

5TH SCIENTIFIC MEETING

COST ACTION CA20121

**BENCH TO BEDSIDE TRANSITION FOR PHARMACOLOGICAL REGULATION OF
NRF2 IN NON-COMMUNICABLE DISEASES (BENBEDPHAR)**

TRANSLATING NRF2 RESEARCH INTO CLINICAL PRACTICE

University of Graz | Austria

October 12-13, 2023

Venue

Meerscheinschlössl

Mozartgasse 3 | 8010 Graz | Austria

Local Organizers

Christina Morgenstern | Brigitte Winklhofer-Roob | University of Graz

Christina Unteregger | Harald Sourij | Medical University of Graz



O-14: Immunomodulatory properties of HYCOs, Nrf2 activators that simultaneously release carbon monoxide (CO) to cells and tissues

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HYCOs are a novel class of hybrid compounds consisting of fumaric esters conjugated to carbon monoxide-releasing molecules (CO-RMs). They were designed based on the consideration that fumaric esters are known to activate the transcription factor Nrf2 and that CO possesses potent anti-inflammatory properties. The dual action of these hybrids has shown promising therapeutic effects in animal models of psoriasis and multiple sclerosis. We have recently started with the group of Drs Motterlini and Foresti in France a collaborative research project relevant to the BenBedPharm COST Action, focusing on the immunomodulatory effects of HYCOs. These effects were examined *in vitro* in cultures of myeloid-derived cells (macrophages and dendritic cells), lymph node cells, immune cells isolated from the inflamed central nervous system, and microglia. By assessing the production of immunoactive molecules, including nitric oxide, reactive oxygen species and cytokines, we provide evidence that HYCOs display immunomodulatory effects in all cell populations examined *in vitro*. Moreover, we were able to demonstrate that HYCOs are efficient in ameliorating type 1 diabetes in an animal model of this autoimmune disease. Our results indicate that HYCOs are Nrf2 activators with promising immunomodulatory therapeutic properties.

Dorđe Miljković is a Research Professor and the Head of the Department of Immunology at the Institute for Biological Research "Siniša Stanković", University of Belgrade. He studies cellular and molecular mechanisms involved in the pathogenesis of autoimmune diseases. His current main research interests are: role of gut immune cells in autoimmunity, mechanisms of autoimmunity progression/regulation, cell-based therapy of autoimmunity, modulation of autoimmune diseases by synthetic and natural compounds.