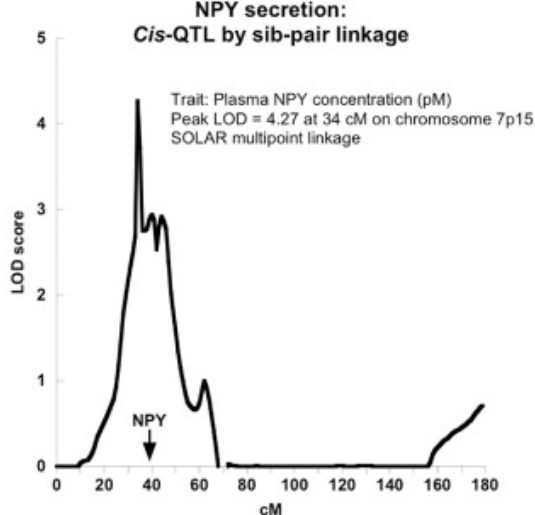
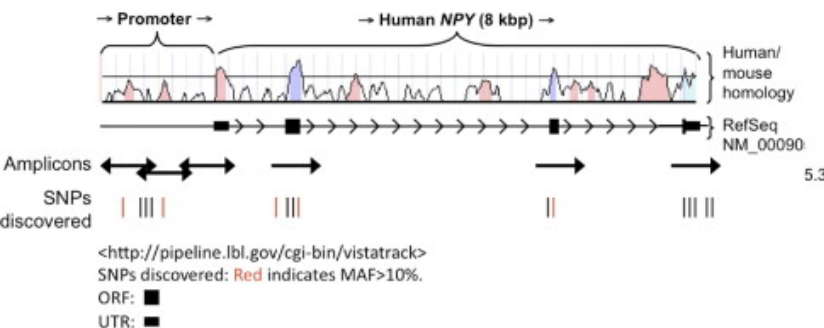


A



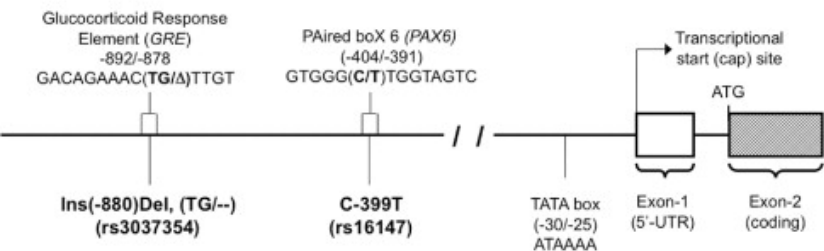
B

### Human *NPY*: Systematic polymorphism determination by re-sequencing



C

### Genetic variation in the proximal human *NPY* promoter: Impact on domains and motifs

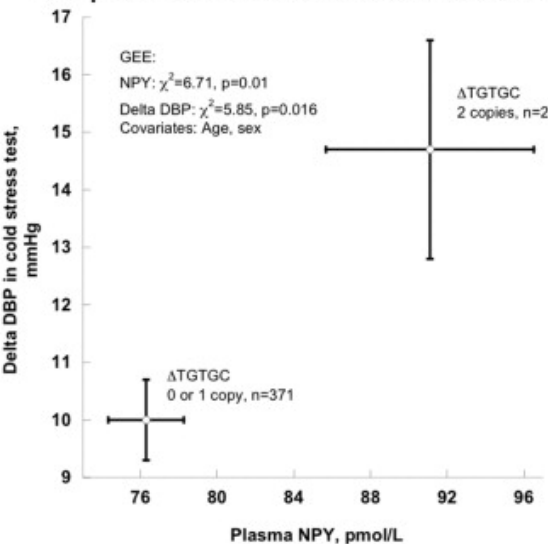


NCBI RefSeq clone: NM\_000905.2

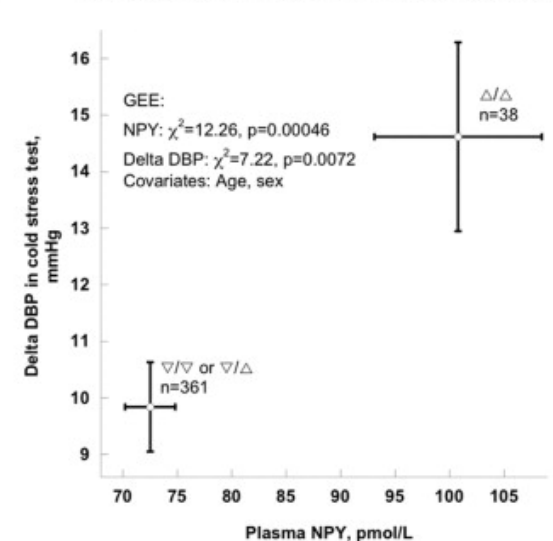
**Bold:** Polymorphic base(s).

G/C-rich domains: -49/-41, -59/-54, -105/-98, -119/-111, -126/-121, -188/-181, -213/-206, -251/-246, -335/-329, -482/-475, -494/-489, -518/-513, -615/-606

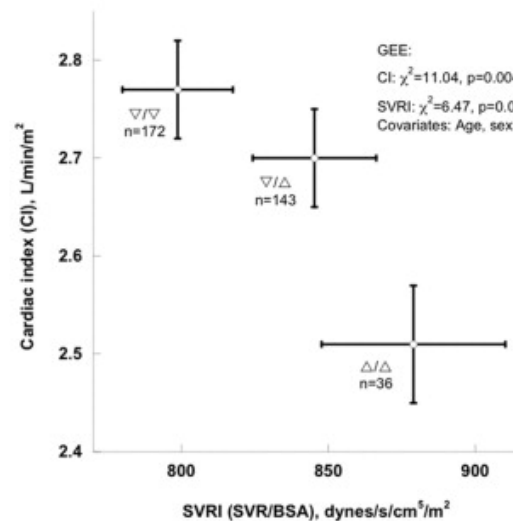
**A** Association of *NPY* haplotype  $\Delta$ TGTGC with plasma NPY and delta DBP in cold stress test



**B** Association of *NPY* promoter polymorphism  $\nabla$ -880 $\Delta$  with plasma NPY and  $\Delta$ DBP in cold stress test



**C** *NPY* promoter variant  $\nabla$ -880 $\Delta$  in twin and sibling pairs:  
Deletion variant predicts higher SVRI with lower CI



A

## *NPY* promoter common variant $\nabla$ -880 $\Delta$ (Ins/Del, TG/--): Disruption of a glucocorticoid response element (GRE) motif

### GRE and $\nabla$ -880 $\Delta$ across species

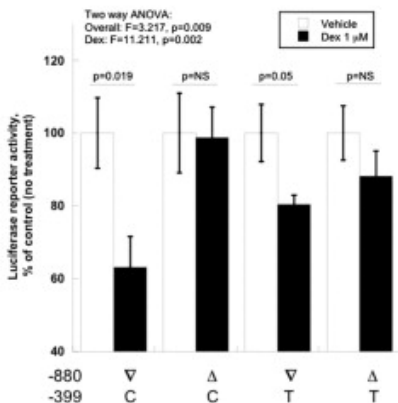
	6 bp direct	3 bp spacer	6 bp inverted	Match
GRE motif	GGTACANNNTGTTCT			
Human TG	<b>GACAGAAAC</b> TGTTGT			8/12
Human --	<b>GACAGAAAC</b> --TTGT			6/12
Chimp	<b>GACAGAAAC</b> TGTTGC			7/12
Orangutan	<b>GACAGAAAC</b> --TTGC			5/12
Marmoset	<b>GGGAGAAAT</b> TGTTGT			9/12
Horse	<b>CAGAGAAAT</b> TGCTGT			6/12
Dog	<b>AGGAGAAAT</b> TCCCGT			4/12


  
 $\nabla$ -880 $\Delta$   
 (rs3037354)

**Bold:** Sequence identity with GRE motif.  
 GRE: Glucocorticoid Response Element.

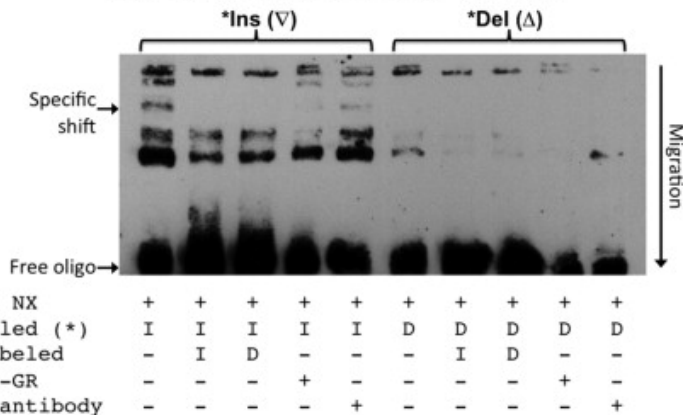
### Glucocorticoid effect on *NPY* promoter

$\nabla$ -880 $\Delta$ /C-399T haplotype expression in chromaffin cells



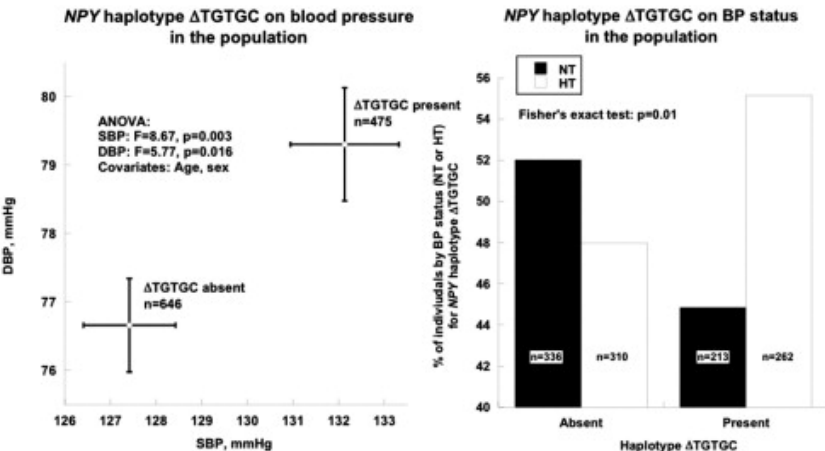
B

## Glucocorticoid receptor interaction with *NPY* promoter Ins/Del variant $\nabla$ -880 $\Delta$ (TG/--): EMSA.

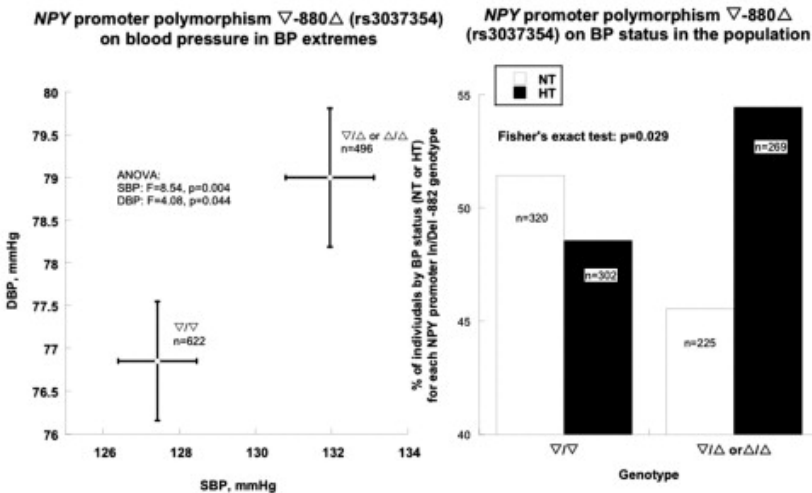


I: Insertion of TG ( $\nabla$ )  
 D: Deletion of TG ( $\Delta$ )  
 GR: Glucocorticoid Receptor  
 Ctl: Control  
 NX: Nuclear Extract

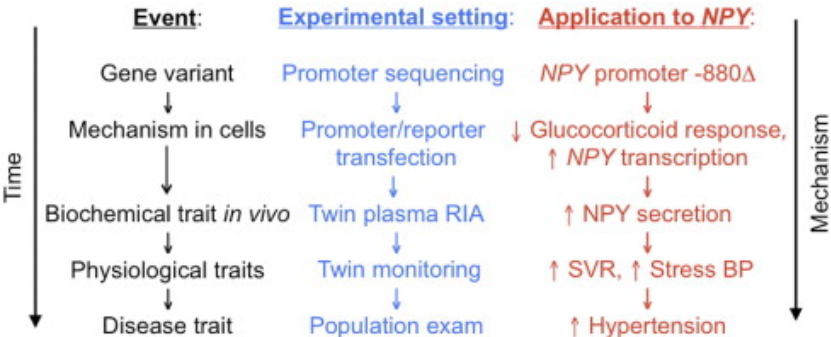
# A *NPY* haplotype $\Delta$ TGTGC on BP in the population



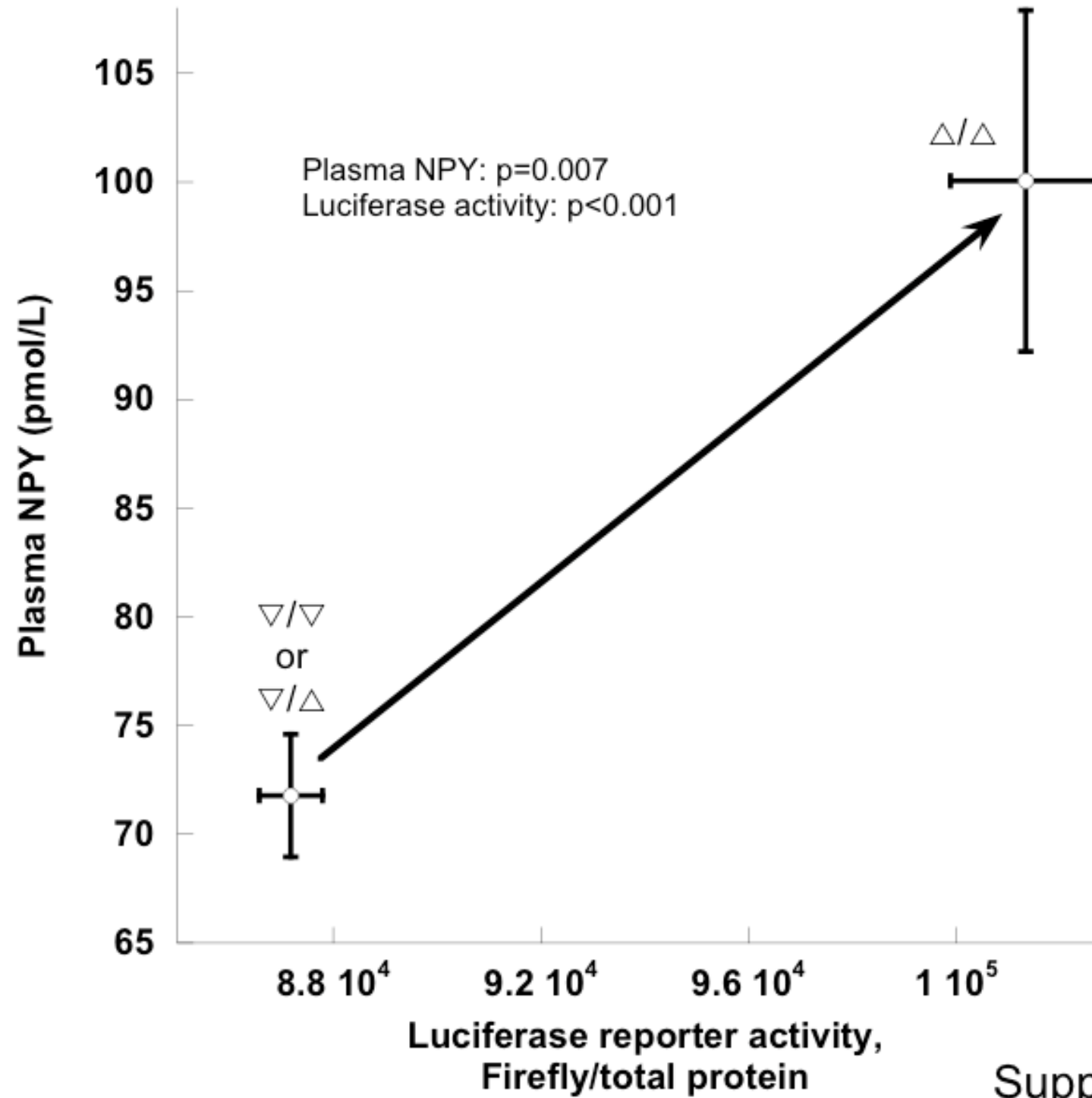
# B *NPY* promoter variant $\nabla$ -880 $\Delta$ in the population: Deletion variant predicts higher SBP/DBP and hypertension



# Human *NPY* promoter genetic variant $\nabla$ -880 $\Delta$ : Schema for effects on autonomic and disease traits



***NPY* promoter variation:  
Coordinate directional functions *in cella* and *in vivo***



Supplementary Figure 6