

Title: MOLECULAR INSIGHTS INTO THE NEUROPROTECTIVE EFFECTS OF CHLOROGENIC ACIDS
MEDIATED BY THE PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR PPARALPHA

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The peroxisome proliferator-activated receptor PPARalpha has been associated to neuroprotection against Parkinson's and Alzheimer's diseases [1]. PPARalpha binds a wide variety of ligands [2], including FDA-approved drugs, suggesting that PPARalpha could be used as an alternative therapeutic target against neurodegeneration. Endogenous ligands of PPARalpha include fatty acids (such as oleic acid, whose concentration is pathologically increased in several neurodegenerative diseases) and their derivatives (such as OLHA, the conjugate of oleic acid and histamine) [3]. In addition, PPARalpha exogenous ligands span from drugs against diabetes and hyperlipidemia to food molecules, such as cinnamic acid [4,5] and the closely related chlorogenic acids (CGAs). Using molecular simulations, we have investigated the binding determinants of CGA-related compounds. Our computational results, in combination with experiments on brain slices, show that these novel PPARalpha ligands could bind to the receptor similarly to known endogenous agonists and drugs. In the long term, this molecular information may be used as a stepping stone for designing PPARalpha-based neuroprotective therapies.

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[5] Prorok T et al. (2019) Neurochem. Res. 44(4):751-762.