Kidney genes expression in hypertensive ISIAH rats

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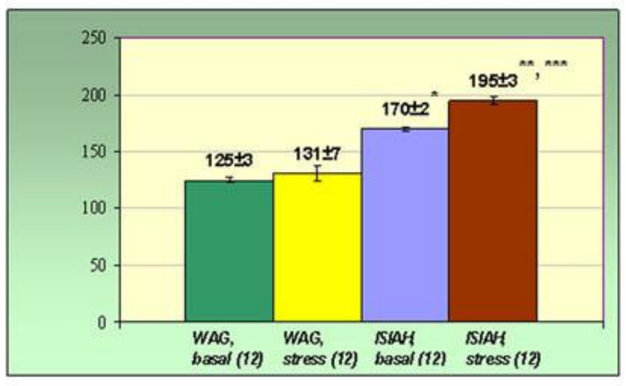
Motivation and Aim

The present study was perfomed to detect the key genes involved in the hypertensive phenotype manifestation in the ISIAH rats with inherited stress-induced arterial hypertension.

ISIAH rats was selected for increased response of systolic arterial blood pressure to a mild emotional stress caused by 30 min restriction in a cylindrical wire-mesh cage,

Basal and stress-induced BP levels in WAG and ISIAH rat strains



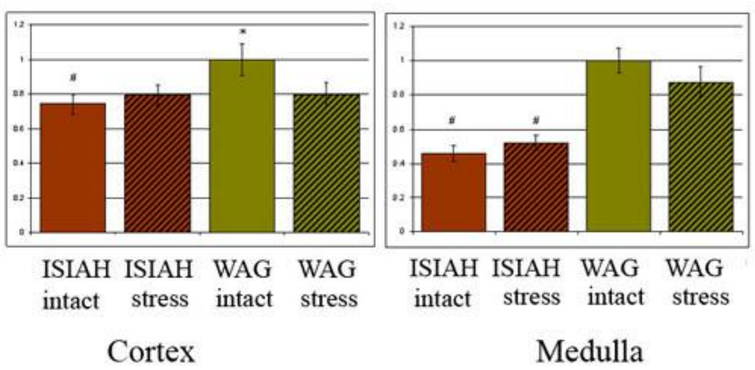
Methods

RT-PCR was performed on ABI PRISM 7000 Sequence Detector System (Applied Biosystems, USA) using a reagent kit with SYBR GreenI and reference dye ROX (Sintol, Moscow) according to manufacturer's recommendations. In each experiment studied cDNA with primers for the target gene (4 Repeats for each sample cDNA) and similar samples with primers for comparing gene (also four repeats) were placed samples in the one plate. Each cDNA sample was analyzed for the two plates. The relative level of gene expression was determined by ΔΔCt.

The results of measurement of the normotensive rats of WAG were used as a calibrator. The data obtained by RT-PCR were analised with 7000 System SDS software application in automatic mode.

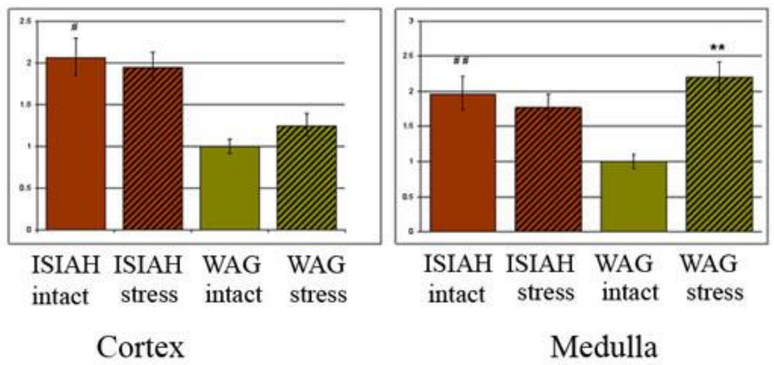
Microarray analisis (RatRef-12 expression Bead Chips, Illunina) was perfomed. Data aquisition and analys was done by BeadStudio software using gene expression module rank invariant normolization and p value < 0.01. Kidney cortex and meddula were taken from hypertensive ISIAH (n=3) and normotensive WAG (n=3) rats to detect the differentially expressed genes. Obtained data were analised by web tools DAVID.

mRNA expression of *Comt* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)



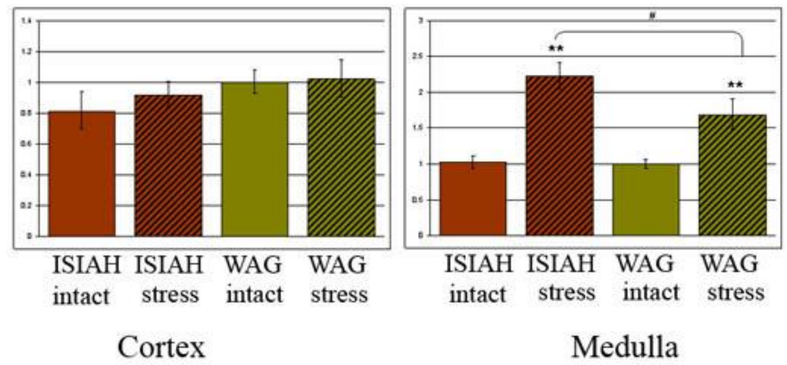
Catechol-O-methyltransferase (Comt) - catalyzes the methylation of catecholamines, causing their inactivation. Comt an enzyme that is found in many tissues, it has the highest activity in the liver and kidneys.

mRNA expression of *Egfr* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)

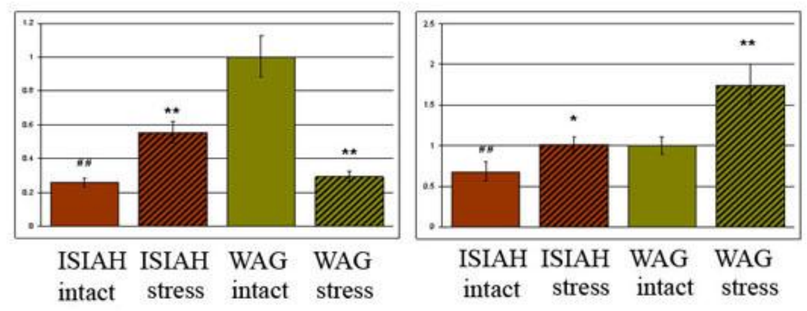


Egfr - (epidermal growth factor receptor) - is important regulators of cell proliferation and transformation. Egfr expression was demonstrated in renal vessels in particular in the afferent and efferent arterioles and in the cylindrical epithelium and mesangium. Egfr can transactivate vasoconstrictors such as: ANG II, endothelin, 1-β adrenergic agents and induces intracellular calcium mobilization.

mRNA expression of *α-ENaC* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)

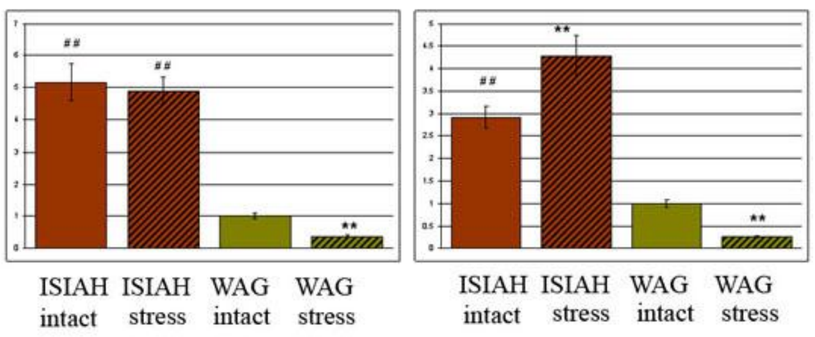


mRNA expression of *b-ENaC* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)

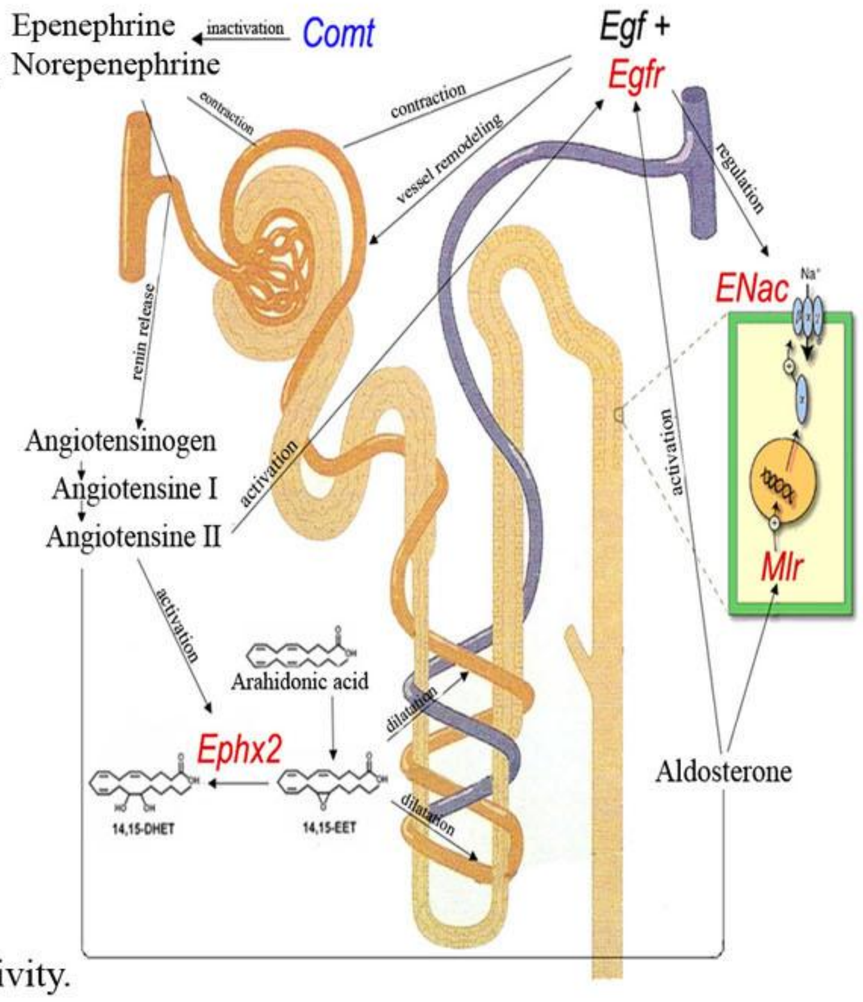


ENaC (sodium channel) - a class of ion channels, whose main function is the regulation of sodium reabsorption. It is involved in the maintenance of sodium balance, extracellular fluid volume in the body, and blood pressure.

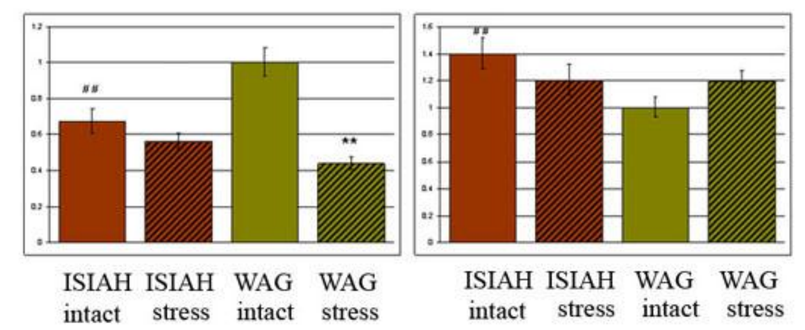
mRNA expression of *Ephx 2* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)



Ephx2 coding soluble hydrolase (sHE). sHE catalyzes degradation of endogenous epoxylipid (derivatives of arachidonic acid metabolism), such as epoxyeicosatrienoic acids (EETs) to their inactive derivatives - diols. sHE has the highest activity in the kidney. EETs are vasodilators, controls blood pressure and renal hemodynamics by adjusting the ion transport in the tubules of the kidney. EETs also inhibit platelet aggregation, increases fibrinolysis and has anti-inflammatory activity.



mRNA expression of *Mlr* gene in the cortex and medulla of the kidneys of ISIAH and WAG rats (n = 5)



Aldosterone interacts with its mineralocorticoid receptor (Mlr) and directly upregulates the mRNA levels of ENaC- .

Conclusion

Gene symbol	*Gene*	*mRNA expression ISIAH\WAG*	*Gene symbol*	*Gene*	*mRNA expression ISIAH\WAG*
cell adhesion molecule			*cell adhesion molecule*		
Cldn16	claudin 16	0.51	*Cldn9*	claudin 9	0.30
Cldn9	claudin 9	0.39	*RT1-A1*	RT1 class Ia, locus A1	7.82
RT1-A1	RT1 class Ia, locus A1	6.09	*RT1-Ba*	RT1 class II, locus Ba	0.27
RT1-CE15	RT1 class I, CE15	8.43	*Tyrosine metabolisme*		
			Aox1	aldehyde oxidase 1	0.25
			Comt	catechol-O-methyltransferase	0.22

Gene Ontology

Kidney cortex (n=3) 126 differentially expressed genes
25 related to ion binding
Kidney medulla (n=3) 65 differentially expressed genes
15 related to ion binding