SESSION X

AGING

Friday (September 17, 2021; 10:45 – 13:55)

Chair:

Prof. Zbigniew Kmiec
Department of Histology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland

DETAILED SESSION X SCHEDULE

Opening lectures (Friday, September 17, 2021; 11:10 – 12:15; *virtual stream A/B*)

S10.L1 AGE-RELATED CHANGES IN THE REGULATION OF ENERGY BALANCE: THE ROLE OF ALTERED HYPOTHALAMIC NEUROPEPTIDE ACTIVITY IN THE DEVELOPMENT OF MIDDLE-AGED OBESITY AND AGING ANOREXIA. **M. Balasko, M. Szekely, E. Petervari** (Institute for Translational Medicine, Medical School, University of Pecs, Pecs, Hungary).

S10.L2 NK CELLS AT THE CROSSROADS OF INNATE AND ADAPTIVE IMMUNITY IN THE PROCESS OF AGING. **L. Kaszubowska** (Medical University of Gdansk, Gdansk, Poland).

Oral presentations (Friday, September 17, 2021; 12:15 – 13:55; *virtual stream A/B*)

S10.L3 THE POSITIVE EFFECT OF 12 WEEKS OF DANCE TRAINING ON THE AMYLOID PRECURSOR PROTEIN, SEROTONIN CONCENTRATION AND PHYSICAL PERFORMANCE IN ELDERLY WOMEN. **E. Rodziewicz-Flis[1], M. Kawa[1], W. Skrobot[2], D.J. Flis[3], J.J. Kaczor[3]** ([1]Departments of Manual and Physical Therapy, Gdansk University of Physical Education and Sport, Gdansk, Poland, [2]Functional Diagnostic and Kinesiology, Gdansk University of Physical Education and Sport, Gdansk, Poland, [3]Physiology and Biochemistry, Gdansk University of Physical Education and Sport, Gdansk, Poland).

S10.L4 DIFFERENT MOVEMENT CADENCES INDUCES PSYCHOPHYSIOLOGICAL CHANGES IN ELDERLY MEN. **W. Barbosa[1], P. Zovico, C. Reis[1], R. Rica[2], D. Bocalini[1]** ([1]Laboratorio de Fisiologia e Bioquimica Experimental, Universidade Estacio de Sa, Vitoria, ES, Brasil, [2]Centro de Educacao Fisica e Desporto, Universidade Federal do Espirito Santo (UFES), Vitoria, ES, Brasil).

S10.L5 POTENTIAL ROLE OF SEX HORMONE-BINDING GLOBULIN IN THE DEVELOPMENT OF ENDOTHELIAL DYSFUNCTION IN OLDER MEN. **M. Grandys[1], J. Majerczak[2], M. Frolow[3], R. Nizankowski[3], S. Chlopicki[4,5], J.A. Zoladz[1]** ([1]Department of Muscle Physiology, Chair of Physiology and Biochemistry, University School of Physical Education, Krakow, Poland, [2]Department of Neurobiology, Poznan University of Physical Education, Poznan, Poland, [3]Laboratory of Clinical Pharmacology of Endothelium, Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Krakow, Poland, [4] Jagiellonian Centre for Experimental Therapeutics, Jagiellonian University, Krakow, Poland, [5]Department of Experimental Pharmacology, Chair of Pharmacology, Jagiellonian University Medical College, Krakow, Poland).

S10.L6 OXI-INFLAMMATORY RESPONSE IN AGEING. **E. Wacka, B. Morawin, A. Tylutka, A. Zembron-Lacny** (Department of Applied and Clinical Physiology, Collegium Medicum University of Zielona Gora, Zielona Gora, Poland).

S10.L7 INFLUENCE OF DEHYDRATION ON LIPID METABOLISM OF AGED MALE RATS. **S.Q.Cognuck[1], W.L. Reis[2], M.S. Silva[1], S.V. Zorro[3], G. Almeida-Pereira[1], L.K. de Barba[1], L.L.K. Elias[1], J. Antunes-Rodrigues[1]** ([1]Physiology Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil, [2]Department of Physiological Science, Center of Biological Sciences, Federal University of Santa Catarina, Florianopolis, Brazil, [3]Medical Clinic Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil).

S10.L8 FENOFIBRATE-INDUCED WHITE ADIPOSE TISSUE BROWNING IS REDUCED IN OLD AGE. **A. Wronska, A. Zubrzycki, Z. Kmiec** (Department of Histology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland).

Session summary

Poster session ((Friday, September 17, 2021; 10:45 – 11:05; *virtual stream C*)

S10.P1 ELASTASES IN THE DEVELOPMENT OF CHRONIC INFLAMMATION WITH AGE. **L.M. Samokhina[1], V.V. Lomako[2]** ([1]GD National Institute of Therapy of L.T. Malaya name of National Academy of Medical Sciences of Ukraine, Laboratory of Immuno-biochemical and Molecular Genetic Studies, Kharkiv, Ukraine, [2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S10.P2 AGE ASPECTS OF VASOCONSTRICTION DEVELOPMENT IN RATS **L.M. Samokhina[1], V.V. Lomako[2]** ([1]GD National Institute of Therapy of L.T. Malaya name of National Academy of Medical Sciences of Ukraine, Laboratory of Immuno-biochemical and Molecular Genetic Studies, Kharkiv, Ukraine, [2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine, Department of Cryophysiology, Kharkiv, Ukraine).

S10.L1

AGE-RELATED CHANGES IN THE REGULATION OF ENERGY BALANCE: THE ROLE OF ALTERED HYPOTHALAMIC NEUROPEPTIDE ACTIVITY IN THE DEVELOPMENT OF MIDDLE-AGED OBESITY AND AGING ANOREXIA

M. BALASKO, M. SZEKELY, E. PETERVARI

Institute for Translational Medicine, Medical School, University of Pecs, Pecs, Hungary

The number of people aged 65 or older is projected to grow to nearly 1.5 billion by 2050. Long-term regulation of body weight (BW) and body composition shows two different trends: obesity develops typically in the middle-aged, whereas old age is characterized by anorexia, weight loss and sarcopenia. Both trends imply world-wide public health burdens. As most mammals also show similar trends in their long-term BW development, a dysregulation of energy homeostasis may also contribute to these phenomena. Therefore, the investigation of regulatory alterations in energy balance during the course of aging, are of outstanding importance. Earlier studies demonstrated the potential role of age-related shifts in the responsiveness to such peripherally administered anorexigenic and hypermetabolic (catabolic) mediators as cholecystokinin in the development of the above mentioned BW trends. The present work summarizes the outcomes of studies carried out in the Laboratories of Energy Balance and Experimental Gerontology of the Institute for Translational Medicine of the Medical School, University of Pecs Hungary, with regard to the age-related changes in key central catabolic mediator systems, such as leptin, alpha-melanocyte stimulating hormone (alpha-MSH) and corticotropin-releasing peptide (CRF). Age-related changes in the anorexigenic and hypermetabolic responsiveness to intracerebroventricular leptin, alpha-MSH and CRF administrations were recorded in different age-groups of normally fed male Wistar rats (from young adult to old groups, from 3 to 24 months of age, respectively). The expressions of the long form of the leptin receptor (Ob-Rb) in the arcuate nucleus and those of CRF in the paraventricular nucleus of the hypothalamus (PVN) were assessed by quantitative RT-PCR along with immunohistochemical detection of type 4 melanocortin receptors in the PVN. The anorexigenic responsiveness to all these central mediators showed a common pattern, diminished efficacy in the middle-aged and increased efficacy in the aging/old groups. The hypermetabolic responsiveness changed similarly in case of leptin and alpha-MSH. The hypothalamic receptor mRNA expressions for leptin and alpha-MSH and those for mRNA of CRF showed a similar pattern. Age-related changes in major central catabolic neuropeptide systems promote the development of middle-aged obesity and aging anorexia and cachexia. Future research needs to investigate the underlying causes and identify preventive measures.

S10.L2

NATURAL KILLER CELLS AT THE CROSSROADS OF INNATE AND ADAPTIVE IMMUNITY IN THE PROCESS OF AGING

L. KASZUBOWSKA

Medical University of Gdansk, Gdansk, Poland

Aging is associated with many physiological changes, which include both innate and adaptive arms of the immune system. These age-related alterations occur at the cellular as well as humoral level of the immunity. However, they reflect rather age-related remodeling of the immune system at multiple structural and functional levels instead of a complete, unidirectional decline of the immune system functions. Natural killer (NK) cells are key effector lymphocytes of innate immunity provided with cytotoxic activity involved in antiviral and anticancer response. These lymphocytes reveal also some regulatory properties as they are capable of activating other cells of both innate and adaptive immunity by secretion of cytokines and chemokines. They appeared also to reveal both adaptive and memory-like phenotypes. The process of aging observed in immune system usually corresponds to chronic increase in proinflammatory status. In healthy aging this process is followed by anti-inflammatory response to maintain homeostasis. This phenomenon is associated with a general trend of raising the basal levels of cellular protective proteins to cope with stressors that accompany aging. It was also observed in NK cells of the oldest seniors and concerned increased expression of cellular protective proteins SIRT1, HSP70 and SOD2 which expression level corresponded to longevity. Moreover, the oldest seniors seem to reveal well-developed adaptive stress response in NK cells as they present increased, constant level of SIRT1 and intracellular HSP70. However, the age of participants was positively associated with sensitivity of SOD2 to stimulation indicating its distinct role in cellular stress response. Interestingly, T-lymphocytes represented slightly different pattern of cellular protective proteins expression, i.e. SIRT1, HSP70 and SOD2 as compared with NK cells and NKT-like cells. Thus, the specific pattern of cellular protective proteins' expression in NK cells of the oldest seniors may suggest an important role of these cells in the process of aging and their involvement in maintaining immune homeostasis to cope with higher levels of chronic stress compared to younger counterparts.

Author for correspondence: Lucyna Kaszubowska (lucyna.kaszubowska@gumed.edu.pl)

S10.L3

THE POSITIVE EFFECT OF 12 WEEKS OF DANCE TRAINING ON THE AMYLOID PRECURSOR PROTEIN, SEROTONIN CONCENTRATION AND PHYSICAL PERFORMANCE IN ELDERLY WOMEN

E. RODZIEWICZ-FLIS[1], M. KAWA[1], W. SKROBOT[2], D.J. FLIS[3], J.J. KACZOR[3]

[1]Department of Manual and Physical Therapy, Gdansk University of Physical Education and Sport, Gdansk, Poland,
[2]Department of Functional Diagnostic and Kinesiology, Gdansk University of Physical Education and Sport, Gdansk, Poland,
[3]Department of Physiology and Biochemistry, Gdansk University of Physical Education and Sport, Gdansk, Poland

A sedentary lifestyle is a risk factor for deterioration of physical functions, higher fall risk and may lead to the development of neurodegenerative diseases. One of the best known factor, that could contribute to healthy aging is physical activity. Its' beneficial effect on age-related changes in cognitive processes, neurodegenerative diseases and physical performance may be associated with modifying circulating protein and/or hormone concentrations. The aim of the study was to examine if 12 weeks of dance training could attenuate the risk of falls, improve physical functions and modify the circulating concentration of amyloid precursor protein and serotonin in serum of elderly women. 20 older women (aged 73.3 ± 1.5) were randomly assigned into two groups: dance training (DG; n=10) and control group (CG; n=10). The training was performed 3 times a week for 12 weeks. To assess the study aims Time up and go test (TUG), 6 minutes walk test (6MWT), plasma amyloid precursor protein (APP) and serum serotonin (5-HT) concentration were performed. Women in the DG improved distance performed during the walking test as well as TUG test time. The improvement in physical functions in the training group was associated with an increase in APP and a decrease in 5-HT concentrations. No changes in the above parameters were observed among the CG. Results indicate that the training intervention could have a beneficial effect on physical functions among older women. Moreover, physical training may be an important factor in modifying the concentration of circulating proteins associated with neurodegenerative disorders.

Author for correspondence: Jan Kaczor (jan.kaczor@awf.gda.pl)

S10.L4

DIFFERENT MOVEMENT CADENCES INDUCES PSYCHOPHYSIOLOGICAL CHANGES IN ELDERLY MEN

W. BARBOSA[1], P. ZOVICO, C. REIS[1], R. RICA[2], D. BOCALINI[1]

[1]Laboratorio de Fisiologia e Bioquimica Experimental, Universidade Estacio de Sa, Vitoria, ES, Brasil,
[2]Centro de Educacao Fisica e Desporto, Universidade Federal do Espirito Santo (UFES), Vitoria, ES, Brasil

Although the effectiveness of Brazilian Public Gyms (BPG) is a consolidated public health program to promote and facilitate active behavior, the program still lacks information on changes in training load parameters elderly using BPG devices. Fifteen physically independent elderly men participated voluntarily in this study. Three 30-minute exercise sessions were randomly distributed with low (L: 1 movement every 2 seconds), medium (M: 1 movement per second) and high (H: 2 movements per second) cadence with 30“ of stimulus and 30“ of recovery using the following devices: elliptical, rower, surf and leg press. Heart rate (HR), perceived exertion (PE) and recovery (PR), pleasure (PP), number of movements (NM) were evaluated before and immediately after the three sessions. The difference between the parameters were analyzed by analysis of variance and t test with significance level $p < 0.05$. Results: Differences ($p < 0.0001$) were found to absolute (L: 107 ± 12 <M: 130 ± 9 <H: 149 ± 5; bpm) and relative heart rate ($F=49.49$; $p < 0.0001$). The B (60 ± 9%) cadence presented values lower than M (75 ± 3%) and H (91 ± 3%) that also differed from each other. Significant differences ($p < 0.01$) to area under curve of PE (L: 75 ± 26, M: 115 ± 16, H: 154 ± 4) and PR (L: 173 ± 16, M: 139 ± 12, H: 97 ± 6; UA) were identified around cadences. Statistical differences ($p < 0.01$) were found in NM (L: 435 ± 13 < M: 883 ± 191 <H: 1726 ± 53), PE after 30 min of the session (L: 4.2 ± 0.7 <M: 5.7 ± 0.7 <H: 7.4 ± 0.5). In relation to PP, the M (–4.29 ± 0.38%) cadence provided a smaller ($p < 0.01$) reduction compared to cadences L (–21.43 ± 0.49%) and H (–48.81 ± 0.90%) cadency that differed from each other. Conclusion: the performance of different cadences induced different responses in training load indicators in proportion to their speed of execution in the elderly submitted to the exercise session in BPG. However, the moderate cadence provided an increase in HR with values considered safe to perform the exercise.

Author for correspondence: (welmoalcantara@hotmail.com)

S10.L5

POTENTIAL ROLE OF SEX HORMONE-BINDING GLOBULIN IN THE DEVELOPMENT OF ENDOTHELIAL DYSFUNCTION IN OLDER MEN

M. GRANDYS[1], J. MAJERCZAK[2], M. FROLOW[3], R. NIZANKOWSKI[3], S. CHLOPICKI[4,5], J.A. ZOLADZ[1]

[1]Department of Muscle Physiology, Chair of Physiology and Biochemistry, University School of Physical Education, Krakow, Poland, [2]Department of Neurobiology, Poznan University of Physical Education, Poznan, Poland, [3]Laboratory of Clinical Pharmacology of Endothelium, Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Krakow, Poland, [4]Jagiellonian Centre for Experimental Therapeutics (JCET), Jagiellonian University, Krakow, Poland, [5]Department of Experimental Pharmacology, Chair of Pharmacology, Jagiellonian University Medical College, Krakow, Poland

Sex hormone-binding globulin (SHBG) is a transport plasma glycoprotein for sex steroid hormones that regulates their biological activity and metabolic clearance. However, it has been also postulated that SHBG level may be related to increased risk of cardiovascular diseases, but this association is far from being fully understood. In this study we have determined serum SHBG concentration in relation to markers of arterial stiffness and early atherosclerosis in young (22.2 ± 2.6 years, n=12) and older, physically non-active subjects (61.0 ± 7.9 years, n=11). Serum SHBG concentration was assessed by electrochemiluminescence immunoassay and markers of arterial stiffness and atherosclerosis were determined noninvasively using applanation tonometry (pulse wave velocity (PWV), arterial stiffness (AI)), infrared photoplethysmography (stiffness index (SI)) and ultrasound technique (carotid intima-media thickness (cIMT)). We demonstrated that serum SHBG concentration was almost 2 fold higher in older men (27.90 ± 9.62 vs. 50.53 ± 17.54 nmol/L in young and older men respectively, $p < 0.001$), what was accompanied by higher level of PWV, AI, SI and cIMT in older men ($p < 0.001$). Moreover, serum SHBG concentration was significantly positively correlated to all markers of arterial stiffness (PWV, AI, SI, $p < 0.001$) as well as to cIMT ($p < 0.03$). We have concluded that elevated serum SHBG concentration may be a valuable biomarker of arterial stiffness and cardiovascular risk in ageing men.

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Author for correspondence: Marcin Grandys (marcin.grandys@awf.krakow.pl)

S10.L6

OXI-INFLAMMATORY RESPONSE IN AGEING

E. WACKA[1], B. MORAWIN[1], A. TYLUTKA[1], A. ZEMBRON-LACNY[1]

[1]Department of Applied and Clinical Physiology, Collegium Medicum University of Zielona Gora, Zielona Gora, Poland

Aging is a process caused by many factors, such as lifestyle, malnutrition, decreased synthesis of anabolic hormones and growth factors, intensification of inflammatory processes, oxidative stress, etc. In recent years, special attention has been paid to chronic low-grade inflammation as one of the factors enhancing senescence of vascular endothelial cells. The study was designed to demonstrate the impact of chronic low-grade inflammation on the regenerative potential of blood vessels in older adults. Blood samples were collected from 60 individuals (females n=42, males n=18) aged 70.4 ± 5.5 years. Serum oxi-inflammatory markers such as C-reactive protein (CRP), oxidised LDL (oxLDL) and 3-nitrotyrosine (3NT) as well as conventional atherogenic markers such as triglycerides (TG), total cholesterol (TC), high-density lipoproteins (HDL) and low-density lipoproteins (LDL) were determined. Moreover, the numbers of endothelial progenitor cells (EPC) as well as CD34 and CD38 hematopoietic cells were measured by using ELISE kits. Statistical analyses were performed by the software Statistica 13.1 (StatSoft Inc., Tulsa, OK, USA). The protocol of the study was approved by the ethics committee at Medical University of Poznan, Poland (No 550/11), in accordance with the Helsinki Declaration. We obtained high levels of TC >150 mg/dL, LDL >130 mg/dL and non-HDL >130 mg/dL were found in 50% of subjects from taking the hypolipidemic drugs (only 10% of group). Despite dyslipidaemia, oxLDL and 3NT demonstrated the low concentrations 319 ± 284 ng/mL and 1.29 ± 0.81 nmol/mL possibly due to subjects' daily physical activity which improves nitro-oxidative metabolism; approx. 60% of them achieved the result of gait speed above 1.3 m/s. Interestingly, female demonstrated significantly higher concentration of oxLDL (404 ± 290 ng/mL) than male (119 ± 130 ng/mL). This confirms that female sex increases the risk of LDL oxidation thus atherogenesis in old age. However, the opposite tendency was observed for CD34 and CD38 (female 22.43 ± 11.16 ng/mL and 1.28 ± 0.90 ng/mL; male 18.36 ± 8.05 ng/mL and 0.72 ± 0.12 ng/mL). High levels of CRP >5 mg/L was found in 20% of individuals. These findings demonstrate that oxi-inflammation impairs the recovery of blood vessels, and an assessment of CD34 and CD38 hematopoietic cells can be a useful tool for monitoring of the vascular regenerative potential. However, the role of progenitor cells in vascular diseases needs to be part of further studies including relatively high number of subjects.

Author for correspondence: Eryk Wacka (e.wacka@cm.uz.zgora.pl)

S10.L7

INFLUENCE OF DEHYDRATION ON LIPID METABOLISM OF AGED MALE RATS

S. QUIROS COGNUCK[1], W.L. REIS[2], M.S. SILVA[1], S.V. ZORRO[3], G. ALMEIDA-PEREIRA[1], L.K. DE BARBA[1], L.L.K. ELIAS[1], J. ANTUNES-RODRIGUES[1]

[1]Physiology Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil, [2]Department of Physiological Science, Center of Biological Sciences, Federal University of Santa Catarina, Florianopolis, SC, Brazil, [3]Medical Clinic Department, Ribeirao Preto Medicine School, University of Sao Paulo, Ribeirao Preto, Sao Paulo, Brazil

Dehydration produces energy metabolism alterations. Our objective was to determinate the effect of dehydration in the lipid metabolism of old male rats. Male rats of 3- and 18-month-old were submitted to water deprivation (WD) for 48 hours. Retroperitoneal white adipose tissue (R-WAT) weight, lipidogram assay, plasma palmitic acid, glycerol, and the relative expression of proliferator-activated receptor alpha (*P-para*), hormone-sensitive lipase (*HSL*), and aquaporin 7 (*Aqp7*) mRNA in R-WAT were determined. Rats showed no difference in glycerol level, *P-para*, and *HSL* expression. The 18-month-old WD rats had lower weight of R-WAT, total cholesterol, and palmitic acid than respective control. The 3-month-old WD rats showed less expression of *Aqp7* mRNA than their respective controls. Both 3- and 18-month-old WD rats showed lower plasma triglyceride. We concluded that age influence lipid metabolism of dehydrated rat.

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Author for correspondence: Susana Quiros Cognuck (susana.cognuck@gmail.com)

S10.L8

FENOFIBRATE-INDUCED WHITE ADIPOSE TISSUE BROWNING IS REDUCED IN OLD AGE

A. WRONSKA, A. ZUBRZYCKI, Z. KMIEC

Department of Histology, Faculty of Medicine, Medical University of Gdansk, Gdansk, Poland

The hypolipemic drug fenofibrate (FN) is known to act through peroxisome proliferator-activated receptor alpha (PPARα) which may stimulate mitochondrial oxidative metabolism. The aim of this study was to examine whether FN affects the thermogenic activity of brown adipose tissue (BAT) as well as browning of white adipose tissue (WAT), and whether these effects depend on age. Young adult (4-month-old) and old (24-month-old) Wistar rats were fed with either standard rodent chow (control animals) or the same chow supplemented with FN in two doses: 0.5% and 0.1% by weight, for 30 days (n=8–10 young or old animals in every group). Snap-frozen samples of epididymal WAT (eWAT) and intarscapular BAT were analysed for gene expression (qPCR) and protein content (Western blotting). In BAT of young rats, treatment with 0.5% FN increased the protein content of CITED1, a transcription factor involved in thermogenic activation and a marker of adipocyte browning. However, neither UCP1 nor PGC-1α proteins were significantly upregulated. The mRNA expression of Ucp1, Pgc-1α, and PGC-1α downstream targets Cpt1b and Acadm decreased after 0.5% FN. In BAT of old rats, the treatment affected neither the studied proteins' content nor mRNA levels. In eWAT of young rats, UCP1 and CITED1 tended to increase after FN, with Pgc-1α, Cpt1b, and Acadm mRNA levels likewise increased. In eWAT of old rats, similar changes in mRNA were observed. We concluded that fenofibrate did not activate the thermogenic function of brown adipose tissue, but modestly stimulated mitochondrial oxidative metabolism and "browning" of white adipose tissue in young adult rats. Aging blunted both these effects.

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Author for correspondence: Agata Wronska (agata.wronska@gumed.edu.pl)

S10.P1

ELASTASES IN THE DEVELOPMENT OF CHRONIC INFLAMMATION WITH AGE

L.M. SAMOKHINA[1], V.V. LOMAKO[2]

[1]GD L.T. Malaya National Institute of Therapy of National Academy of Medical Sciences of Ukraine,
Laboratory of Immuno-biochemical and Molecular Genetic Studies; Kharkiv, Ukraine,
[2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine,
Department of Cryophysiology, Kharkiv, Ukraine

Chronic inflammation develops with age, and this condition is a strong risk factor for multiple organ pathology. The development of inflammation is associated with the functioning of elastases: serine (EC 3.4.21.37) of neutrophilic origin (El), cysteine or thiol (EC 3.4.22) of endothelial (EEl) origin, and metalloelastase (MEl) or matrix metalloprotease 12 (EC 3.4.24.65) of macrophage origin. The aim was to investigate the activity of elastases of various origins and the elastase inhibitory activity of α-1-proteinase inhibitor (EIA α-1-PI) in the tissues of male rats of different ages. The work was performed on white outbred rats (Rattus norvegicus) 3, 6, and 24 months old according to the bioethics rules (n=6 in each group). The elastases activity and EIA α-1-PI were determined in the nuclear-free fractions of 10% homogenates of tissues of the cerebral cortex (CC), lungs, heart, liver and kidneys by highly sensitive (10^{-10} g) enzymatic methods (Samokhina L.M., 2014, 2015; ISBN: 978-3-659-63483-3; ISBN 978–3–659–33949–3). It was noted that El activity decreases with age at 6 and 24 months in the tissues of internal organs, which may be the result of a loss of compensatory reserve, but increases in CC at 6 and 24 months and in the kidneys at 24 months, which may be due to a decrease in antioxidant protection and lead to the inflammation, as well as destruction and vasoconstriction. An increase EEl, EIA α-1-PI at 6 months and a decrease at 24 months was shown, which can be considered as links of the body's compensatory response. The MEl activity increased in CC at 24 months, decreased in the lungs, which may be a consequence of oxidative stress and the participation of MEl in the pathological changes.

Author for correspondence: L. Samokhina (lub.samokhina@gmail.com)

S10.P2

AGE ASPECTS OF VASOCONSTRICTION DEVELOPMENT IN RATS

L.M. SAMOKHINA[1], V.V. LOMAKO[2]

[1]GD L.T. Malaya National Institute of Therapy of National Academy of Medical Sciences of Ukraine,
Laboratory of Immuno-biochemical and Molecular Genetic Studies; Kharkiv, Ukraine,
[2]Institute for Problems of Cryobiology and Cryomedicine of National Academy of Sciences of Ukraine,
Department of Cryophysiology, Kharkiv, Ukraine

Angiotensin II (AII) plays a key role in the regulation of blood pressure and vascular tone. In tissues of rats, rabbits, mice, AII is formed with the chymase participation at a high concentration of AI. Tonin forms AII directly from angiotensinogen. The calpains activity promotes an increase in AII-induced left ventricular hypertrophy and vascular remodeling. The aim of this work is to study the activity of chymase, tonin, and calpains in the tissues of male rats of different ages. The work was performed with using white rats (Rattus norvegicus) 3, 6, 24 months, n=6 in each group. The activity of chymase, tonin and calpains was determined in blood serum and non-nuclear fractions of 10% homogenates of tissues of the cerebral cortex (CC), lungs, heart, liver and kidneys by highly sensitive enzymatic methods (ISBN: 978-3-659-63483-3); (ISBN 978-3-659-33949-3). It was noted that the chymase activity is higher at 24 months in blood serum, CC and liver, which may indicate the chymase release by mast cells, and (given the species specificity of rat chymase to degrade AII) promote vasodilation, at least in CC; in the kidneys the chymase activity decreases in 24 months, suggesting the development of local vasoconstriction. The tonin activity in 6 months is higher than at 3 months, indicating also the vasoconstriction development, and decreases at 24 months (except for CC). The calpains activity increases at 6 months (in the lungs, heart, liver, and kidneys) and 24 months (in all tissues except the heart), maximum - in the lungs. The calpains activation promotes endothelial dysfunction, cardiovascular diseases, structural and functional changes in the kidneys, inflammation, etc. The high calpains activity in the lungs at 24 months can be induced by increased respiration, is associated with the development of tissue inflammation and edema, and an increase in pulmonary vascular permeability.

Author for correspondence: L. Samokhina (lub.samokhina@gmail.com)