European Journal of Clinical Investigation

ESCI
EUROPEAN SOCIETY FOR CLINICAL INVESTIGATION

Volume 49, April 2019, Issue S1, Pages: 1-234. Special Issue.

DOI: 10.1111/eci.13109

WILEY

ABSTRACT

POSTERS

P001-T | Disruption of IDH2 attenuates LPS-induced inflammation and lung injury

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Acute lung injury (ALI) is an acute failure of the respiratory system with unacceptably high mortality, for which effective treatment is urgently necessary. Infiltrations by immune cells, such as leukocytes and macrophages, are responsible for the inflammatory response in ALI, which is characterized by excessive production of pro-inflammatory mediators in lung tissues exposed to various pathogen-associated molecules such as lipopolysaccharide (LPS) from microbial organisms. Alpha-Ketoglutarate (alpha-KG) is a key metabolic intermediate and acts as a pro-inflammatory metabolite, which is responsible for LPS-induced proinflammatory cytokine production through NF-kappaB signaling pathway. Mitochondrial NADP+-dependent isocitrate dehydrogenase (IDH2) has been reported as an essential enzyme catalyzing the conversion of isocitrate to alpha-KG with concurrent production of NAPDH. Therefore, we evaluated the role of IDH2 in LPS-induced ALI using IDH2-deficient mice. We observed that LPS-induced inflammation and lung injury is attenuated in IDH2-deficient mice, leading to a lengthened life span of the mice. Our results also suggest that IDH2 disruption suppresses LPS-induced proinflammatory cytokine production, resulting from an inhibition of the NF-kappaB signaling axis in an alpha-KG-dependent manner. In conclusion, disruption of IDH2 leads to a decrease in alpha-KG levels, and the activation of NF-kappaB in response to LPS is attenuated by reduction of alpha-KG levels, which eventually reduces the inflammatory response in the lung during LPS-induced ALI. The present study supports the rationale for targeting IDH2 as an important therapeutic strategy for the treatment of systemic inflammatory response syndromes, particularly ALI.

P002-T | Effects of decrease in intracellular Ca^{2+} concentration on electrical characteristics of premotor interneurons of training snails

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The Ca^{2+} plays an important role in formation of conditioning. The intracellular Ca^{2+}, which is stored in the endoplasmic reticulum and mitochondria, is involved in the regulation of many intracellular reactions. The changes of the level of intracellular calcium concentration by the influx and uptake transport from the endoplasmic reticulum and mitochondria can regulate short-term and long-term forms of plasticity. In present study we analyzed the influence of a decrease in the intracellular Ca^{2+} concentration on the maintenance of the excitable changes of snails premotor interneurons after learning.

It was found that after decreasing of intracellular Ca^{2+} level by the calcium chelators EGTA the threshold potential significantly increased by 3.3 mV in the group of untrained snails and tended to increase, but not significantly in a group of trained snails. Application of membrane-penetrating calcium ion chelator BAPTA-AM did not lead to specific changes of electrical characteristics of trained snails. This difference in actions of both chelators pointed on different pathways of influence of intracellullar Ca^{2+} concentration on neuron excitability. Our results suggested that the decrease of intracellullar Ca^{2+} level was not involved in maintenance of the excitability of interneurons after training. As we showed earlier the changes of intracellullar Ca^{2+} level was more critical on the stage of formation of the conditioning.

Supported RFBR (grant 18-015-00274).