FENS Regional Meeting

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National Neuroscience Society of Romania

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Abstract Book

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Thursday, July 11, 2019

13:45-15:00

Room Atlantic 1
Room Atlantic 2

POSTER SESSION 2

P263

MOLECULAR MECHANISMS OF ETHYL PYRUVATE TOLEROGENIC EFFECTS ON DENDRITIC CELLS

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Aims: Tolerogenic dendritic cells (tolDC) have immuno-regulatory properties and they are a promising prospective therapy for multiple sclerosis, as well as for other autoimmune diseases. Ethyl pyruvate (EP) is a redox analogue of dimethyl fumarate (Tecfidera), a drug for multiple sclerosis treatment. We have recently shown that EP has the ability to direct DC towards tolDC in both murine and human DC. Therefore, we expanded our investigation to determine which mechanisms are responsible for EP-imposed tolerance in DC. Therefore, we examined Nrf2 signalling pathway, HO-1 and NQO1 enzymes, and NF-κB transcription factor.

Methods: C57BL/6 mice bone marrow derived DC were cultivated for 8 days in the presence of 20 ng/mL of GM-CSF without (immature DC - iDC) or with EP added on days 3 and 6 (EP-DC). In order to induce maturation, iDC and EP-DC were incubated for 15min - 4 h with 100 ng/mL lipopolysaccharide (mature - mDC and tEP-DC, respectively). After that, immunocitochemistry staining was performed.

Results: Maturation of DC led to reduction of the Nrf2 and HO-1 expression, yet this reduction was prevented by EP. Also, the NQO1 expression was higher in EP-DC in comparison to iDC. However, the expression in tEP-DC was lower than in mDC, but still higher than in iDC. Finaly, unlike mDC had higher levels of nuclear NF-κB than iDC, tEP-DC had lower expression compared to EP-DC.

Conclusions: EP exercises its tolerogenic potential on DC through the up-regulation of anti-oxidative signaling pathways, as well as through the inhibition of proinflammatory transcription factor NF-κB.