

The Antihypertensive Drug Telmisartan Protects Oligodendrocytes from Cholesterol Accumulation and Promotes Differentiation by a PPAR- γ -Mediated Mechanism

Antonietta Bernardo ^{1,*}, Mariagiovanna Malara ², Lucia Bertuccini ³, Chiara De Nuccio ⁴, Sergio Visentin ¹ and Luisa Minghetti ⁴

¹ National Center for Research and Preclinical and Clinical Evaluation of Drugs, Istituto Superiore di Sanità, 00169 Rome, Italy; sergio.visentin@iss.it

² Institute for Anatomy and Cell Biology, Ulm University, 89081 Ulm, Germany; mariagiovanna.malara@uni-ulm.de

³ Core Facilities, Istituto Superiore di Sanità, 00169 Rome, Italy; lucia.bertuccini@iss.it

⁴ Research Coordination and Support Service, Istituto Superiore di Sanità, 00169 Rome, Italy; chiara.denuccio@iss.it (C.D.N.); luisa.minghetti@iss.it (L.M.)

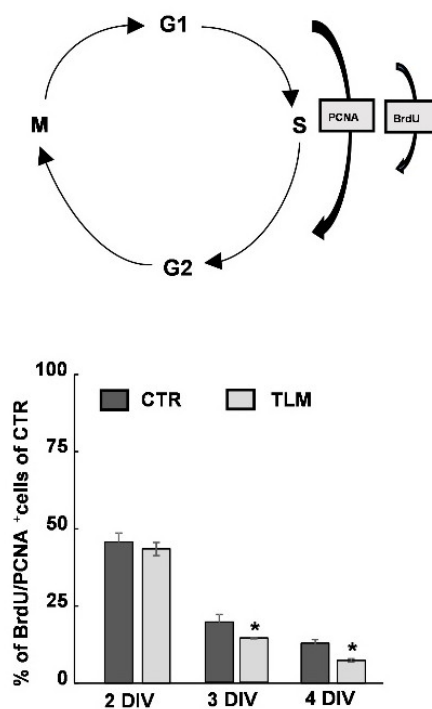


Figure S1. Effects of TLM on OP proliferation. The OPs were treated with TLM for 2, 3 or 4DIV and cell proliferation was evaluated. A schematic representation of the cell cycle phases with proliferation markers used is shown. The percentage of BrdU- and PCNA-positive cells compared to the total cells are shown below. The data represent the means \pm SEM of 3-4 experiments (* p <0.001 vs CTR).

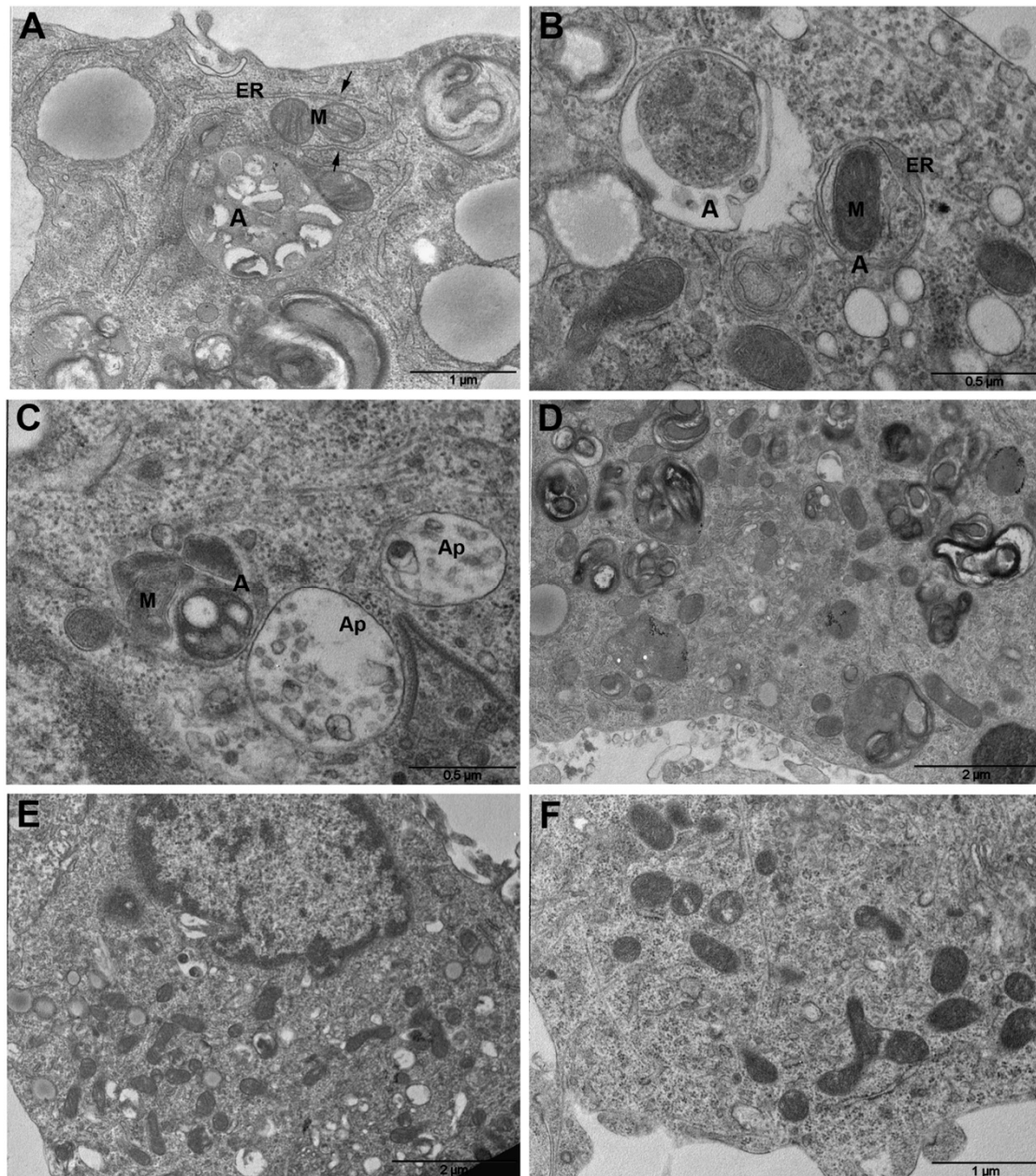


Figure S2. TEM analysis of the impaired autophagy induced by the cholesterol transport inhibitor U18666A in OP cultures. TEM micrographs of cells treated with U18666A are shown in A-D. In **panel A** the arrows indicate a phagophore (endoplasmic reticulum (ER) elongation around two mitochondria (M)). In **panel B** two newly formed autophagosomes (A) in which the cytoplasmic material and a mitochondrion are still intact are shown. Two amphisomes (Ap) and an autophagosome (A) are shown in **panel C**. In the micrograph the progression of digestion is evident, but the mitochondrion residue is still distinguished. In **panel D**, the altered autophagy is represented by many autolysosomes engulfing the cell cytoplasm. In **panel E**, TEM micrograph of an oligodendrocyte treated by U18666A and TLM is shown. The absence of autophagosomes engulfing the cell cytoplasm is evident. In **panel F** shows TEM micrograph of an untreated oligodendrocyte.