NITRIC OXIDE MEDIATES THE EFFECTS OF CHRONIC STRESS ON PURINERGIC P2X7 AND ADENOSINE A2B RECEPTOR EXPRESSION IN BONE MARROW CELLS

Sanja Momčilović[1], Andrija Bogdanović[2], Maja Milošević[1], Dragana Marković[1], Aleksandra Jauković[1], Diana Bugarski[1], Sanja Vignjević Petrinović[1]
[1]Institute for Medical Research, National Institute of Republic of Serbia, University of Belgrade, Belgrade, Serbia, [2]Clinic of Haematology, University Clinical Centre of Serbia, Belgrade, Serbia

INTRODUCTION:

- Insufficient tissue oxygenation under chronic stress conditions causes anemia and triggers a process called stress erythropoiesis (SE). However, despite a marked increase in the number of erythroid progenitors, anemia remains persistent during chronic stress.
- Chronic stress induces SE by altering local production of nitric oxide (NO) in the bone marrow.
- Purinergic P2X7R and adenosine A2B (ADORA2B) receptors are expressed on hematopoietic progenitors and activation of ADORA2B regulates erythroid lineage commitment, while P2X7R activation leads to erythroid progenitor cell apoptosis in the hypoxic microenvironment.

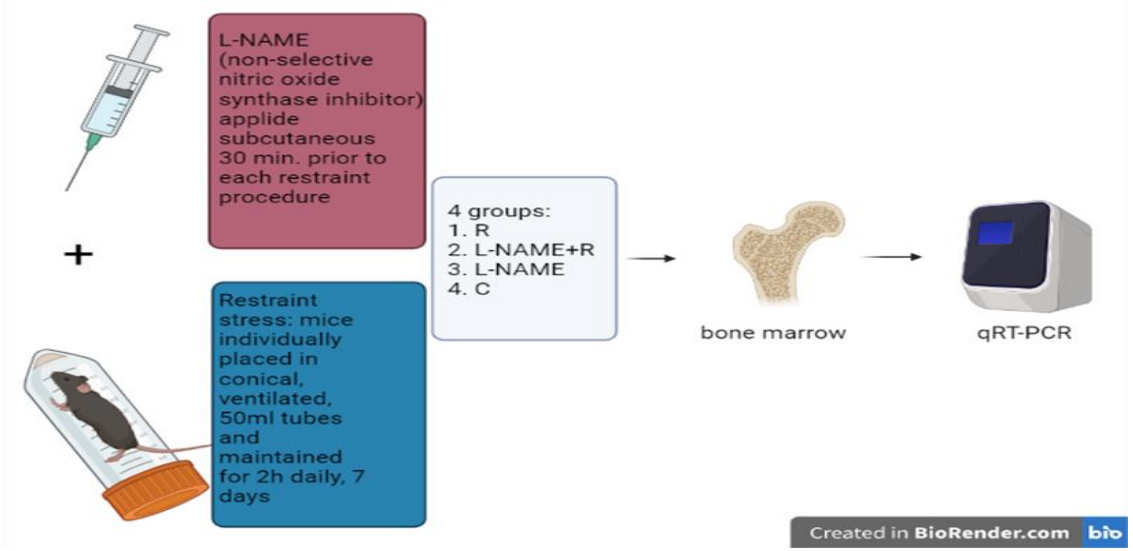
OBJECTIVES:

This study was aimed to examine:

- the effects of chronic psychological stress on the expression of P2X7R and ADORA2B receptors in the bone marrow
- potential role for NO in obtained stress-induced changes

METHOD:

Experimental design

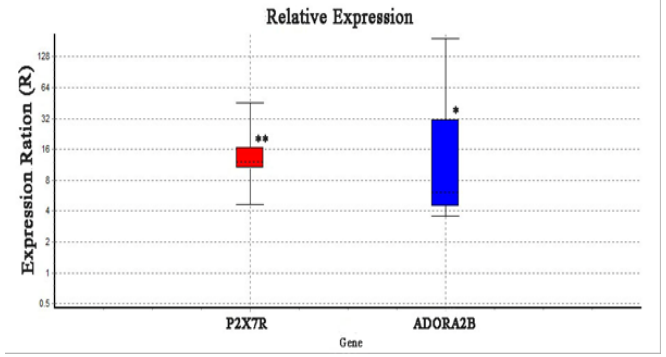


1. R-mice subjected to daily restraint stress for 7 consecutive days;
2. L-NAME + R-animals treated with L-NAME prior to daily Restraint;
3. L-NAME-mice received only the daily dose of L-NAME
4. C-controls

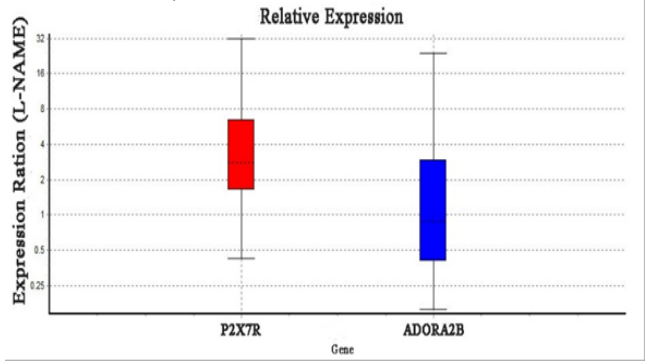
RESULTS:

- Chronic exposure to restraint stress significantly increased the expression of P2X7R ($P<0.01$) and ADORA2B ($p<0.05$) genes in the bone marrow.
- The subcutaneous injection with NO synthase inhibitor L-NAME for 7 consecutive days under basal conditions did not alter the expression of these receptors ($p>0.05$) in the bone marrow.
- Blockade of NO biosynthesis prior to daily stress completely prevented stress-induced increase in P2X7R and ADORA2B mRNA levels within bone marrow microenvironment.

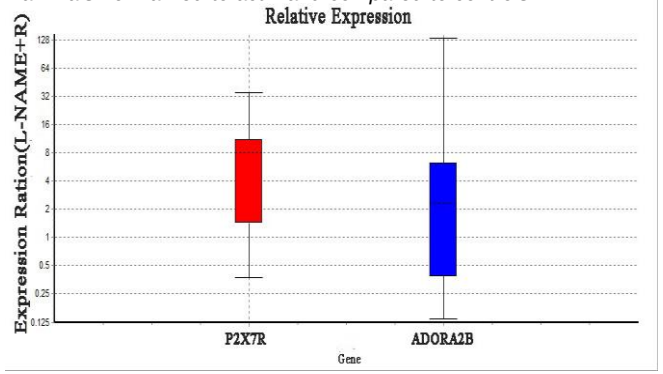
*a) Relative expression mRNK of P2X7R and ADORA2B gene in the bone marrow of restrained animals normalized to actin and compared to controls *p<0,05; **p<0,01*



b) Relative expression mRNK of P2X7R and P2X7R gene in the bone marrow animals treated with L-NAME normalized to actin and compared to controls.



c) Relative expression mRNK of P2X7R and ADORA2B gene in the bone marrow of L-NAME pretreatment and then restrained animals normalized to actin and compared to controls.



CONCLUSIONS:

Obtained results demonstrate an interplay between NO and purinergic signaling in bone marrow of chronically stressed animals, indicating a physiological significance of this interaction in the regulation of either cellular adaptation or apoptosis under chronic stress conditions