COMPARATIVE PROTEOMIC ANALYSIS OF RENAL TISSUE OF NORMOTENSIVE AND HYPERTENSIVE RATS

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Comparative proteomic analysis of kidney tissue from normotensive (WKY) and spontaneously hypertensive (SHR) rats revealed quantitative and qualitative changes in renal proteins. The number of renal proteins specific for WKY rats (blood pressure 110–120 mm Hg) was 13–16. There were 20–24 renal proteins specific for SHR (blood pressure 180 mm Hg and more). The total number of identified renal proteins common for both rat strains included 972–975 proteins. A pairwise comparison of all possible (SHR-WKY) variants identified 8 proteins specific only for normotensive (WKY) animals, and 7 proteins specific only for hypertensive ones (SHR). Taking into consideration their biological roles, the lack of some enzyme proteins in hypertensive rats (for example, biliverdin reductase A) reduces the production of molecules exhibiting antihypertensive properties, while the appearance of others (e.g. betaine-homocysteine S-methyltransferase 2, septin 2, etc.) can be interpreted as a compensatory reaction. Renal proteins with altered relative content (with more than 2.5-fold change) accounted for no more than 5% of all identified proteins. Among the proteins with an increased relative content in the hypertensive animals, the largest group consisted of proteins involved in the processes of energy generation and carbohydrate metabolism, as well as antioxidant and protective proteins. In the context of the development of hypertension, the identified relative changes can apparently be considered compensatory. Among the proteins with the most pronounced decrease in the relative content in the hypertensive rats, the dramatic reduction in acyl-CoA medium-chain synthetase-3 (ACSM3) appears to make an important contribution to the development of renal pathology in these animals.

Key words: arterial hypertension; WKY and SHR rats; renal tissue proteomic profiling

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INTRODUCTION

The spontaneously hypertensive rats (SHR) represent a convenient model reproducing the major symptoms of essential hypertension in humans [1]. Increased blood pressure in these animals begins at 6–7 weeks of age, reaching the level of stable hypertension by 17–19 weeks [1]. Similar to hypertension in humans, the development of hypertension in SHR is accompanied by renal damage similar to nephropathy in hypertensive patients [2–4]. The susceptibility of SHR to hypertensive kidney disease has been associated with both specific [4] and multiple independent genomic loci [5]. Although comparison of the relative content of renal proteins in SHR animals and the control strain of rats (Wistar Kyoto; WKY), used for creation of the SHR strain, has been carried out in a number of studied [6, 7], the role of differentially expressed proteins in the development of renal pathology still remains insufficiently studied [6].

Therefore, the aim of this study was to perform a proteomic analysis of the kidneys of SHR animals (with the blood pressure level of 180 mmHg) and normotensive WKY rats.

MATERIALS AND METHODS

Reagents

The following reagents were used in this study: ammonium bicarbonate, dithiothreitol, urea, guanidine hydrochloride, sodium chloride, Triton X-100, 4-vinylpyridine, Coomassie brilliant blue G-250 (Merck, USA); formic acid, sodium hydroxide (Acros Organics, USA), acetonitrile (Fisher Chemical, UK); isopropanol, trifluoroacetic acid (Fluka, USA); tris-(2-carboxyethyl)phosphine (Pierce, USA); modified trypsin (mass spectrometry grade, Promega, USA). Other reagents of the highest purity available were from local suppliers.

Experimental Animals

Male 14-week-old WKY rats (n=6; blood pressure 110–120 mm Hg) and SHR (n=5; blood pressure 180 mm Hg or more) were used in experiments. The animals were obtained from the Nursery of the laboratory animals (Pushchino branch of the M.M. Shemyakin and Yu.A. Ovchinnikov Institute of Bioorganic Chemistry RAS). The animals were decapitated under light ether anesthesia; the kidneys were quickly removed, immediately frozen and stored at -70°C until the study.

Preparation of Lysates of Kidney Homogenates

Kidney tissue was homogenized using a Heidolph SilentCrusher homogenizer (50,000 rpm) in 0.05 M potassium phosphate buffer (pH 7.4) and diluted in it to the final protein concentration of 30 mg/ml. To evaluate relative quantitative changes in renal proteins the same amount of total protein was used during sample preparation; it was controlled using the Bradford method [8]. After incubation in the presence of 3% Triton X-100 (4°C, 1 h), the lysates were diluted 3 times with the same buffer and centrifuged for 30 min at 16,000 *g* to obtain a cleared supernatant.

Sample preparation for mass spectrometric analysis (protein extraction, alkylation and trypsinolysis) was carried out as described previously [9].

Mass Spectrometric Analysis and Statistical Data Processing

The conditions for mass spectrometric analysis are given in detail in [10]. Proteins were identified by 2 or more peptides; their amino acid sequences were identified on the basis of tandem mass spectra, and the identified proteins were registered at least in two of three technical replicates.

To identify differences in the distribution of proteins in samples, statistical analysis based on the LFQ (Label Free Quantitation) values of the identified proteins was used. Determination of proteins that were statistically significantly different between samples was carried out using a Volcano plot created by Perseus application using Log2(LFQ) values with the cutoff parameters FDR = 0.05 and S0 = 1 (difference in LFQ content more than two times). Using a Volcano plot based on a *t*-test, proteins with peptide signal intensities differed significantly between samples have been identified. The Supplementary Materials list the most significant proteins with a difference in the LFQ content of more than two times and (-Log P) >1.3.

RESULTS AND DISCUSSION

Venn diagrams constructed during pairwise comparisons of renal samples from SHR-WKY rats illustrate the similarities and differences in the protein composition of the compared samples. Figure 1 shows such a diagram for one of the pairs of samples. In other cases, almost identical results have been obtained: proteins specific to animals of the WKY strain varied in the range of 13–16, proteins specific to SHR varied in the range 24–28; 972–975 proteins were common proteins for both strains.

All possible pairwise comparisons resulted in identification of 8 proteins, which were found exclusively in the kidneys of control rats (Fig. 2, Table 1). For half of these proteins, good evidence

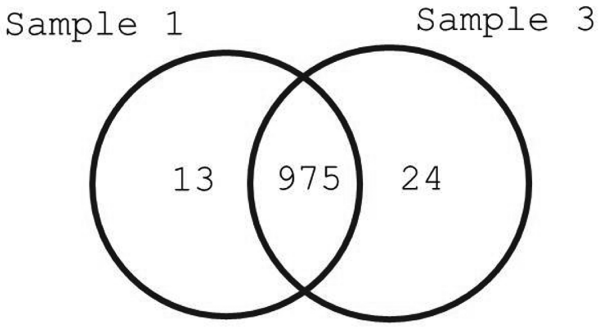

Figure 1. Distribution of protein identifications between samples 1-3 (control and hypertensive rats).

exists in the literature for their association with hypertension and/or renal failure. These include phosphopyruvate hydratase [11], Ras-related protein Rab-11A [12], a kinesin-like protein [13], and biliverdin reductase A [14]. In the context of the development of hypertension, biliverdin reductase A (BVRA) is of particular interest. This enzyme (EC 1.3.1.24) catalyzes the reduction of biliverdin to bilirubin, which lowers blood pressure, improves renal blood flow and acts as a selective ligand for PPARα receptors that promote blood pressure lowering [14]. Mice lacking the gene encoding this enzyme are characterized by a 100-fold decrease in the bilirubin level and an increase in parameters of endogenous oxidative stress [15]. In this regard, the lack of detectable amounts of BVRA in SHR apparently contributes to the development of hypertension.

Among 7 proteins found exclusively in the kidneys of the hypertensive rats, they all were associated with the development of cardiovascular pathology (Fig. 3, Table 1). These include multidrug and toxin extrusion protein 1 [15], prefoldin (subunit 5) [16, 17], coatomer (delta subunit) [18], ubiquitin-conjugating enzyme E2 V2 [19], septin-2 [20, 21], prominin 1 [22, 23], and betaine homocysteine S-methyltransferase 2 (BHMT2) [24, 25]. For example, the enzyme betaine-homocysteine S-methyltransferase (EC 2.1.1.5) catalyzes homocysteine remethylation to methionine using betaine as a methyl group donor. Taking into consideration known data on the association of homocysteine with blood pressure levels [24, 26], as well as the decrease in plasma betaine levels in hypertensive patients on dialysis [26], the detection of BHMT2 specifically in the kidneys of the hypertensive rats indicates an important role of this enzyme in the development of hypertension. Septin-2, a member of a highly conserved family of cytoskeletal GTPases, attenuates some effects of the pressor hormone angiotensin II on cells [27].

Besides qualitative differences, significant changes in the relative protein content were found in the kidney proteomes of hypertensive (SHR) rats as compared to control normotensive rats (WKY). Figure 4 shows, as an example, a Volcano diagram comparing proteins

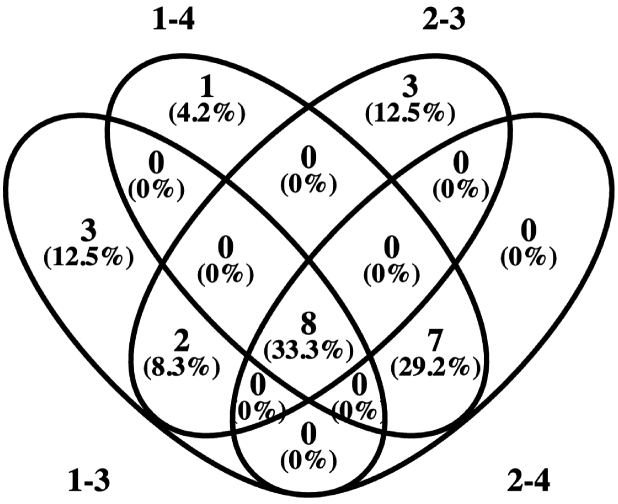

Figure 2. A Venn diagram. Proteins found exclusively in the kidneys of control rats (data from four experiments).

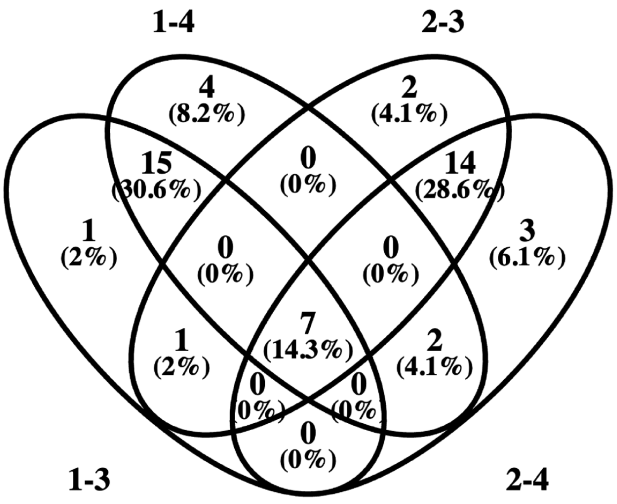

Figure 3. A Venn diagram. Proteins found exclusively in the kidneys of hypertensive rats (data from four experiments).

Table 1. Proteomic identification of renal proteins found exclusively in control normotensive and hypertensive rats (results of four experiments)

#	Uniprot accession No.	Uniprot gene name	Uniprot protein name	Function	Localization	Role in cardiovascular pathology (refs.)
Found exclusively in control rats						
1	A0A8I5ZMA1	*Eno2*	Phosphopyruvate hydratase	1	C	[11]
2	A0A8I6AA65	*Rab11a*	Ras-related protein Rab-11A	2	PM, Ve, G, M	[12]
3	A0A8L2QCP8	*Kif5b*	Kinesin-like protein	2	Ve, Mch, Mictotub	[13]
4	A0A142BM04	*unreviewed*	Anti-F4/80 kappa light chain variable region	4	C	—
5	A0JN30	*Cnpy2*	Canopy FGF signaling regulator 2	3	ER	—
6	D3ZRN3	*Actbl2*	Actin, beta-like 2	2	C	—
7	Q6AZ33	*Blvra*	Biliverdin reductase A	3	C	[14]
8	Q9JJI4	*Mup4l1*	Alpha-2u globulin	3	Mch, S	—
Found exclusively in hypertensive rats						
1	A0A8I5ZRP9	*Slc47a1*	Multidrug and toxin extrusion protein 1	2	M	[15]
2	A0A8I5Y1V4	*Pfdn5*	Prefoldin subunit 5	4	C	[16, 17]
3	A0A8I5ZSE6	*Arcn1*	Coatomer subunit delta	2	C, M, G, Ve	[18]
4	A0A0G2JU07	*Ube2v2*	Ubiquitin conjugating enzyme E2 V2	6	N, C	[19]
5	A0A8L2QCZ9	*Septin2*	Septin-2	2	C, M	[20, 21]
6	A0A8I6GLV7	*Prom1*	Prominin 1	3	M	[22, 23]
7	F1LMG2	*Bhmt2*	Betaine-homocysteine S-methyltransferase 2	6	N, C	[24, 25]

Here and in other tables, the numbers in the column "Function" indicate the following functional groups of proteins: *1*. Proteins/enzymes involved in the processes of energy generation and carbohydrate metabolism. *2*. Proteins involved in the formation of the cytoskeleton, transport and exocytosis. *3*. Proteins involved in signal transduction and regulation of enzyme activity. *4*. Antioxidant and protective proteins/enzymes. *5*. Proteins involved in regulation of gene expression, cell division, and differentiation. *6*. Enzymes involved in metabolism of proteins, amino acids and other nitrogenous compounds. *7*. Enzymes involved in lipid metabolism. Localization of proteins: C – cytoplasm, N – nucleus, M – membranes, PM – plasma membrane, Mch – mitochondria, ER – endoplasmic reticulum, G – Golgi complex, L – lysosomes, Mictotub – microtubules, Ve – vesicles, Per – peroxisomes, S – secretory proteins, Extra – extracellular space.

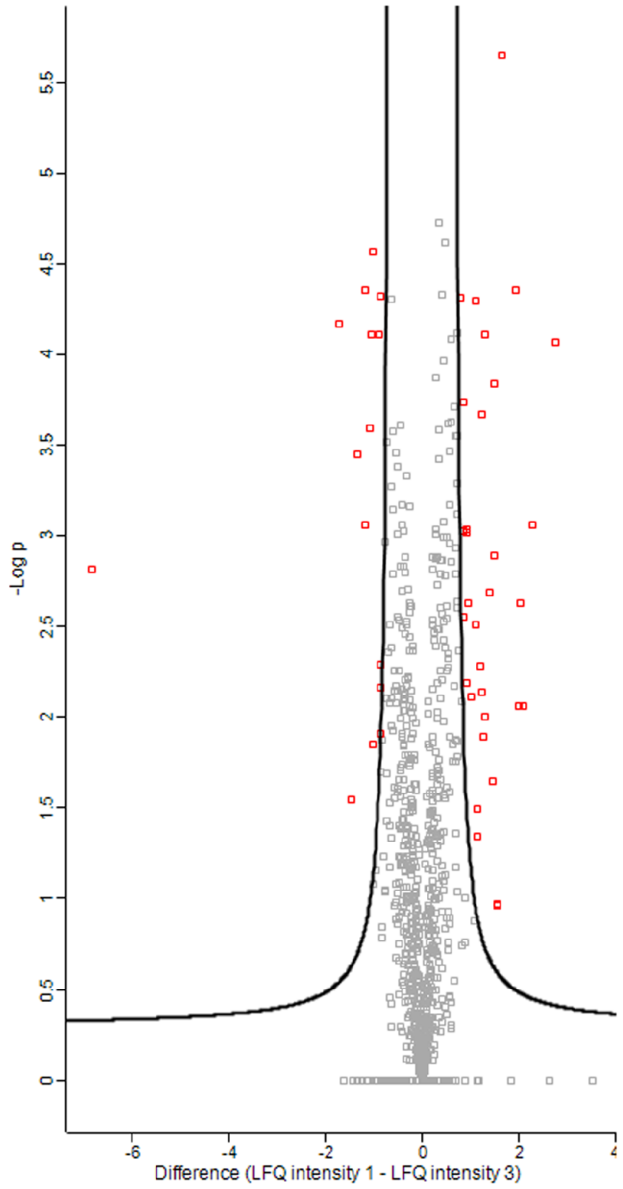

Figure 4. A Volcano diagram comparing proteins of samples 1-3. The x-axis shows log2(LFQ) difference range, the y-axis shows statistical significance, proteins with statistically significant differences are marked in red, proteins with statistically insignificant differences are marked in gray. Points in the area of negative values belong to proteins whose peptide signal intensity is higher in sample 3. Points in the area of positive values belong to proteins whose peptide signal intensity is higher in sample 1. The color version of this figure is available in the electronic version of the article.

from samples 1–3. Tables 2 and 3 list proteins whose content increases (Table 2) or decreases (Table 3) in the kidneys of the hypertensive rats as compared to control animals. These tables (2 and 3) show the proteins whose relative abundance changes are the most pronounced and are shown for at least two pairs of experiments. All the significant results of changes in the relative protein content in the kidneys of SHR rats compared to control animals are given in Supplementary Materials (Tables S1–S8).

Tables 2 and 4 show that among the proteins whose relative content increased in hypertensive animals, the largest group included proteins involved in the processes of energy generation and carbohydrate metabolism. These are cytochrome *c* oxidase, subunits of the NADH dehydrogenase complex, ATP synthase, as well as dihydrolipoyl dehydrogenase, a component of multienzyme mitochondrial complexes of keto acid dehydrogenases (Table 2, Fig. 5). In SHR animals, the relative content of most of these proteins increased by 6–8 times as compared to control rats. This is consistent with data on an increase in ATP production in the mitochondria of SHR kidney proximal tubule cells compared to WKY [37]. Interestingly, in the context of increased activity of the pyruvate dehydrogenase complex (PDH) in the kidneys of hypertensive rats [37], our experiments revealed an increase in the relative content of not only dihydrolipoyl dehydrogenase (the E3 component of PDH), but also the pyruvate transport protein responsible for pyruvate transport through the inner mitochondrial membrane (Table 2, Fig. 5).

The hypertensive rats had significantly higher relative levels of renal antioxidant and protective proteins than in control normotensive rats. For example, the relative contents of superoxide dismutase and glutathione S-transferase were almost 7-fold and 4-fold higher than in control normotensive rats, respectively (Table 2, Fig. 5). There is evidence in the literature that changes in the activity of both of these enzymes correlate with the development of hypertension [31, 28]. The content of immunoglobulin light chain kappa was strongly increased (almost 15 times) in SHR animals (Table 2, Fig. 5).

In the hypertensive rats, compared to control animals, the relative content of calmodulin was more than 7-fold than in control normotensive rats. This is consistent with previously published data on increased activity of this regulatory protein in the kidneys and hearts of hypertensive animals [35].

The highest (almost 18-fold) change in the relative content of SHR renal proteins was found for type VI collagen. This protein is the main component of the basement membrane. Certain evidence exists in the literature that specific nephropathy in patients with hypertension is accompanied by deposition of this protein in the renal glomeruli [29].

A 2-fold (or more pronounced) reduction in the relative renal protein content in the hypertensive animals was observed for proteins belonging to various functional groups (Tables 3, 4, Fig. 6). In the vast majority of cases, these proteins are known to play a certain role in the development of cardiovascular pathology [33, 38–53]. The most pronounced decrease in the kidneys of SHR rats was observed in the relative content of renal mitochondrial acyl-CoA medium-chain synthetase-3 (ACSM3) (ACSM3, 0.007 versus 1 in the control, i.e. decreased by more than 140 times) (Table 3, Fig. 6). Knockout

Table 2. Proteomic identification of renal proteins with increased relative content in hypertensive rats in comparison with normotensive rats (proteins with the most pronounced relative increase versus control are shown)

#	Uniprot accession No.	Uniprot gene name	Uniprot protein name	Function	Localization	-Log(P-value)	Fold change	Role in cardiovascular pathology (refs.)
1	P01835	*IGKC*	Ig kappa chain C region, B allele	4	C	2.108	14.777	—
2	G3V983	*Gstm1*	Glutathione S-transferase	4	C, Mch, ER, N, PM	3.688	4.181	[28]
3	F1LQM1	*Mup4l1*	Alpha-2u-globulin (L type)	3	S	4.546	7.095	—
4	A0A8I5ZTR6	*Col6a3*	Collagen type VI alpha 3 chain	2	S	3.150	17.816	[29]
5	Q6PDV1	*Lyz2*	Lysozyme	6	C	4.358	3.846	[30]
6	B5DEL8	*Ndufs5*	NADH dehydrogenase [ubiquinone] iron-sulfur protein 5	1	Mch, M	2.940	3.379	—
7	Q6LDS4	*Sod1*	Superoxide dismutase [Cu-Zn]	4	Mch, L	6.249	6.879	[31]
8	P12075	*Cox5b*	Cytochrome *c* oxidase subunit 5B, mitochondrial	1	Mch	2.752	8.146	[32]
9	P38718	*Mpc2*	Mitochondrial pyruvate carrier 2	2	Mch	2.126	7.222	[33]
10	G3V7Y3	*Atp5f1d*	ATP synthase F1 subunit delta	1	Mch	2.741	5.788	[34]
11	A0A8I5ZR70	*Rdx*	Radixin	2	PM, C, M	3.592	4.508	—
12	P25093	*Fah*	Fumarylacetoacetase	6	C	1.318	3.651	—
13	A0A8I6AN99	*Ubb-ps1*	Ubiquitin B, pseudogene 1	6	C, N	3.153	3.008	—
14	Q5RJN0	*Ndufs7*	NADH dehydrogenase [ubiquinone] iron-sulfur protein 7, mitochondrial	1	Mch	3.415	4.395	—
15	P0DP31	*Calm3*	Calmodulin-3	3	C	2.299	7.432	[35]
16	A0A8I5ZTF9	*Akr1b1*	Aldo-keto reductase family 1 member B1	7	C	4.428	4.815	—
17	B2RZC1	*Rbp4*	Retinol-binding protein	2	S	3.032	3.379	—
18	A0A8I5ZXS2	*Dld*	Dihydrolipoyl dehydrogenase	1	Mch, Ve	3.551	3.010	—
19	P27139	*Ca2*	Carbonic anhydrase 2	3	C, PM	4.595	2.867	[36]
20	P20760	*Igg-2a*	Ig gamma-2A chain C region	4	PM	4.614	4.316	—
21	P11030	*Dbi*	Acyl-CoA-binding protein	7	ER, G	1.579	3.620	—

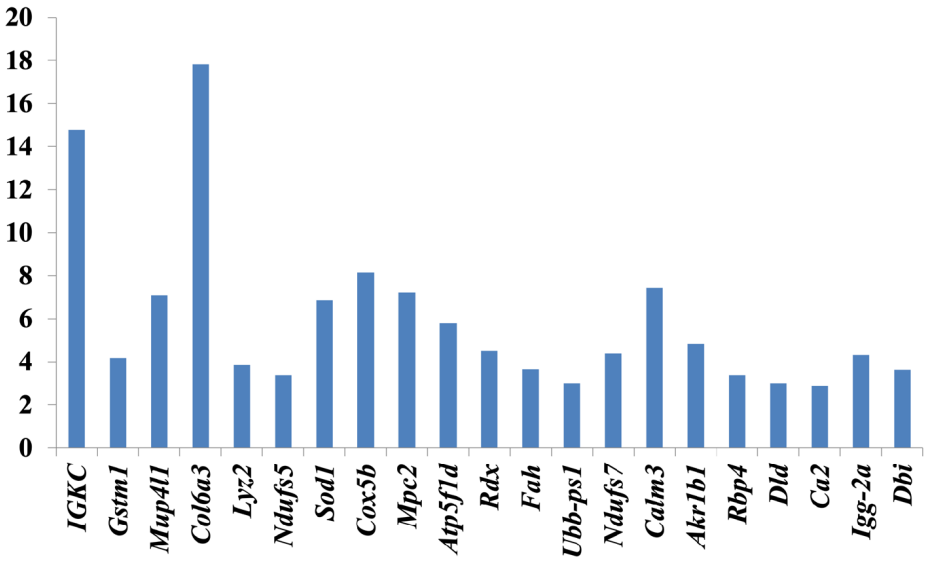

Figure 5. Renal proteins of hypertensive rats with the most pronounced increase in the relative content as compared to control animals (are indicated using gene names of corresponding proteins).

Table 3. Proteomic identification of renal proteins with decreased relative content in hypertensive rats in comparison with normotensive rats (proteins with the most pronounced relative increase versus control are shown)

#	Uniprot accession No.	Uniprot gene name	Uniprot protein name	Function	Localization	-Log(P-value)	Fold change	Role in cardiovascular pathology (refs.)
1	Q9WVK3	*Pecr*	Peroxisomal trans-2-enoyl-CoA reductase	7	Per	4.372	0.289	—
2	Q6SKG1	*Acsm3*	Acyl-coenzyme A synthetase ACSM3, mitochondrial	7	Mch	2.896	0.007	[38]
3	Q91ZW6	*Tmlhe*	Trimethyllysine dioxygenase, mitochondrial	6	Mch	3.879	0.294	[39]
4	P07171	*Calb1*	Calbindin	3	C, N, S	4.868	0.414	[40, 41]
5	A0A8I6AI74	*Ywhah*	Tyrosine 3-monooxygenase/ tryptophan 5-monooxygenase activation protein, eta	3	C	3.447	0.394	—
6	D4A1D8	*Surf4*	Surfeit locus protein 4	2	ER, G, M	2.363	0.296	—
7	A0A8I5ZLR0	*Gstt3*	Glutathione transferase	4	C, Mch, ER, N, PM	4.597	0.420	[42, 43]
8	A0A8L2UH84	*Pebp1*	Phosphatidylethanolamine binding protein 1	3	C	4.114	0.483	—
9	A0A8I6A9U0	*Fgb*	Fibrinogen beta chain	3	S	2.934	0.408	—
10	Q562C3	*Gcat*	Glycine C-acetyltransferase (2-amino-3-ketobutyrate-coenzyme A ligase)	6	Mch, N	2.240	0.483	[44, 45]
11	A0A8I6AH82	*Xylb*	Xylulose kinase	1		2.691	0.481	[46]
12	D4A4D5	*Rplp2*	Large ribosomal subunit protein P2	5	C	2.480	0.325	—
13	P85971	*Pgls*	6-phosphogluconolactonase	1	C	2.326	0.399	[47]
14	A0A0G2JUM0	*Sult1c2*	Sulfotransferase	4	C, L	2.983	0.471	[48, 49]
15	D4AE56	*Ptges2*	Prostaglandin E synthase 2	7	M	1.782	0.403	[50]
16	A0A8I6A9B3	*Hspa12a*	Heat shock protein family A (Hsp70) member 12A	4	C, M, Mch	1.870	0.386	[51]
17	D3ZNJ5	*Inmt*	Indolethylamine N-methyltransferase	4	C	3.379	0.162	—
18	A0A8L2R5Y9	*Arl8b*	Small monomeric GTPase	3	C, M	2.096	0.430	[52]
19	A0A8I5ZV58	*Aass*	Aminoadipate-semialdehyde synthase	6	Mch	2.941	0.410	[53]
20	B2RYS0	*Cox7a2*	Cytochrome *c* oxidase subunit 7A2, mitochondrial	1	Mch	3.207	0.228	[32]

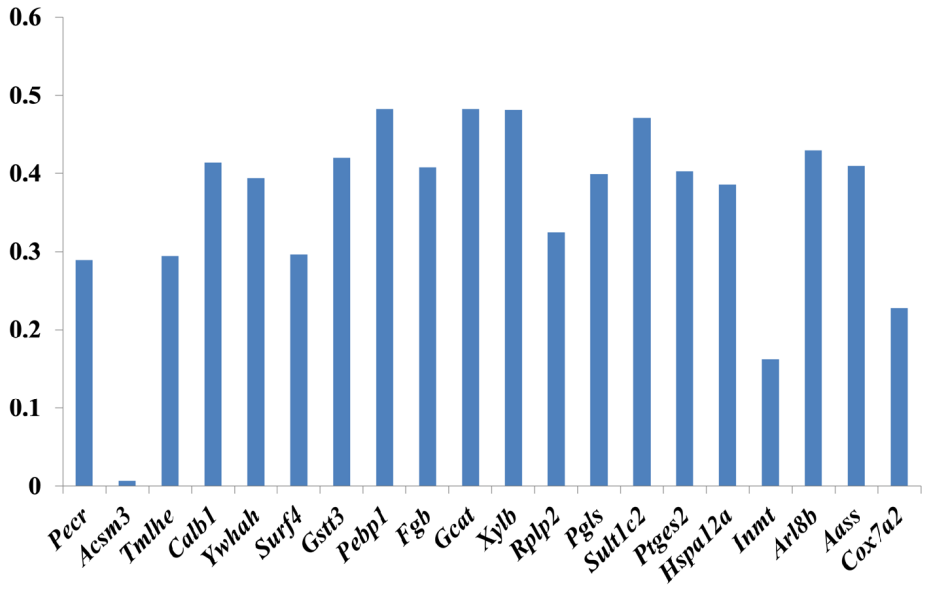

Figure 6. Renal proteins of hypertensive rats with the most pronounced decrease in the relative content as compared to control animals (are indicated using gene names of corresponding proteins).

Table 4. Functional distribution of renal proteins with altered relative content in hypertensive (SHR) rate in comparison of control normotensive (WKY) rats

Functional groups	Increased relative content	Decreased relative content
1. Proteins/enzymes involved in the processes of energy generation and carbohydrate metabolism	5	3
2. Proteins involved in the formation of the cytoskeleton, transport and exocytosis	4	1
3. Proteins involved in signal transduction and regulation of enzyme activity	3	5
4. Antioxidant and protective proteins/enzymes	4	4
5. Proteins involved in regulation of gene expression, cell division, and differentiation	0	2
6. Enzymes involved in metabolism of proteins, amino acids and other nitrogenous compounds	3	3
7. Enzymes involved in lipid metabolism	2	3
Total	21	20

of the gene encoding this enzyme in mice was accompanied by impaired glucose and lipid metabolism, mitochondrial dysfunction with a decrease in ATP formation and an increase in reactive oxygen species [54]. Taking these data into account, it appears that a dramatic decrease in ACSM3 contributes to the development of metabolic syndrome, which, in turn, provokes the further development of renal pathology [55].

CONCLUSIONS

Proteomic profiling of the kidneys of normotensive WKY rats and hypertensive rats (SHR), revealed quantitative and qualitative changes in a number of renal proteins. The qualitative changes were found for 8 proteins specific for normotensive rats and 7 proteins specific for the hypertensive rats. Taking into consideration their biological role, the absence of some enzyme proteins in hypertensive rats (for example, biliverdin reductase A) reduces the production of molecules exhibiting antihypertensive properties, while the appearance of others (e.g., betaine-homocysteine S-methyltransferase 2, septin 2, etc.) can be interpreted as a compensatory reaction. Proteins whose relative content changed in the kidneys by at least 2.5 times accounted for no more than 5% of all identified proteins. Among the proteins with an increased relative content in hypertensive animals, the largest group consisted of proteins involved in the processes of energy generation and carbohydrate metabolism, as well as antioxidant and protective proteins. These changes can also be considered as compensatory for the development of hypertension. Among the proteins with the most pronounced decrease in the relative content in the hypertensive rats, the dramatic reduction in acyl-CoA medium-chain synthetase-3 (ACSM3) appears to make an important contribution to the development of renal pathology in these animals.

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COMPLIANCE WITH ETHICAL STANDARDS

The experiments were carried out in compliance with generally accepted norms of humane treatment of laboratory animals. The work was carried out in accordance with the Order of the Ministry of Health of the Russian Federation No. 199n of April 1, 2016 “On Approval of the Rules for Good Laboratory Practice” and the Directive 2010/63/EU of the European Parliament and of the Council of the European Union of September 22, 2010 on the protection of animals used for scientific purposes.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

Supplementary materials are available in the electronic version at the journal site (pbmc.ibmc.msk.ru).

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СРАВНИТЕЛЬНЫЙ ПРОТЕОМНЫЙ АНАЛИЗ ПОЧЕЧНОЙ ТКАНИ НОРМОТЕНЗИВНЫХ И ГИПЕРТЕНЗИВНЫХ КРЫС

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Сравнительный протеомный анализ почечной ткани нормотензивных (WKY) и гипертензивных (SHR) крыс выявил количественные и качественные изменения ряда белков. Специфичные для животных линии WKY (артериальное давление 110–120 мм рт. ст.) белки почек варьировали в диапазоне 13–16, специфичные для SHR (артериальное давление 180 мм рт. ст. и более) — 24–28, а общее число идентифицированных для обеих линий белков составило 972–975. При попарном сравнении всех возможных (SHR-WKY) вариантов идентифицированы 8 белков, специфичных только для нормотензивных животных, и 7 — только для гипертензивных. С учётом их биологической роли, отсутствие одних белков-ферментов у крыс-гипертоников (например, биливердинредуктаза А) снижает выработку молекул, проявляющих гипотензивные свойства, а появление других (бетаин-гомоцистеин S-метилтрансфераза 2, септин 2 и др.) может быть интерпретировано как компенсаторная реакция. На долю белков, относительное содержание которых менялось в почках не менее 2,5 раз, пришлось не более 5% всех идентифицированных белков. Среди белков, относительное содержание которых увеличивалось у гипертонических животных, наибольшую группу составляли белки, участвующие в процессах генерации энергии и углеводного обмена, а также антиоксидантные и защитные белки. В контексте развития гипертонии выявленные изменения, по-видимому, могут рассматриваться как компенсаторные. Среди белков, относительное содержание которых у крыс-гипертоников снизилось наиболее сильно, драматическое снижение ацил-КоА-синтетазы среднецепочечных жирных кислот (ACSM3), по-видимому, вносит важный вклад в развитие почечной патологии у этих животных.

Полный текст статьи на русском языке доступен на сайте журнала (http://pbmc.ibmc.msk.ru).

Ключевые слова: артериальная гипертония; крысы WKY и SHR; протеомное профилирование ткани почек

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