results". At the top, it shows the patient's information: Patient ID: 123456, DOB: Jan. 1, 1999, Name: Sue Sample, Indication: Future hypertension therapy, and Kit ID: GCE123. Below this is a "Recommended Treatments" section with four numbered points: 1. Primary recommendation: consider a selective β-blocker. If co-morbidity for β-blockade is present consider a Ca²⁺ channel blocker. 2. If the above recommendation is not effective or appropriate for the patient, consider therapy with an ACE inhibitor. 3. If the above recommendation is not effective or appropriate for the patient, consider therapy with an angiotensin-II (AII) receptor blocker. 4. If the above recommendation is not effective or appropriate for the patient, consider thiazide or a thiazide-like diuretic. A note at the bottom of this section says "Do not start or stop taking any medications without first consulting your provider." Below this is a "Functionality of Organ Systems" section with three categories: Nonfunctional allele (red), Moderately functional (blue), and Functional allele (green). Under the "Cardiac System" heading, it says: "The patient demonstrates the greatest functionality in the genes that encode receptors that control cardiac function, specifically the β₁-adrenergic receptors, and the genes that encode CYP2D6 (which metabolizes some β-blockers). The patient is most likely to respond to β-blockade, specifically a selective β-blocker. If co-morbidity for β-blockade is present consider a Ca²⁺ channel blocker." A note below states: "Note: A system's functionality may not correlate to its responsiveness." Under the "Vascular System" heading, it says: "Following this, the patient demonstrates functionality in the renin-angiotensin-aldosterone system, specifically the ACE gene and the..." A note below states: "ACE rs1799752 NC_000017.11:g.63488543**".

PRESCRIBE THERAPY MOST
LIKELY TO WORK

AN 'EVIDENCE FIRST' MISSION



Journal of
Clinical Medicine

Article

Relationship between a Weighted Multi-Gene Algorithm and Blood Pressure Control in Hypertension

Pamela K. Phelps^{1,†}, Eli F. Kelley^{2,†}, Danielle M. Walla¹, Jennifer K. Ross¹, Jerad J. Simmons¹, Emma K. Bulock¹, Audrie Ayres¹, Monica K. Akre³ , Ryan Sprissler^{3,4}, Thomas P. Olson^{3,5}

The Effect of Genetically Guided Mathematical Prediction and the Blood Pressure Response to Pharmacotherapy in Hypertension Patients

Eli F Kelley¹ , Thomas P Olson^{2,3}, Timothy B Curry^{2,3}, Ryan Sprissler^{2,4} and Eric M Snyder²

¹School of Kinesiology, University of Minnesota, Minneapolis, MN, USA. ²Geneticure, Inc., Rochester, MN, USA.

³College of Medicine and Science, Mayo Clinic, Rochester, MN, USA.

⁴Department of Genetics, University of Arizona Genomics Core, Tucson, AZ, USA.



Research Article

Hypertension: An Open Access

Snyder EM, et al. Hypertens Open Acc: HTOA-103.
DOI: 10.29011/HTOA-103.100008

Association of a Multi-Gene Panel with Blood Pressure Medication Success in Patients with Hypertension: A Pilot Study

Eric M Snyder¹, Ryan Sprissler^{1,2}, Micah Johnson³, Greg D Beenken³, Timothy Curry⁴, Nicholas Cassuto⁵, Eli F Kelley³, Thomas P Olson^{1,5}



Journal of Medical Economics

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Economic evaluation of a pharmacogenomic multi-gene panel test to optimize anti-hypertension therapy: simulation study

Eli F. Kelley, Eric M. Snyder, Nimer S. Alkhatib, Scott C. Snyder, Ryan Sprissler, Thomas P. Olson, Monica K. Akre & Ivo Abraham

The importance and challenges of developing a pharmacogenetics test for hypertension

Eric M Snyder¹, Eli F Kelley², Ryan Sprissler^{1,3} & Thomas P Olson^{*1,4}

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³University of Arizona Genomics Core, Tucson, Arizona, AZ 85721 USA

⁴Division of Cardiovascular Diseases, Mayo Clinic College of Medicine, Rochester, MN 55905, USA

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CLINICALLY DEMONSTRATED IMPROVEMENTS OVER STANDARD OF CARE

~1300 patients, 4 clinical trials, 5 peer-reviewed papers

- **UNITEDHEALTH GROUP DATA: \$3100 LESS PER PT PER YEAR**
- **47% LOWER OVERALL COST**
- **97% UNDER CONTROL IN <6 MONTHS**
- **36% LOWER BLOOD PRESSURE**
- **43% LESS SERIOUS ADVERSE EVENTS**
- **64% LESS SPENDING ON HOSPITALIZATIONS**

SAMPLE REPORT:

One Page.

Actionable.



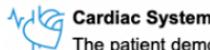
Patient ID: 123456 DOB: Jan. 1, 1950 Name: Sue Sample
Indication: Future hypertension therapy. Kit ID: GCE123

Recommended Treatments

- Primary recommendation: consider a **selective β-blocker**. If co-morbidity for **β-blockade** is present consider a **Ca⁺ channel blocker**.
- If the above recommendation is not effective or appropriate for the patient, consider **therapy with an ACE inhibitor**.
- If the above recommendation is not effective or appropriate for the patient, consider **therapy with an angiotensin-II (AII) receptor blocker**.
- If the above recommendation is not effective or appropriate for the patient, consider **thiazide or a thiazide-like diuretic**.

Do not start or stop taking any medications without first consulting your provider.

Functionality of Organ Systems*



Cardiac System

The patient demonstrates the greatest functionality in the genes that encode receptors that control cardiac function, specifically the β_1 -adrenergic receptors, and the genes that encode CYP2D6 (which metabolizes some β -blockers). The patient is most likely to respond to β -blockade, specifically a selective β -blocker. If co-morbidity for β -blockade is present consider a Ca^+ channel blocker.

Nonfunctional allele ❌ Moderately functional ⓘ Functional allele** ✓

Less	Responsiveness to treatment*	More	
Gene Name	SNP ID	HGVS ID	Result
ADRB1	rs1801252	NC_000010.11:g.114044277A>G	AA ✓
ADRB1	rs1801253	NC_000010.11:g.114045297G>C	CC ✓
ADRB2	rs1042713	NC_000005.10:g.148826877G>A	GG ✓
ADRB2	rs1042714	NC_000005.10:g.148826910G>C	GC ⚡
CYP2D6	rs3892097	NC_000022.11:g.42128945C>T	TC ⚡



Vascular System

Following this, the patient demonstrates functionality in the renin-angiotensin-aldosterone system, specifically the ACE gene and the angiotensin-II receptor. The patient is most likely to respond to therapy with an ACE inhibitor, and may respond to therapy with an angiotensin-II (AII) receptor blocker.

Less Responsiveness to treatment* More

Gene	SNP ID	HGVS ID	Result
ACE	rs1799752	NC_000017.11:g.63488543***	-/+ ✓
Angiotensin-I (a)	rs5051	NC_000001.11:g.230714126C>T	TT ✓
Angiotensin-I (b)	rs699	NC_000001.11:g.230710048A>G	CC ✓
Angiotensin-I (c)	rs7079	NC_000001.11:g.230702585G>T	CC ✗
A-II Receptor	rs5186	NC_000003.12:g.148742201A>C	CA ⚡
Renin	rs12750834	NC_000001.11:g.204171656G>A	AG ✓



Renal System

The final line of therapy is informed by the patient's functionality in the genes that encode for channels/enzymes important in Na^+ reabsorption in the kidney. The patient is most likely to respond to a diuretic, specifically thiazide or a thiazide-like diuretic.

Less Responsiveness to treatment* More

Gene	SNP ID	HGVS ID	Result
Alpha Adducin	rs4961	NC_000004.12:g.2904980G>T	GT ✓
SCNN1A	rs2228576	NC_000012.12:g.6347896T>C	TC ⚡
SLC12A3	rs1529927	NC_000016.10:g.56870675C>G	GG ✗
WNK1(a)	rs1159744	NC_000012.12:g.825679C>G	GG ✓
WNK1(b)	rs2107614	NC_000012.12:g.793913T>C	CC ✓
WNK1(c)	rs2277869	NC_000012.12:g.907744T>C	TT ✗

This test was authorized by Dr. Sam Sample, NPI #1234567890.

Comments: Thank you for using Geneticure!

Mario J. Soto

Sample Director, PhD
Laboratory Director

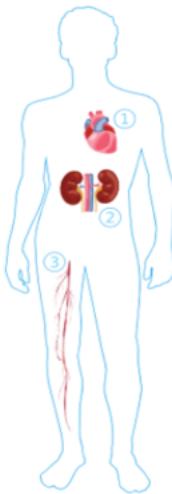
Troy L. Gray

Sample Consultant, MD
Clinical Consultant

THIS IS NOT PHARMACOGENOMICS (PGX).

THIS IS PATENTED INTEGRATED COMPUTATIONAL GENOMIC MEDICINE.

"Inch-Wide, Mile-Deep" Approach to Solve a Physiologic Problem for a Specific Disease



WE USE THE GENETIC TARGETS OF
INTEGRATIVE PHYSIOLOGY

$$\Sigma \div$$

COMBINED WITH PROPRIETARY AND
EVIDENCE-BASED WEIGHTED
ALGORITHMS



TO PINPOINT THE CORRECT MEDICATION
SELECTION THAT TARGETS THE CORRECT
ORGAN SYSTEM(S)

ECONOMICS

- \$1100 LIST, \$452 COST TO PROVIDERS OR PATIENTS
- 16X RETURN ON INVESTMENT FOR PAYERS, IN <3 YEARS
- COMPARABLE TEST PRICING
 - PrismRA Rheumatoid Arthritis Medication Response: \$5000
 - Grail Cancer Screening: \$950
 - Genesight Mental Health PGx \$330
 - Gut Biome \$150-\$500



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Economic evaluation of a pharmacogenomic multi-gene panel test to optimize anti-hypertension therapy: simulation study

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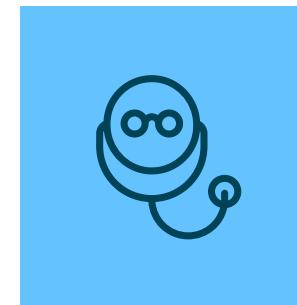
NEXT GENERATION PRECISION MEDICINE ACHIEVING THE QUADRUPLE-AIM:



IMPROVED OUTCOMES



LOWER COST



CLINICIAN EFFICIENCIES



PATIENT EXPERIENCE

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 1.800.DNA.8109

