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ABSTRACT BOOK

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"Precision medicine for healthy ageing"

Barcelona, Spain

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Guest Editor:

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Contents

Abstract number

PL | Plenary speakers

PL-1-PL-5

Workshop invited speakers

W1 | Phagocyte biology
W2 | Mitochondria, ageing and disease
W2/W4 | Mitochondria, ageing and disease & Hepato-Gastroenterology/Lipids
W3 | Cardiology-CIBERCV
W4/W7 | Hepato-Gastroenterology/Lipids & Obesity-CIBEROBN
W5/W7 | Omics & Obesity-CIBEROBN
W6 | Precision nutrition
W7 | Obesity-CIBEROBN

W1-L1-W1-L19
W2-L1-W2-L18
W2/W4-L1-W2/W4-L4
W3-L1-W3-L18
W4/W7-L1-W4/W7-L7
W5/W7-L1-W5/W7-L14
W6-L1-W6-L9
W7-L1-W7-L4

Oral presentations

W1 | Phagocyte biology
W2 | Mitochondria, ageing and disease
W3 | Cardiology-CIBERCV
W4/W7 | Hepato-Gastroenterology/Lipids & Obesity-CIBEROBN
W7 | Obesity-CIBEROBN

W1-O1-W1-O15
W2-O1-W2-O10
W3-O1-W3-O14
W4/W7-O1-W4/W7-O10
W7-O1-W7-O4

Posters by theme

W1 | Phagocyte biology
W1 | Phagocyte biology
W2 | Mitochondria, ageing and disease
W2 | Mitochondria, ageing and disease
W2 | Mitochondria, ageing and disease
W3 | Cardiology-CIBERCV
W3 | Cardiology-CIBERCV
W3 | Cardiology-CIBERCV
W4 | Hepato-Gastroenterology/Lipids
W5 | Omics
W6 | Precision nutrition
W7 | Obesity-CIBEROBN
W7 | Obesity-CIBEROBN
W9 | Miscellaneous Medical Topics

Poster session 1
Poster session 2
Poster session 1
Poster session 2
Poster session 3
Poster session 1
Poster session 2
Poster session 3
Poster session 3
Poster session 2
Poster session 3
Poster session 1
Poster session 3
Poster session 3

P1-T-P20-T
P21-T-P35-T
P36-T-P55-T
P56-T-P72-T
P1-F-P34-F
P73-T-P102-T
P103-T-P128-T
P35-F-P68-F
P69-F-P90-F
P129-T-P161-T
P91-F-P99-F
P162-T-P191-T
P100-F-P125-F
P126-F-P142-F

Posters by session

W1 | Phagocyte biology
W2 | Mitochondria, ageing and disease
W3 | Cardiology-CIBERCV
W7 | Obesity-CIBEROBN
W1 | Phagocyte biology
W2 | Mitochondria, ageing and disease
W3 | Cardiology-CIBERCV
W5 | Omics
W2 | Mitochondria, ageing and disease
W3 | Cardiology-CIBERCV
W4 | Hepato-Gastroenterology/Lipids
W6 | Precision nutrition
W7 | Obesity-CIBEROBN
W9 | Miscellaneous Medical Topics

Poster session 1
Poster session 1
Poster session 1
Poster session 1
Poster session 2
Poster session 2
Poster session 2
Poster session 2
Poster session 3
Poster session 3
Poster session 3
Poster session 3
Poster session 3
Poster session 3

P1-T-P20-T
P36-T-P55-T
P73-T-P102-T
P162-T-P191-T
P21-T-P35-T
P56-T-P72-T
P103-T-P128-T
P129-T-P161-T
P1-F-P34-F
P35-F-P68-F
P69-F-P90-F
P91-F-P99-F
P100-F-P125-F
P126-F-P142-F

Poster session 1 Thursday, 31 May, 12:30-14:30

Poster session 2 Thursday, 31 May, 17:30-19:00

Poster session 3 Friday, 1 June, 12:30-14:30

of ZD7288 (an organic blocker) stimulated electrically and also in the absence of this stimulation.

The experiments, which involved the intracellular recording of electrical activities in the working myocardium, were carried out on random-bred albino rats. Isolated right atrial wall from a fragment of the right auricle exhibiting no pacemaker activity was placed in a 3-mL chamber and superfused with Tyrode solution at 38°C at a rate of 10 mL/min. The stimulus duration (1 ms) and repetition rate (5 Hz) corresponded to the normal HR of mature rats. Intracellular AP was recorded via glass microelectrodes with resistance of 25–60 MΩ. The signals were digitized with an E14-140 converter (L-Card) and recorded using PowerGraph 3.3 software (DiSoft). The data were processed with Mini-Analysis 3.0.1 software (Synaptosoft), Microsoft Excel software and Student's *t* test.

ZD7288 significantly increased the duration of action potentials at 50% and 90% repolarization levels in atrial myocardium at a fixed stimulation rate of 5 Hz. The blocker affected neither resting potential nor the upstroke velocity of action potential.

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P124-T | The blockade of If in isolated (Langendorff perfused) heart

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According to modern views, If are responsible for the development of initial, linear, and slow diastolic depolarization in cells of the sinoatrial node. At the same time, a rather small If was identified in both atypical and working cardiomyocytes. Therefore, it remains unclear how the blockade of data currents affects heart function.

This research aim is to investigate dose-dependent effects of the blockade of If: on coronary flow; the inotropy; and the chronotropy in Langendorff perfused heart in adult rats. Isolated hearts were perfused in a Krebs-Henseleit solution – Langendorff (ADInstruments) installation. The coronary flow (CF), systolic pressure in the left ventricle (LVP) and heart rate (HR) were calculated along the curve. The signals were recorded in a PowerLab system (ADInstruments) with the help of LabChart Pro 8.0 software. 10^{-9} – 3×10^{-5} M concentrations range of ZD7288 (Sigma) were used for the blockade of If. The data was processed

statistically using Microsoft Excel software and Student's *t* test.

ZD7288 10^{-9} M increased LVP by 47% ($P \leq 0.05$), decreased HR by 26% ($P \leq 0.05$) and reduced CF by 20% ($P \leq 0.01$). ZD7288 10^{-8} M, 10^{-7} M and 10^{-5} M did not cause significant alterations in the studied parameters of the heart. ZD7288 10^{-6} M led to bradycardia – 23% ($P \leq 0.05$) and did not cause significant changes in LVP and CF. ZD7288 3×10^{-6} M reduced LVP by 14% ($P \leq 0.05$), HR by 11% ($P \leq 0.05$) and did not lead to a change in CF. If blockade 3×10^{-5} M reduced myocardial inotropy by 26% ($P \leq 0.05$), CF by 14% ($P \leq 0.01$) and HR by 19% ($P \leq 0.05$).

The blockade of If in Langendorff perfused hearts of adult rats resulted in different contractility effects. The range in all the studied concentrations of the If blockade reduced both heart function and coronary flow.

Work supported by Program of Competitive Growth of KFU and Russian Foundation for Basic Research (grant No. 17-04-00071).

P125-T | Role of NPY1,5-receptors in the neonatal rats myocardial contractility

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Neuropeptide Y (NPY) is present in the central and peripheral nervous systems and fully satisfies to neurotransmitter criteria, since it is stored in sympathetic vesicles, released by electrical stimulation and acts on specific receptors. In the rat heart there are metabotropic Y1R, Y2R, Y3R, Y4R and Y5R receptors. The density of different receptor subtypes varies in postnatal ontogenesis. Expression of Y1R increased between 10 and 20 days of life. A small number of Y2R is observed in the atria and ventricles only from 20 days of life. In contrast, the highest level of expression of Y5R was found in newborn pups comparing with more adult rats.

The aim of the current study was to determine the role of different subtypes of NPY receptors in the heart contraction in the postnatal development. Registration of isometric contraction of atrial and ventricular myocardial striae of 7- and 100-day-old rats was carried out on a PowerLab device with a force sensor MLT 050/D (ADInstruments).

The selective agonist of Y1R, Leu(31)Pro(34)NPY (10^{-5} – 10^{-13} M), induced an increase in myocardial contraction force in 7-day-old (10^{-6} M) and in 100-day-old rats (10^{-7} M). The selective blocker of Y1R, BIBP 3226,

eliminates the positive effect caused by Leu(31)Pro(34) NPY in all age groups, which indicates the involvement of this receptor subtype in myocardial contractility.

NPY (10^{-6} – 10^{-10} M) reduced the force of myocardial contraction in 7-day-old animals and does not cause significant changes in the parameters of isometric myocardial contraction in 100-day-old rats. NPY in the presence of selective blocker of Y5R, CGP 71683 (1.4 mM), reduced the force of myocardial contraction in 7-day-old animals and did not affect in 100-day-old animals, which indicates the involvement of this receptor subtype in myocardial contractility only in newborn animals.

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P126-T | Developmental changes of ATP influence to rats heart parameters

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ATP can participate in the intercellular signaling, where it acts as a cotransmitter on specific purinoreceptors. In the rat cardiomyocytes have been found ionotropic P2X_{1,2,4,5} and metabotropic P2Y_{1,2,4,6,11} receptors. The results of the studies are contradictory, because ATP rapidly dissociates to adenosine, which acts on its receptors causing a multidirectional effect. During the postnatal development, the percentage of P2X₂ and P2X₆ is kept at the same level with a peak for P2X₃ purinoreceptors at 20 days.

The influence of ATP on the heart has been studied. Registration of isometric contraction of atrial myocardium strips was performed with a preserved sinus node and stimulation of 6 pulses per minute in 7- and 100-day-old rats. Intracellular recording of the electrical activity was performed using glass microelectrodes with a resistance of 30–60 MΩ.

ATP with a concentration of 10^{-4} – 10^{-7} M causes a dose-dependent reduction in the striae of the myocardium of the atria and ventricles. The maximum increase was observed in the concentration of 10^{-7} M in newborns and 10^{-6} M in adult animals. When ATP was added to the strips of the myocardium with a preserved sinus node, a short-term increase in the frequency and force of contraction results was found. Increasing the concentration of the agonist led to a decrease in the strength of contraction of the myocardium strips. Adding this concentration to the atrial

preparation with a preserved sinus node caused a short-term increase in the heart rate, an increase in the duration of 20%, 50%, and 90% of the repolarization.

The increase of myocardial contractility with the addition of ATP is associated with the activation of P2X₁ purinoreceptors which play the most important role in the positive inotropic effect in newborn rats.

Work supported by Program of Competitive Growth of KFU and Russian Foundation for Basic Research (grant No. 17-04-00071).

P127-T | Involvement of α -adrenoreceptors of rats myocardial contractility dopaminergic regulation during postnatal ontogenesis

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The regulatory effect of dopamine, especially in ontogenesis, on myocardial contractility has been given little attention. The function of dopamine is initiated through the activation of dopamine receptors found in the heart of the rat and human. Dopamine also interacts with α - and β -adrenergic receptors. The purpose of this study is to study the effect of different dopamine concentrations on myocardium contractility in 42-, 56- and 100-day-old rats with blocked α -adrenergic receptors.

Registration of isometric contraction of atrial and ventricular myocardial striae of 42-, 56- and 100-day-old rats was carried out on a PowerLab device with MLT 050/D force sensor (ADIstruments). We determined the reaction contraction force of the atrium and ventricle myocardium at dopamine range of 10^{-5} – 10^{-9} M. 10^{-6} M concentration of phentolamine was used for the blockade of α -adrenergic.

Dopamine blockade by phentolamine increased the force of atrial contractions by 8% (10^{-6} M) and in the ventricles by 15% (10^{-5} M) in 42-day-old rats after. All the other dopamine concentrations lead to a decrease in contractility of strips of myocardium of Atria and ventricles.

Phentolamine induced dopamine blockade increased the force of contraction of the Atria and ventricles by 13–20% (10^{-5} , 10^{-6} , 10^{-9} M) in 56-day-old rats. We observed a 19% reduced contraction force of the atrial and ventricular strips of the myocardium after treatment with 10^{-7} and 10^{-8} M concentrations of dopamine.

100-day-old animals, phentolamine induced dopamine blockade increased the force of atrial contractions in the studied range of concentrations (10^{-5} , 10^{-6} , 10^{-7} , 10^{-9} M) and reduces the force of contraction of strips of