



**Supp. Fig. S1.** Pro-ANP processing activity of p.Tyr13Cys, p.Asp95Tyr, p.Leu334Trp and p.Arg525His was analyzed by Western blotting. WT corin and inactive R801A mutant were used as positive and negative controls, respectively. Pro-ANP to ANP conversion was quantified. Data were from 3 independent experiments. n.s.: not significant vs. WT.

**Supplemental Table S1. Characteristics of participants in cohorts 1 and 2**

Characteristics	Cohort 1			Cohort 2		
	Normal (n=300)	Hypertensive (n=401)	<i>p</i> value	Normal (n=377)	Hypertensive (n=368)	<i>p</i> value
Age (year)	39 ± 19	57 ± 14	<0.05	50 ± 10	54 ± 7	0.13
Male (%)	157 (52.3)	268 (66.8)	<0.01	200 (53.1)	152 (41.3)	0.013
SBP (mmHg)	108.2 ± 16.7	147.2 ± 5.9	<0.01	111.6 ± 11.8	135.3 ± 10.1	<0.01
DBP (mmHg)	74.2 ± 8.6	93.6 ± 7.5	<0.01	78.8 ± 3.6	97.8 ± 6.6	<0.01
Blood parameters						
BG (mmol/L)	5.3 ± 0.7	5.3 ± 1.2	0.46	4.9 ± 0.8	5.4 ± 1.3	0.22
TG (mmol/L)	3.8 ± 1.9	3.9 ± 2.6	0.79	3.6 ± 1.9	3.6 ± 3.3	0.83
HDL (mmol/L)	1.5 ± 0.6	1.5 ± 0.5	0.56	1.4 ± 0.5	1.4 ± 0.6	0.68
UA (µmol/L)	277.2 ± 56.4	348.3 ± 86.7	0.07	299.5 ± 76.3	312.6 ± 88.2	0.52
Medical history						
HF	0 (0)	12 (2.9)		0 (0)	13 (3.5)	
Diabetes	0 (0)	22 (5.5)		0 (0)	23 (6.3)	
CVD	0 (0)	8 (2.0)		0 (0)	9 (2.4)	
RF	0 (0)	5 (1.2)		0 (0)	2 (0.5)	

Data are mean ± S.D. In gender distribution, the number and percentage of males are indicated; SBP: systolic blood pressure; DBP: diastolic blood pressure; BG: blood glucose; TG: triglyceride; HDL: high density lipoprotein; UA: uric acid; HF: heart failure; CVD: cerebrovascular disease; RF: renal failure

**Supplemental Table S2. *CORIN* variant p.Arg530Ser in second independent cohort**

	Normal		Hypertension		<i>p</i> value
	Arg530	Ser530 (%)	Arg530	Ser530 (%)	
Second cohort (377 normal; 368 HP)	375	2 (0.53)	359	9 (2.44)	0.0327
First and second cohorts (677 normal; 769 HP)	674	3 (0.47)	750	19 (2.47)	0.0029

HP: hypertensive individuals.

**Supplemental Table S3. Multivariate logistic regression analysis of hypertension association in cohorts 1 and 2**

	p.Arg530Ser	Age and gender adjusted		Multivariable adjusted*	
		OR (95% CI)	<i>p</i> value	OR (95% CI)	<i>p</i> value
Cohort 1	-	1.00 (reference)	0.060	1.00 (reference)	0.034
	+	7.46 (0.92-60.56)		9.59 (1.03-89.35)	
Cohort 2	-	1.00 (reference)	0.049	1.00 (reference)	0.028
	+	4.72 (1.01-22.08)		5.86 (1.21-28.37)	
Cohorts 1 and 2	-	1.00 (reference)	0.004	1.00 (reference)	0.002
	+	6.09 (1.76-21.01)		7.40 (2.04-26.89)	

\*Adjusted for age, blood glucose, cerebrovascular disease, gender, high density lipoprotein, heart failure, renal failure, triglyceride and uric acid. CI: confidence interval; OR: odds ratio.

**Supplemental Table S4. Multivariate logistic regression analysis of hypertension association in cohorts 1 and 2 (HF excluded)**

	p.Arg530Ser	Age and gender adjusted OR (95% CI)	<i>p</i> value	Multivariable adjusted* OR (95% CI)	<i>p</i> value
Cohort 1	-	1.00 (reference)	0.060	1.00 (reference)	0.042
	+	7.46 (0.92-60.64)		10.13 (1.09-94.48)	
Cohort 2	-	1.00 (reference)	0.062	1.00 (reference)	0.04
	+	4.22 (0.88-20.12)		5.37 (1.08-26.65)	
Cohorts 1 and 2	-	1.00 (reference)	0.004	1.00 (reference)	0.002
	+	6.06 (1.75-20.91)		7.27 (2.02-26.19)	

\*Adjusted for age, blood glucose, cerebrovascular disease, gender, high density lipoprotein, renal failure, triglyceride and uric acid. CI: confidence interval; OR: odds ratio.

**Supplemental Table S5. Correlation analysis of hypertension and p.Arg530Ser in cohorts 1 and 2**

	Pearson's correlation		Partial correlation*	
	Correlation coefficient (r)	<i>P</i> value	Correlation coefficient (r)	<i>p</i> value
Cohort 1	0.090	0.022	0.097	0.014
Cohort 2	0.077	0.036	0.088	0.017
Cohorts 1 and 2	0.083	0.002	0.090	0.001

\*Cardiovascular risk factors (high density lipoprotein and triglyceride) were used as confounding variables in the analysis.

**Supplemental Table S6. Corresponding *CORIN* variants in 1000G and ExAC databases**

Variant	Corresponding Variants	
	1000G	ExAC
p.(Ser4ValfsTer26)	rs199972616	4:47839958 C/CT
p.(Tyr13Cys)	rs2289433	4:47839929 C/T
p.(Asp95Tyr)	rs186748019	4:47788868 C/A
p.(Leu334Trp)	rs185899169	4:47685768 A/C
p.(Arg349His)	not found	not found
p.(Arg525His)	rs11934749	4:47667064 T/C
p.(Arg530Ser)	not found	not found
p.(Pro866Ser)	rs575717887	4:47605630 G/A
p.(Thr924Met)	rs532940795	4:47605455 G/A

1000Genomes (1000G) database: [www.internationalgenome.org](http://www.internationalgenome.org)

ExAC database: <http://exac.broadinstitute.org>

**Supplemental Table S7. CORIN variant frequencies in 1000G and ExAC databases**

Variant	Normal in cohort 1 n (%)	1000Genomes		ExAC	
		n (%)	<i>p</i> *	n (%)	<i>p</i> *
p.(Ser4ValfsTer26)	2/300 (0.7)	15/2504 (0.6)	0.70	124/60621 (0.2)	0.13
p.(Tyr13Cys)	153/300 (51)	1284 /2504 (51.3)	0.93	27399/60689 (45.1)	0.04
p.(Asp95Tyr)	2/300 (0.7)	14/2504 (0.56)	0.69	55/60419 (0.09)	0.03
p.(Leu334Trp)	3/300 (1)	3/2504 (0.12)	0.02	46/60593 (0.08)	0.002
p.(Arg349His)	0/300 (0)	-	-	-	-
p.(Arg525His)	109/300 (36.3)	413/2504 (16.5)	<0.001	13788/60581 (22.8)	<0.001
p.(Arg530Ser)	1/300 (0.3)	-	-	-	-
p.(Pro866Ser)	0/300 (0)	1/2504 (0.04)	1	20/60594 (0.03)	1
p.(Thr924Met)	0/300 (0)	2/2504 (0.08)	1	7/60639 (0.01)	1

n: number of individuals; \**p* values vs. normal in cohort 1 by Chi-Test