Supplemental Figure 1: Subject reported survey results. Of the 435 subjects who underwent genotyping, 425 completed a baseline survey regarding their beliefs and attitudes toward genetic testing. All responses were given according to a Likert scale. A) Subjects were asked about their familiarity with pharmacogenomics. B) Subjects were asked whether genetic testing would increase their own efforts to control their blood pressure. C-D) Subjects were asked whether the genetic testing would help their providers select medications and control blood pressure.

Supplemental Table 1: Gene descriptions

Gene	Variants Tested	Biological/Functional Significance	Predicted Phenotype
ADRB1	rs1801253 (c.1165G>C), rs1801252 (c.145A>G)	Encodes β1-adrenoreceptor, polymorphism is associated with greater agonist-promoted downregulation and altered glycosylation of the receptor.	Increased beta-blocker efficacy with increasing copies of the 49S-389R haplotype.
CYP2C9	CYP2C9*2 (c.430C>T), CYP2C9*3 (c.1075A>C), CYP2C9*5 (c.1080C>G) CYP2C9*6 (c.818delA), CYP2C9*8 (c.449G>A), CYP2C9*11 (c.1003C>)	Encodes cytochrome P450 2C9 enzyme, which metabolizes losartan to its active metabolite E3179. E3179 is 10- to 40-fold more potent than its parent compound.	Intermediate or poor metabolizers have reduced efficacy of losartan.
CYP2D6	CYP2D6*2 (c.2850C>T and c.4180G>C), CYP2D6*3 (c.2549delA) CYP2D6*4 (c.1846G>A and c.100C>T), CYP2D6*5 (gene deletion) CYP2D6*6 (c.1707delT), CYP2D6*7 (c.2935A>C) CYP2D6*9 (c.2615_2617delAAG), CYP2D6*10 (c.100C>T and c.4180G>C) CYP2D6*17 (c.1023C>T), CYP2D6*29 (c.3183G>A), CYP2D6*41 (c.2988G>A), CYP2D6*1XN (duplication), CYP2D6*2XN (c.2850C>T, c.4180G>C, duplication) CYP2D6*4XN (c.1846G>A, c.100C>T, duplication)	Encodes cytochrome P450 2D6 enzyme, metabolizes metoprolol and carvedilol to its inactive metabolites.	Poor metabolizers have higher circulating concentrations and increased risk of bradycardia. Ultrarapid metabolizers have a risk of inefficacy.
F7	rs6046 (c.1238G>A; p.Arg413Gln)	Encodes vitamin K dependent clotting factor VII. F7 is the initiator of the extrinsic coagulation pathway. Blood pressure effect possibly related to endothelial homeostasis.	Decreased amlodipine efficacy with increasing copies of A allele in African Americans.
GRK4	rs2960306 (c.194G>T), rs1024323 (c.329C>G)	Encodes G-protein coupled receptor kinase 4 (GRK4). The presence of GRK4 is important for regulation of ADRB1 cell surface expression.	Decreased beta-blocker efficacy associated with increasing copies of the 65L-142V haplotype.
NAT2	NAT2*5 [rs1801280 (c.341T>C)], NAT2*6 [rs1799930 (c.590G>A)], NAT2*7 [rs1799931 (c.857G>A)], NAT2*14 [rs1801279 (c.191G>A)]	Encodes N-acetyletransferase 2, which is responsible for acetylation of hydralazine to its inactive metabolite.	Poor metabolizers have higher circulating concentrations of hydralazine and increased efficacy.
NEDD4L	rs4149601 (c.24G>A)	Encodes member of the Nedd4 family of HECT domain E3 ubiquitin ligases, regulating cell surface expression of the epithelial sodium channel, ENaC. Consists of 3 domains (C2, WW and Hect). C2 domain is a calcium-rich lipid-binding domain responsible for membrane targeting. WW and Hect domains target ENac for internalization	Presence of two G alleles results in increased ENaC activity and increased response to diuretics in Caucasians.

		into the cell and degradation by lysozomes respectively.	
NPHS1	rs3814995 (g.35851310C>T)	Encodes nephrin, the principal structural protein of the glomerular podocytes. NPHS1 mutations result in congenital nephrotic syndrome. Angiotensin receptor blocks decrease renal nephrin expression.	One or more A alleles is associated with increased angiotensin receptor blocker efficacy.
VASP	rs10995 (c.*719G>A)	Encodes vasodilator-stimulated phosphoprotein (VASP). VASP is a substrate for cyclic AMP-and cyclic GMP-dependent protein kinases, regulating smooth muscle contraction.	Increased expression is associated with increased thiazide efficacy.
YEATS4	rs7297610 (g.69430244C>T)	Encodes GAS41, essential for RNA transcription and cell viability including chromatin-modification. Evidence for direct functional/biological significance lacking, possible role with regards to hypertension-associated cell proliferation at the level of the renal tubules.	One or more copies of the T allele is associated with decreased thiazide efficacy.
EBF1/ FGF5/ SH2B3	EBF1 rs4551053 (g.158411534G>A) FGF5 rs1458038 (g.81164723C>T) SH2B3 rs3184504 (c.784T>C)	This 3 gene model was uncovered in the PEAR studies and evidence for direct functional/biological significance is lacking.	Increasing copies of efficacy alleles are associated with increased thiazide efficacy.

Supplemental Table 2: Genotype frequency

Gene	Actionable Genotype	Overall Frequency (N = 382)
ADRB1	Greater beta blocker response (2 copies of 49S-389R)	42 (11.0)
	Standard beta blocker response (1 copy of 49S-389R)	190 (49.7)
	Reduced beta blocker response (0 copies of 49S-389R)	150 (39.3)
CYP2D6	Ultrarapid metabolizer	12 (3.1)
	Normal or indeterminate metabolizer	212 (55.5)
	Intermediate (Reduced) metabolizer	141 (36.9)
	Poor metabolizer	17 (4.5)
CYP2C9	Normal Metabolizer	272 (71.2)
	Intermediate (Reduced) metabolizer (*1/*2)	49 (12.8)
	Intermediate (Reduced) metabolizer (non-*1/*2)	43 (11.2)
	Poor Metabolizer	18 (4.7)
F7	Standard efficacy (G/G allele)	305 (79.8)
	Reduced efficacy (G/A or A/A allele)	77 (20.2)
GRK4	Greater beta blocker response (0 copies of 65L-142V)	166 (43.5)
	Standard beta blocker response (1 copy of 65L-142V)	174 (45.5)
	Reduced beta blocker response (2 copies of 65L-142V)	42 (11.0)
NAT2	Normal or intermediate metabolizer	180 (47.1)
	Poor metabolizer	202 (52.9)
NEDD4L	Increased diuretic efficacy (G/G)	171 (44.8)
	Standard diuretic efficacy (G/A)	173 (45.3)
	Reduced diuretic efficacy (A/A)	38 (9.9)
NPHS1	G/G (Standard ARB efficacy)	243 (63.6)
	G/A or A/A (Increased ARB efficacy)	139 (36.4)
VASP	Standard thiazide efficacy (A/A)	236 (61.8)
	Increased efficacy allele (A/G or G/G)	146 (28.2)
YEATS4	Standard efficacy (C/C)	266 (69.6)
	Reduced efficacy allele (C/T or T/T)	116 (30.4)
EBF1/FGF5/SH2B3	Increased thiazide efficacy (3 or more efficacy alleles)	92 (24.1)
	Standard thiazide efficacy (1 or 2 efficacy alleles)	281 (73.6)
	Reduced thiazide efficacy (0 efficacy alleles)	9 (2.4)

Supplemental Table 3: Cross sectional associations of individual drug-gene interactions with baseline uncontrolled hypertension

Drug-Gene Interaction	Phenotype	uHTN	cHTN	Odds Ratio (CI)	P-value	N[D]	Predicted direction of effect[E]
F7-amlodipine[A]	Normal variant	48	38	1.98 (0.8-5.0)	0.15	114	Odds Ratio > 1
	Reduced efficacy	20	8				
NEDD4L-diuretics[A]	Normal / increased	23	45	1.83 (0.9-3.7)	0.09	130	Odds Ratio > 1
	Reduced efficacy	30	32				
ADRB1-beta blockers	Normal / increased	68	74	1.47 (0.9-2.5)	0.15	236	Odds Ratio > 1
	2 Reduced efficacy alleles	54	40				
GRK4-beta blockers	Normal Variant	107	102	1.19 (0.5-2.7)	0.67	236	Odds Ratio > 1
	Reduced efficacy	15	12				
CYP2C9-losartan[B]	Normal	39	88	**5.2 (1.9-14.7)**	**0.002**	108	Odds Ratio > 1
	Intermediate / Poor	14	6				
CYP2D6-beta blockers[C]	Normal	79	55	**0.55 (0.3-0.95)**	**0.03**	222	Odds Ratio < 1
	Intermediate/ Poor	39	49				
NPHS1-ARB	Normal Variant	35	33	0.77 (0.4-1.7)	0.52	108	Odds Ratio < 1
	Increased efficacy allele	18	22				
VASP-Thiazides[A]	Normal Variant	7	14	0.86 (0.3-2.8)	0.80	51	Odds Ratio < 1
	Increased efficacy allele	9	21				

[A]Denotes the analysis was performed in the relevant population. *F7* was tested in individuals with self-reported African ancetsry. *NEDD4L* and *VASP* were tested in individuals of self-reported European ancestry. [B]*CYP2C9* *1/*2 genotypes were included with normal metabolizers. [B]Ultrarapid and indeterminate metabolizers were excluded from the analysis. [D]Comparisons with sample size below 50 not shown (YEATS4 for thiazides in African Americans and NAT2 for hydralazine). [E]The predicted direction of effect is given based on effect sizes in the literature for each drug-gene pair. Variants predicting reduced efficacy would be predicted to have a higher odds ratio of uncontrolled blood pressure. Variants associated with increased drug efficacy would be predicted to have an odds ratio < 1 for uncontrolled blood pressure.

Supplemental Document 1: Subject Survey

Study ID number: _____ Date: _____

Interviewer: _____

Genetics Opinion Survey – Initial (Read to subject)

By completing this survey you are agreeing to participate in a research study looking at your opinion on genetic testing. This information may be used to make education materials that can be helpful for you and other patients.

How familiar are you with the terms pharmacogenomics, genetic testing or personalized medicine?

- Very familiar
- Somewhat familiar
- Not very familiar
- I have not heard of it

Have you, or has anyone in your immediate family, ever been told that you carried a gene that predisposed you to certain diseases?

- Yes
- No
- I don't know

If a genetic test was available that could tell whether a family member was at higher risk to have their kidneys stop working in the future, would you want them to take the test?

- Yes
- No
- I don't know

Do you believe tests that use genes to predict diseases are mostly accurate and reliable?

- Yes
- No
- I don't know

For each of the following statements, indicate whether you agree or disagree with them:

Understanding my genetic code can help my doctor pick the best medications and proper dose for me.

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- I don't know

Understanding my genetic code *would encourage me* to do more to control my blood pressure and protect my kidneys.

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- I don't know

Understanding my genetic code could prompt my doctor to do more to control my blood pressure and help my kidneys.

- Strongly Agree
- Agree
- Neutral
- Disagree
- Strongly Disagree
- I don't know

How would you describe your health?

- Excellent
- Very Good
- Good
- Fair
- Poor

How would you describe your race and/or ethnicity?

- White
- African-American or Black
- Hispanic
- Asian
- Native American
- Other: _____

How would you describe your highest level of education?

- Some High School (or less)
- High School Graduate or GED
- Some College (no degree)
- Bachelor's degree
- Graduate School (or higher)

Supplemental Document 2: Provider Survey

Study ID number: _____   Date: _____

Interviewer: _____

Genomics Clinician Survey (Post):

1) Has genetic testing impacted your diagnosis or management in this patient?   Yes / No

2) Will you discuss the results with the patient in the next 6 months?   Yes / No