A step forward in understanding oleocanthal anti-inflammatory activity by proteomic analysis in microglial cells

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M.C. Barbalace[I], L. Zallocco[II], I. Rinaldi[I], M. Freschi[I], M. Ronci[III,IV], S. Hrelia[I], C. Angeloni[I], L. Giusti[V]

[I]Department for Life Quality Studies, Alma Mater Studiorum-University of Bologna, Rimini, Italy, [II]Department of Translational Research and New Technologies in Medicine and Surgery, University of Pisa, Pisa, Italy, [III]Department of Medical, Oral and Biotechnological Sciences, University G. D'Annunzio of Chieti-Pescara, Chieti, Italy, [IV]Interuniversitary Consortium for Engineering and Medicine, COIIM, Campobasso, Italy, [V]School of Pharmacy, University of Camerino, Camerino, Italy

Neurodegenerative diseases are devastating disorders affecting millions of people worldwide. Although these diseases exhibit distinct pathogenetic mechanisms, including diverse protein aggregates and genetic variations, they all share a common characteristic: persistent neuroinflammation. Our previous data have demonstrated that oleocanthal (OL), a compound found in extra virgin olive oil, exhibits significant antiinflammatory activity in microglial cells. To better characterize the underlying mechanism of this effect, we evaluated the proteomic profile of microglial BV2 cells pretreated with 10 μM OL and then exposed to 100 ng/mL LPS. Protein extracts were analyzed by 2D electrophoresis and LC/MS/MS was used to identify the spots of interest. About 111 differently expressed proteins were identified between LPS and control, 62 proteins between OL+LPS and LPS, and 31 proteins were present in both comparisons. Of note, the treatment with only OL did not alter the protein pattern compared to control cells. In a general overview of proteins modulated by LPS exposure, it emerges that OL pretreatment can bring the levels of these proteins to values comparable to those of control cells, with a signal-dampening effect. Among these proteins, aconitate decarboxylase 1, cytochrome b5 type B, ubiquitin C-terminal hydrolase L3, ATP synthase F1 subunit alpha, tyrosine 3 /tryptophan 5 monooxygenase activation protein beta and theta, interferoninduced protein with tetratricopeptide repeats 3, cathepsin A were strongly upregulated by LPS and downregulated by OL pretreatment; clathrin light chain A was strongly downregulated by LPS and upregulated by OL pretreatment. Our findings indicate novel molecular targets of LPS. Since OL alone did not modify protein levels, it leads us to hypothesize that it could act through an antagonistic mechanism on TLR4, blocking the LPS signal. This work was supported by MUR-PRIN 2022 (Prot. 20222W7P7S) to Cristina Angeloni.