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DEGLI STUDI
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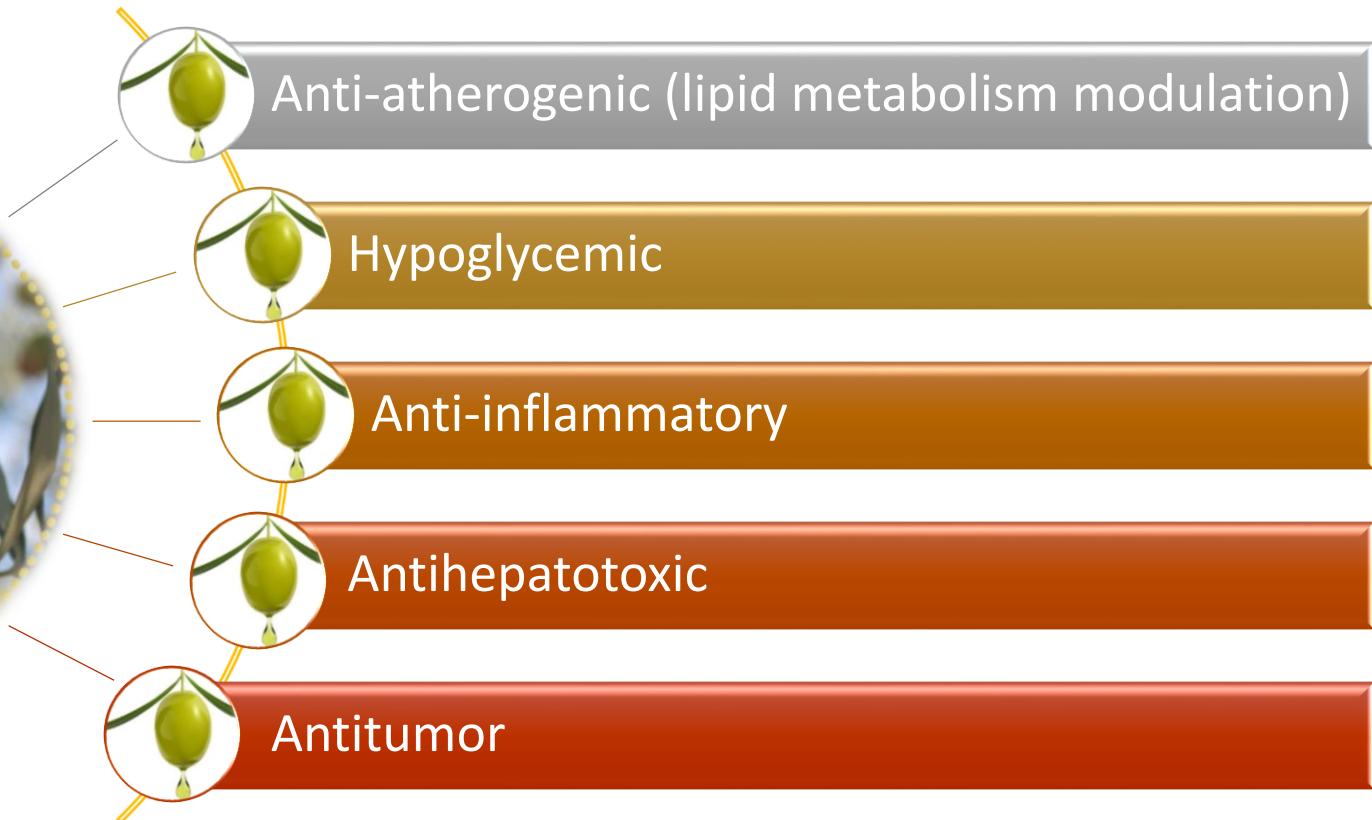
EVOO-polyphenol extracts exert hypocholesterolemic effects through the modulation of the LDLR pathway: in vitro and cellular mechanism of action elucidation

Carmen Lammi

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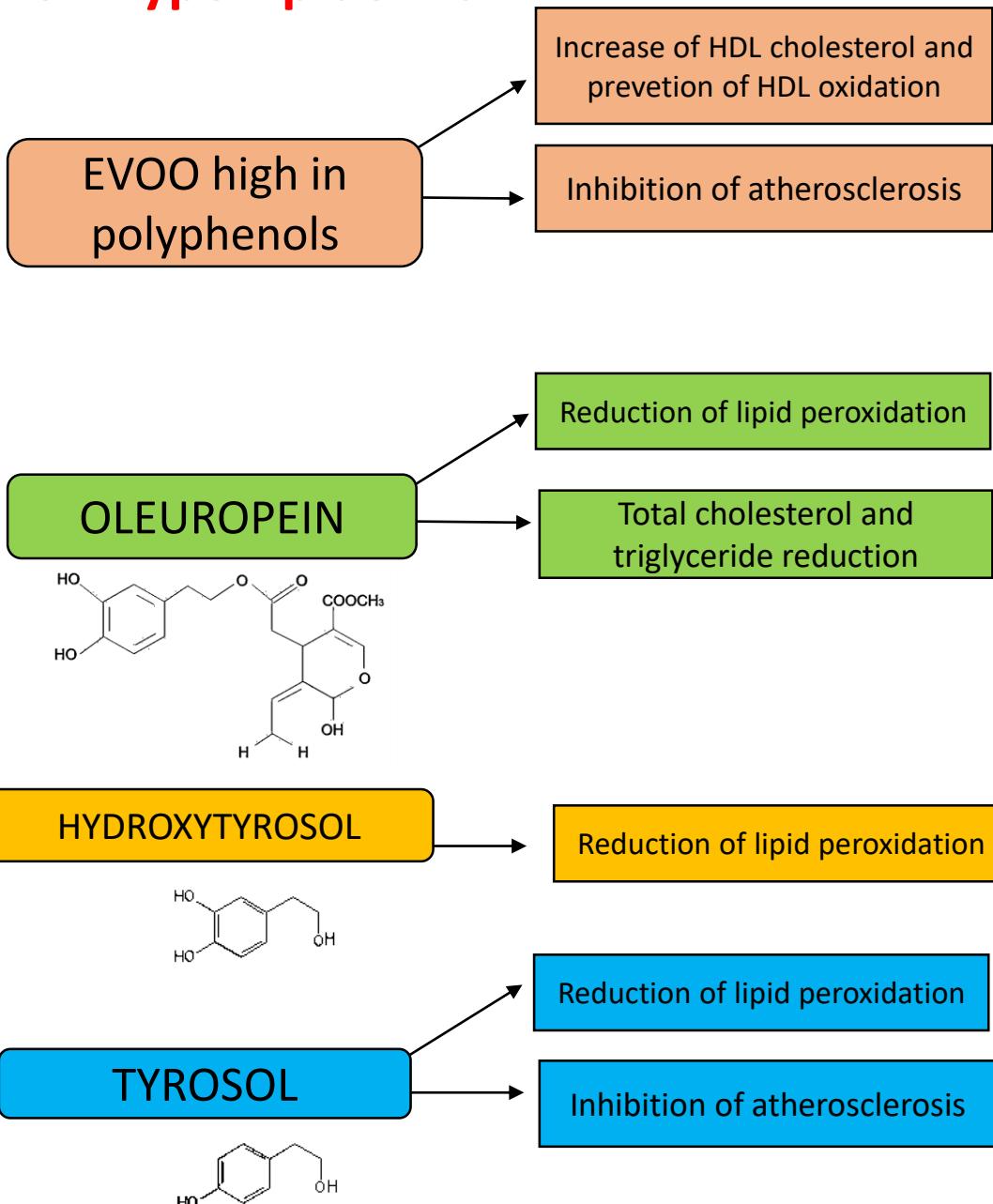
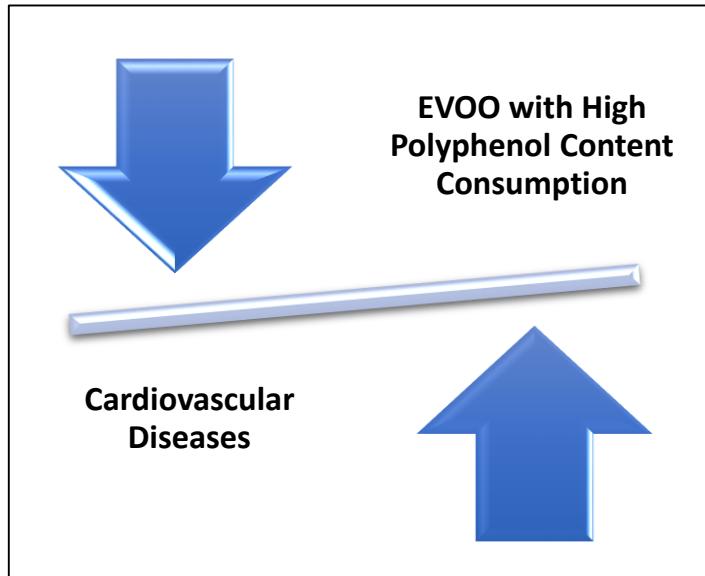


Health-promoting properties of Extravirgin Olive Oil (EVOO) polyphenols



Antioxidant power of these molecules

High Risk Factors: Hyperlipidemia



LDLR

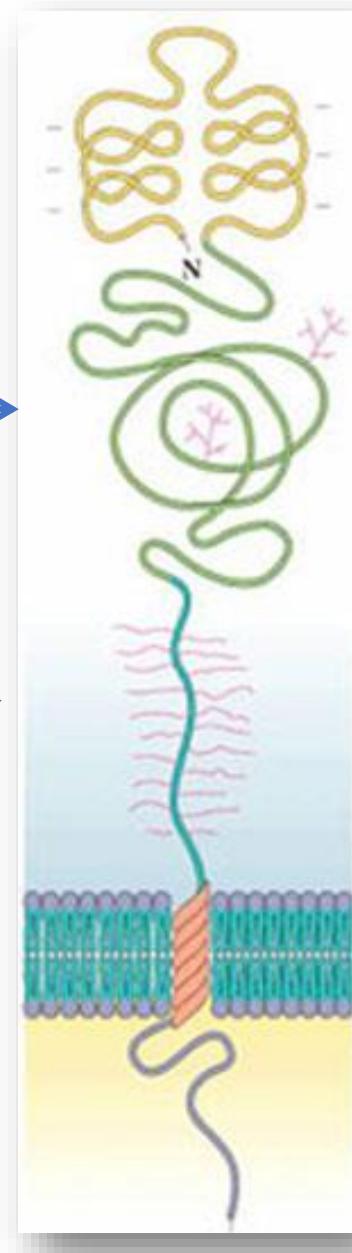
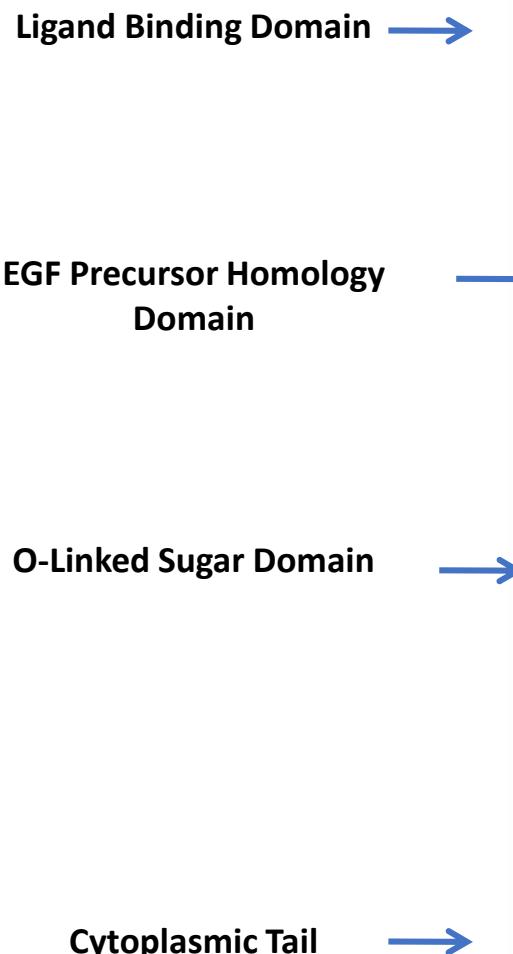
(Low Density Lipoprotein Receptor)

Dyslipidemia, a disorder of lipoprotein metabolism characterized by abnormal lipid amounts in the blood, is a major problem in human health, since it is clearly implicated in atherogenesis and cardiovascular events

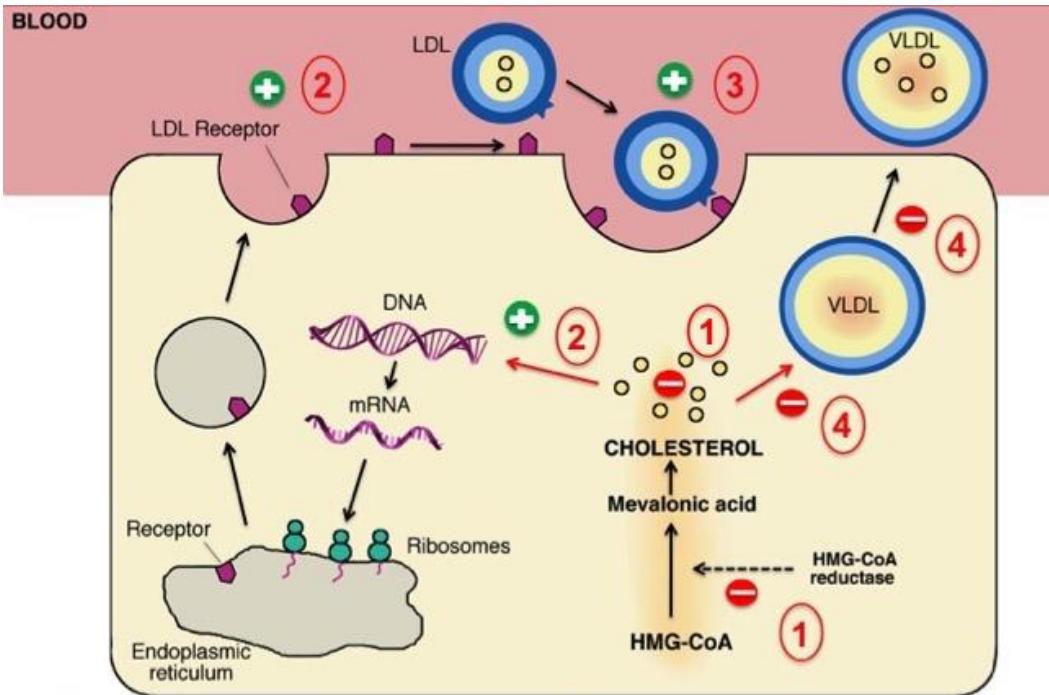


LDL Receptor

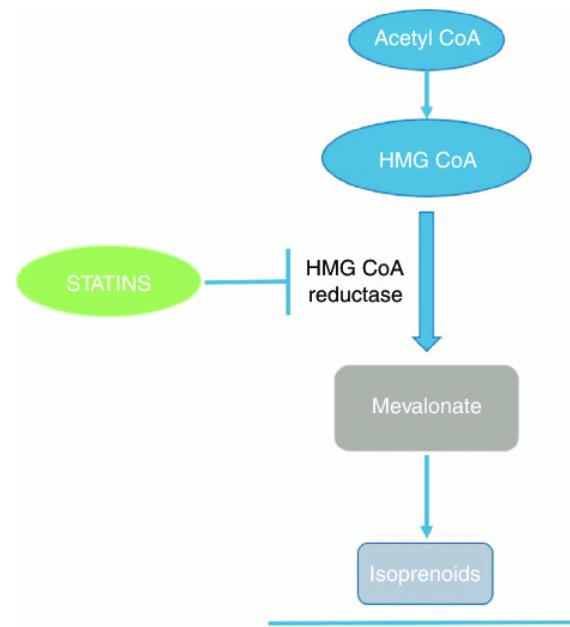
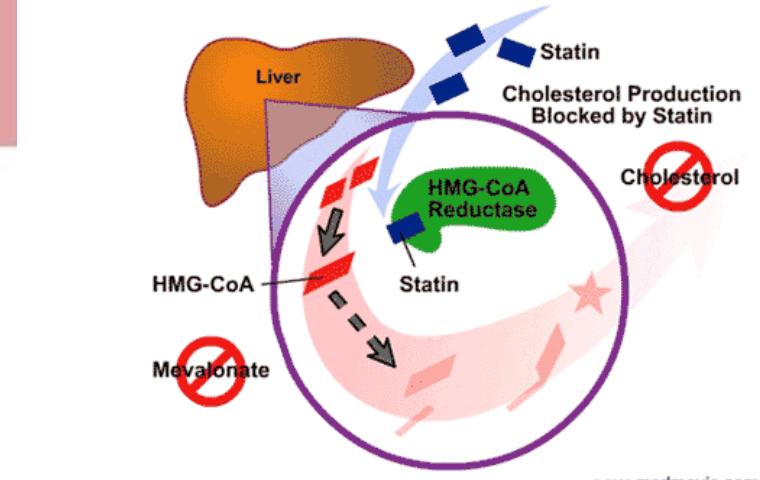
a transmembrane glycoprotein which plays a pivotal role in the binding and endocytosis of circulating LDL increasing its plasma clearance



HMG-CoA reductase *Intracellular pathway*

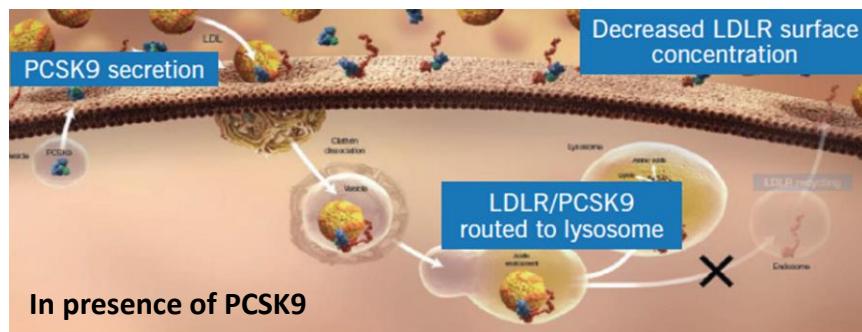
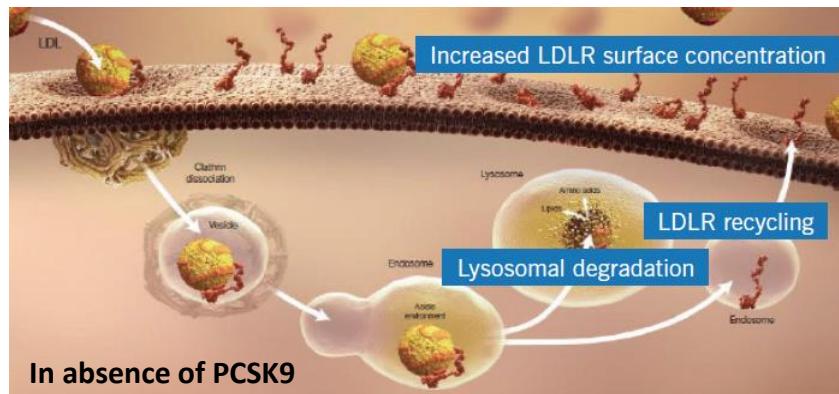


1. The inhibition of HMG-CoA reductase leads to a decreased concentration of intracellular cholesterol
2. LDL receptor level increases
3. The up-take of LDL from blood is enhanced
4. Low intracellular cholesterol decreases the secretion of VLDL

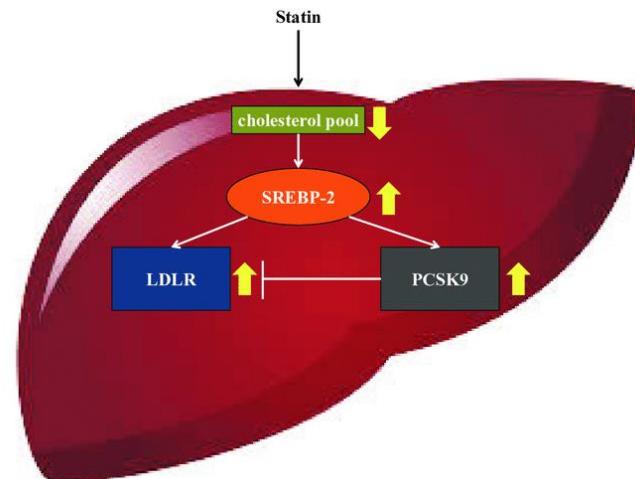


PCSK9

is currently a new target for hypercholesterolemia treatment



Identification of compounds modulating
the intracellular production and secretion of
PCSK9



Statins increase PCSK9 expression, which dampens an effective LDL clearing by promoting LDLR degradation, thereby counteracting their therapeutic effects.

BUO and OMN Extracts Description

TESTED EXTRACTS:

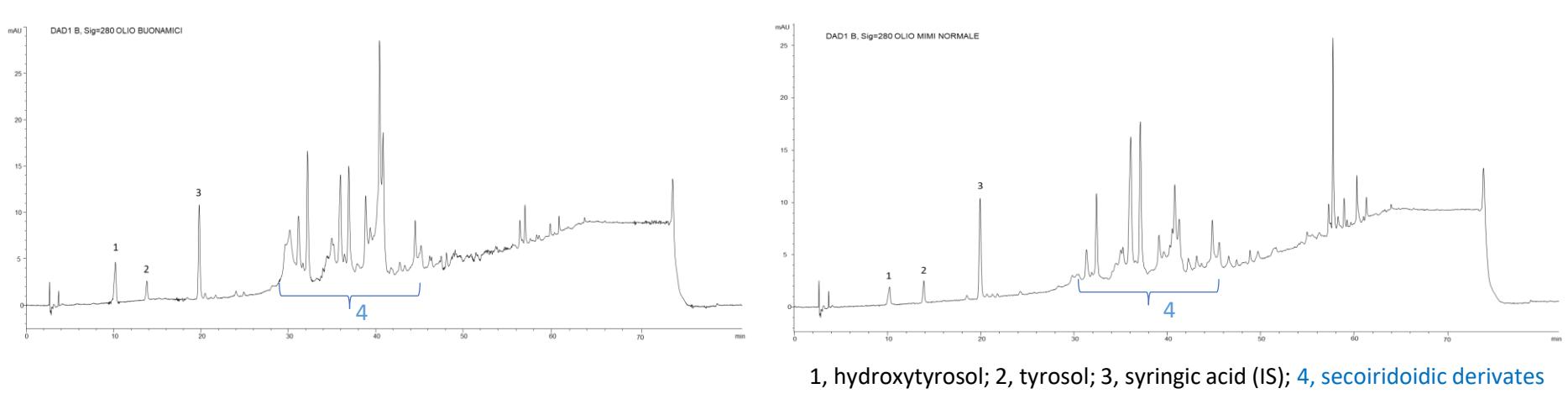
BUO – Sample of Tuscany EVOO (Buonamici, Frantoio cv)

OMN – Sample of Apulian EVOO (Mimi, Coratina cv)



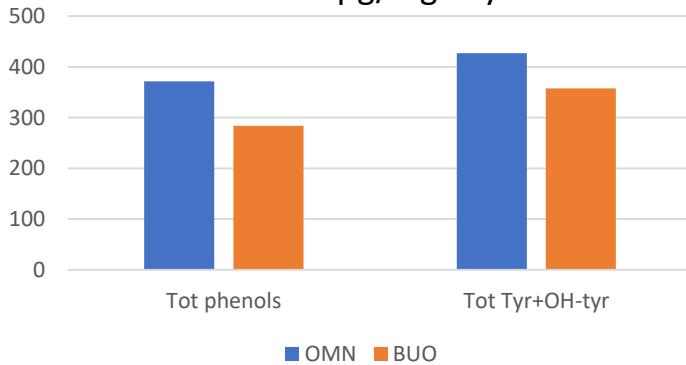
❖ Qualitative

HPLC Profiles of OMN and BUO EVOO Extracts

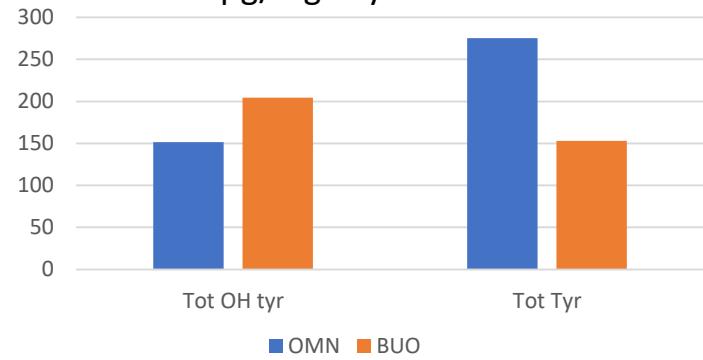


❖ Quantitative

Total Phenols $\mu\text{g}/\text{mg}$ Dry Extract

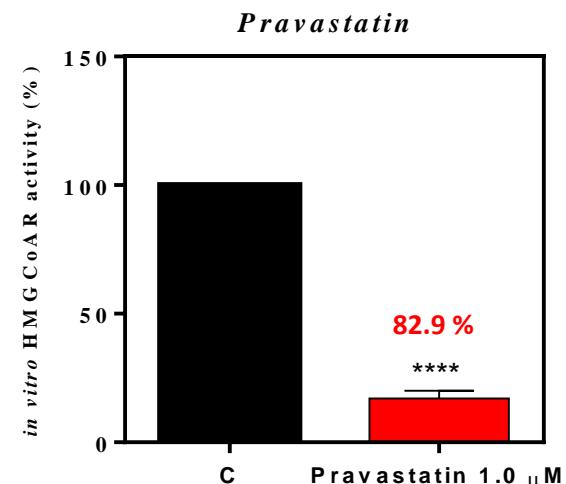
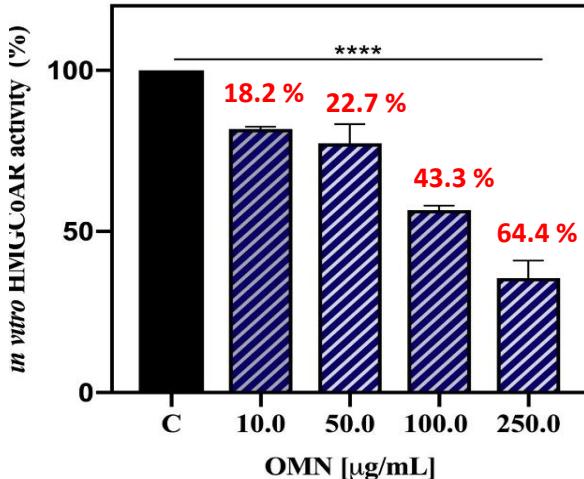
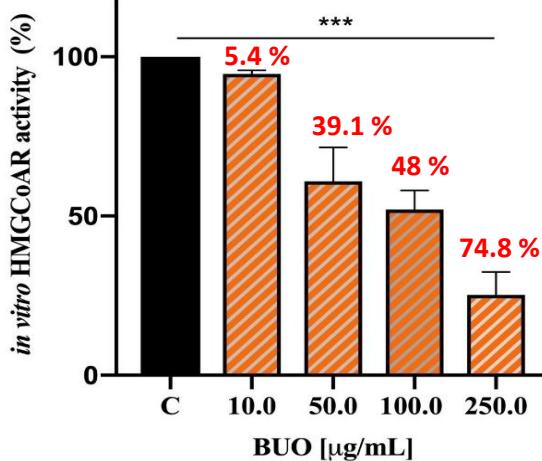
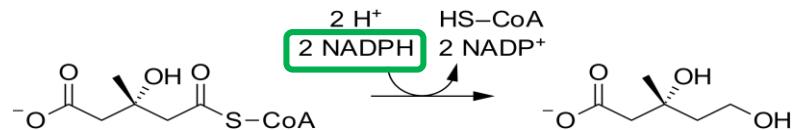
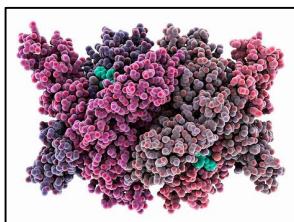


$\mu\text{g}/\text{mg}$ Dry Extract



*Effect of BUO and OMN extracts on the *in vitro* HMGCoAR activity*

HMG-CoA reductase Purified catalytic domain



Nutrition Research
Volume 22, Issue 9, September 2002, Pages 1067-1075

Effects of feeding virgin olive oil or their polyphenols on lipid of rat liver

F Benkhalti ^a, J Prost ^b, E Paz ^c, F Perez-Jimenez ^c, C El modafar ^a, E El Boustani ^a



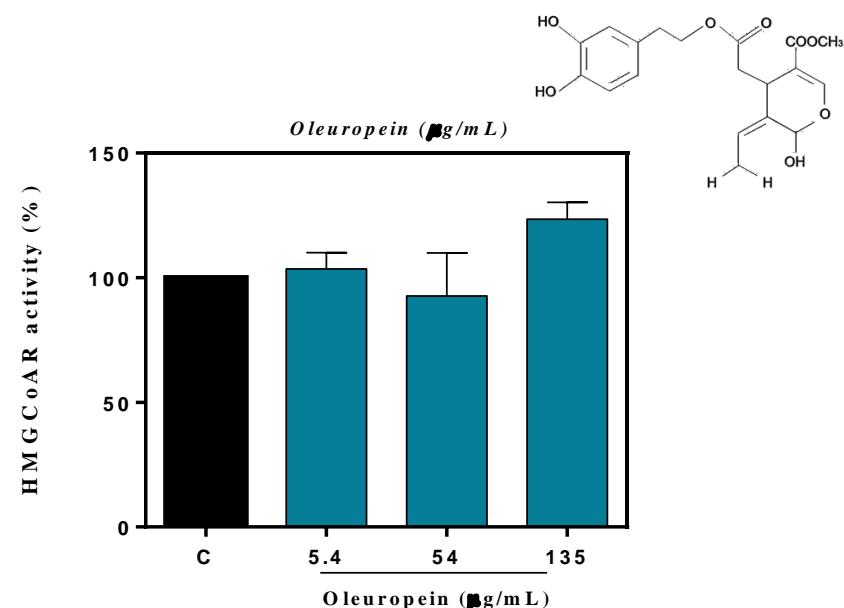
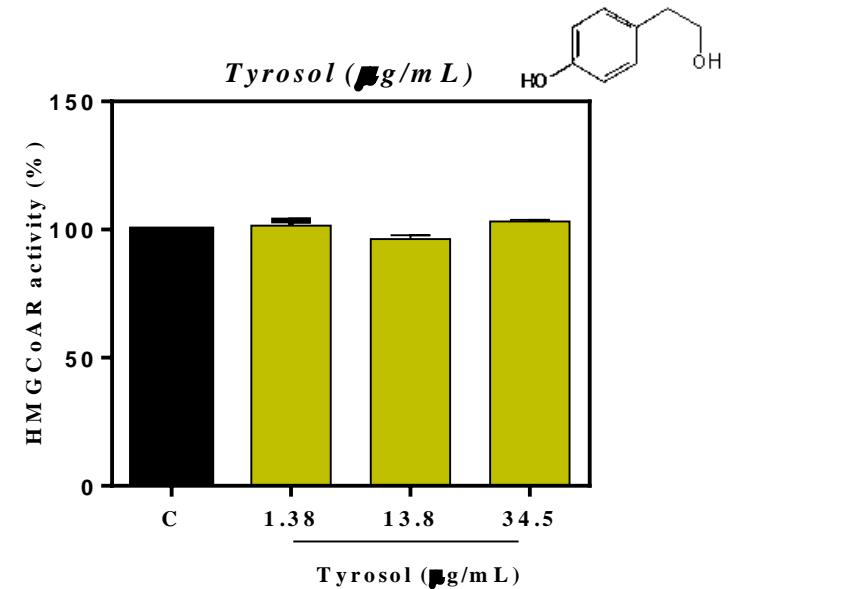
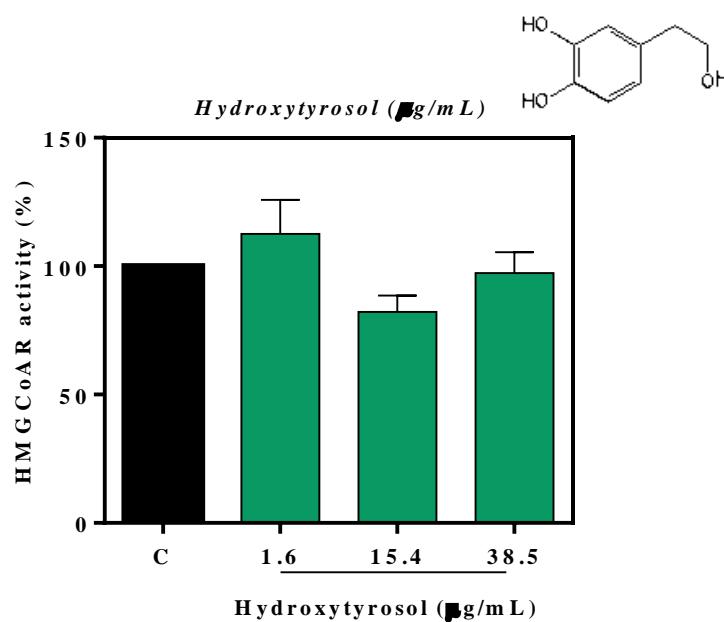
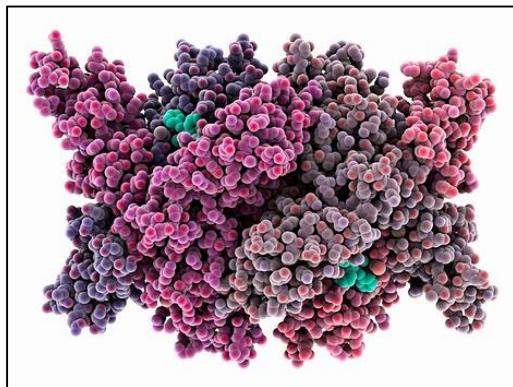
In vivo
study

The activity of HMG-CoA reductase decreased significantly in liver microsome from polyphenols extract-fed rats.

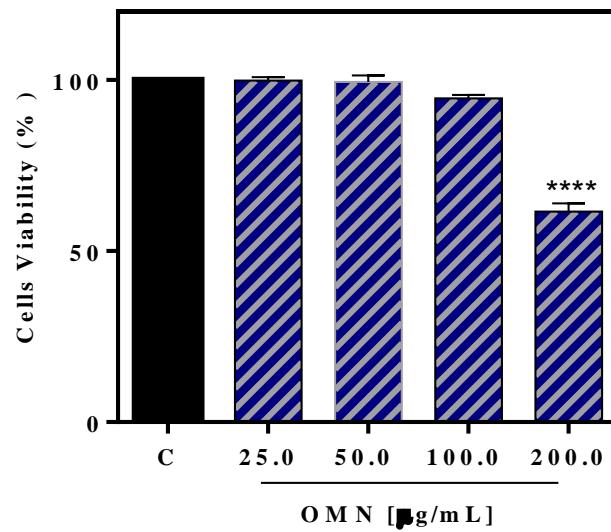
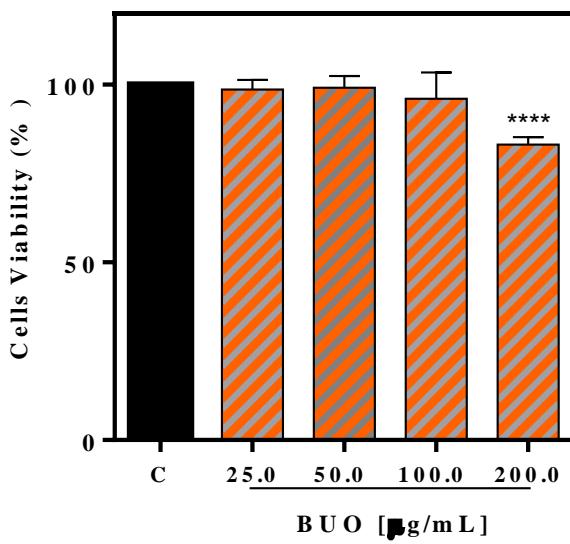
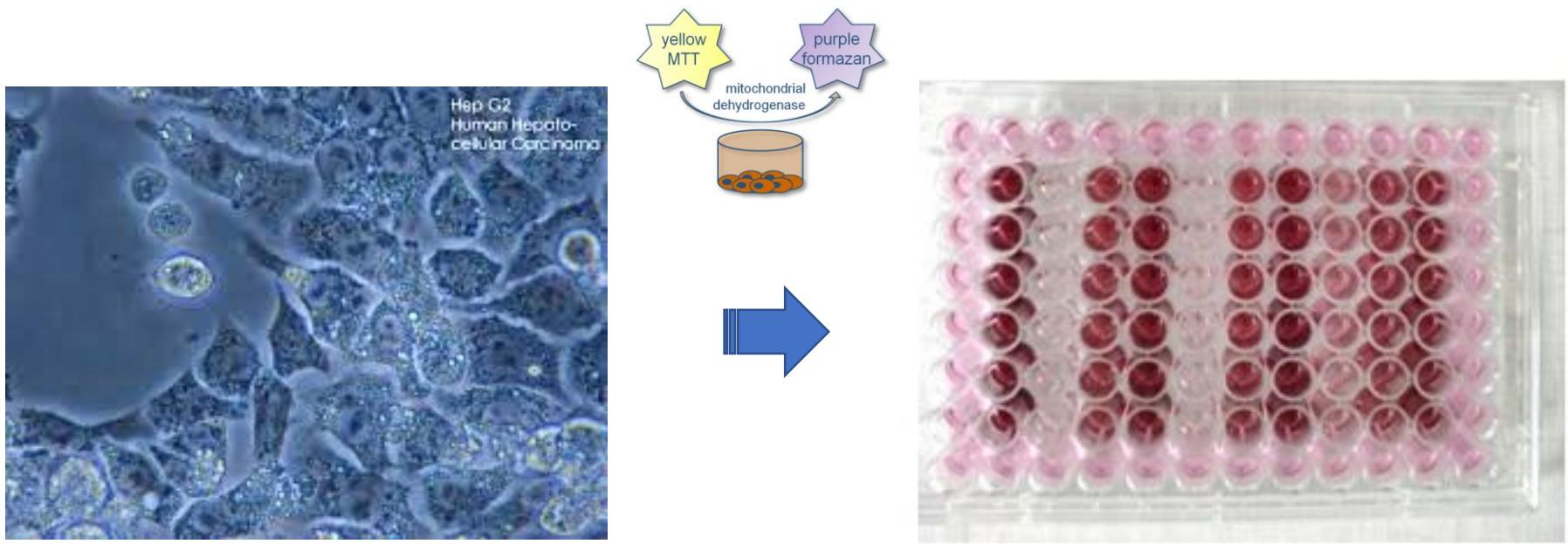


Effect of polyphenols on the in vitro HMGCoAR activity

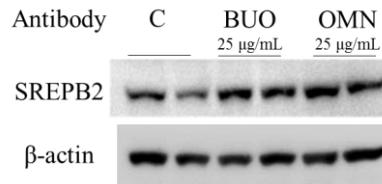
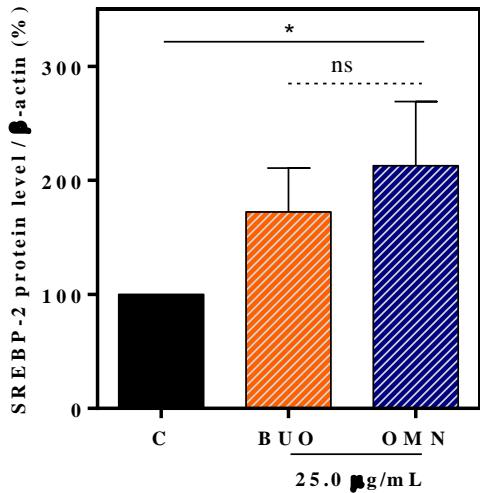
HMG-CoA reductase Purified catalytic domain



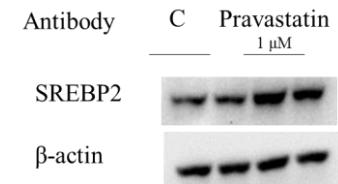
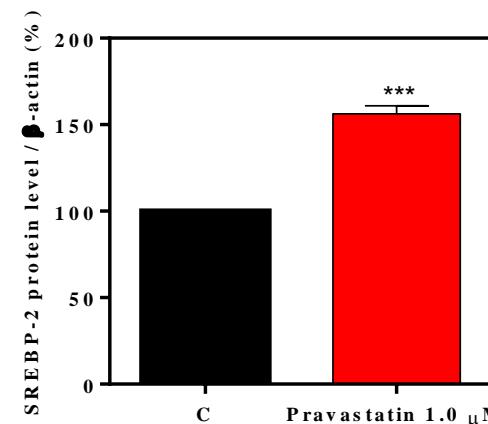
Effect of BUO and OMN on HepG2 cell viability: MTT Experiment



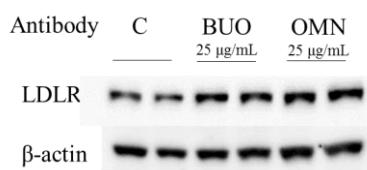
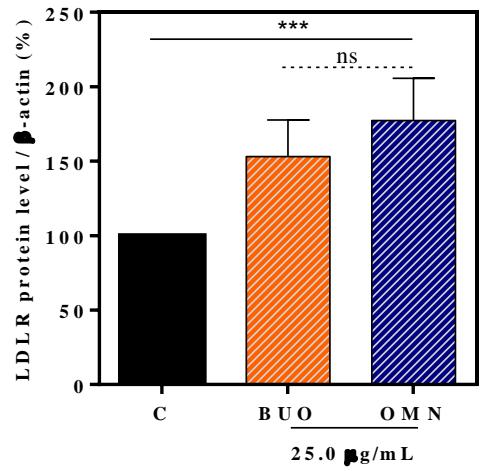
Effect of BUO and OMN extracts on the LDLR Pathway



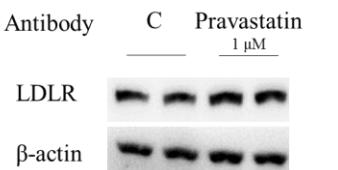
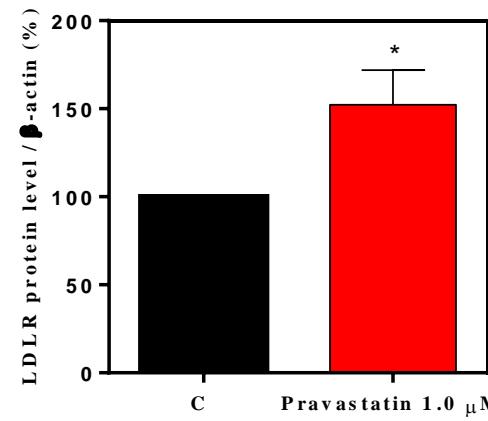
SREBP-2 ↑



SREBP-2 ↑

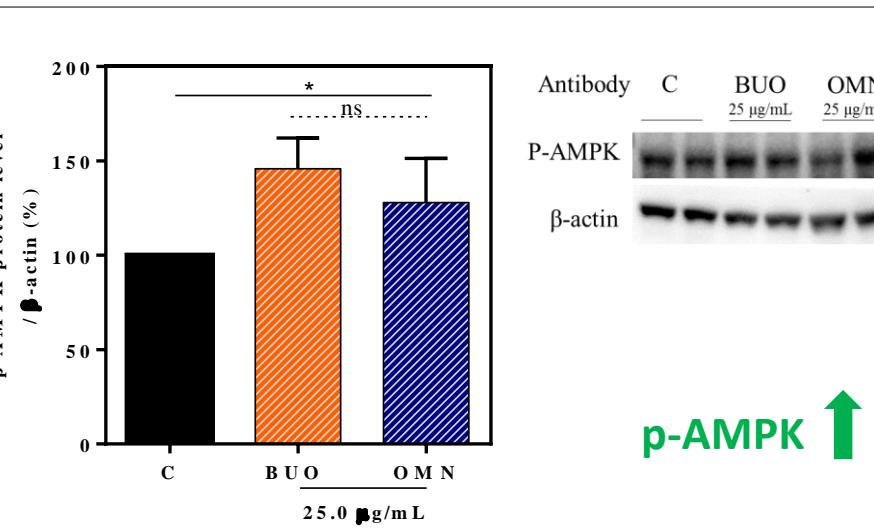
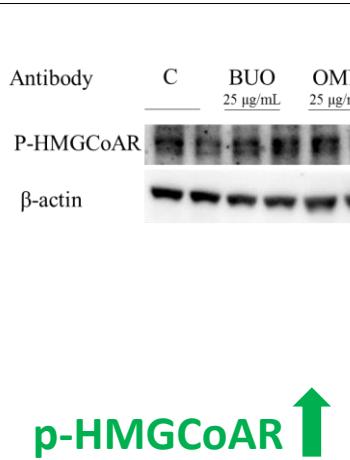
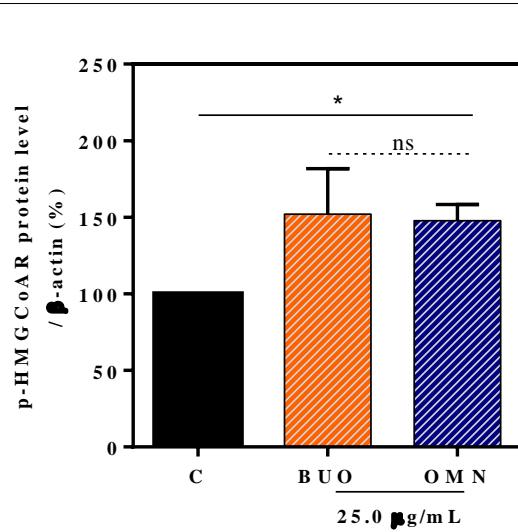
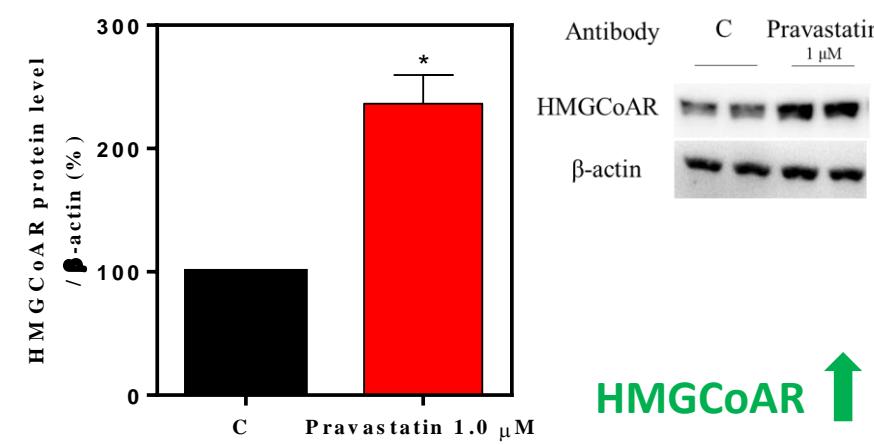
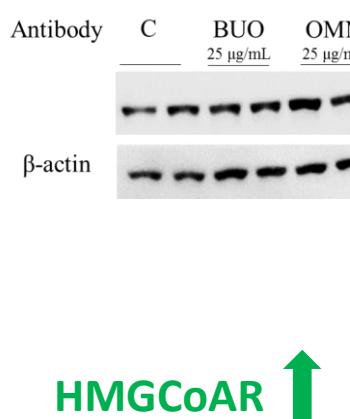
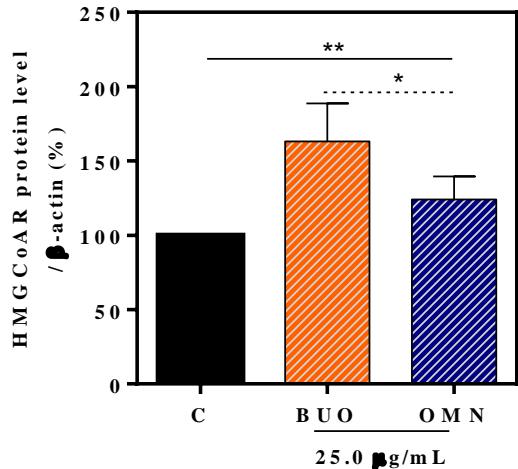


LDLR ↑

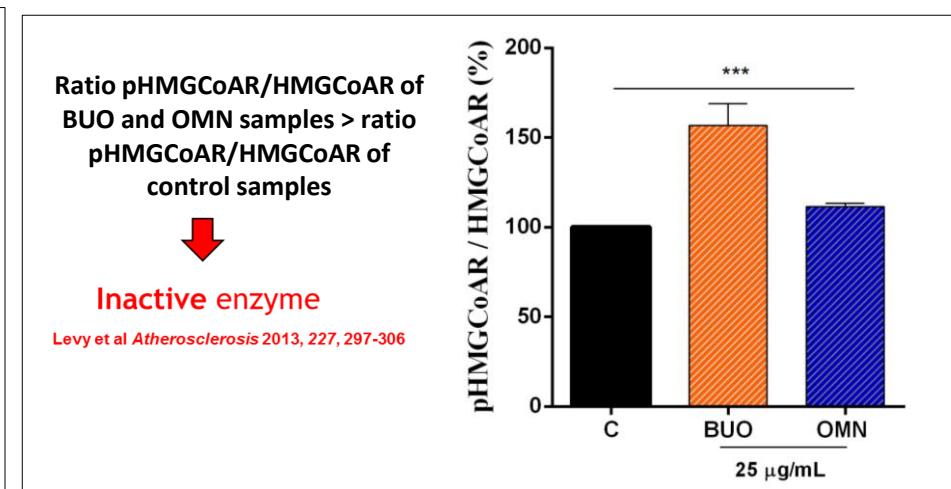
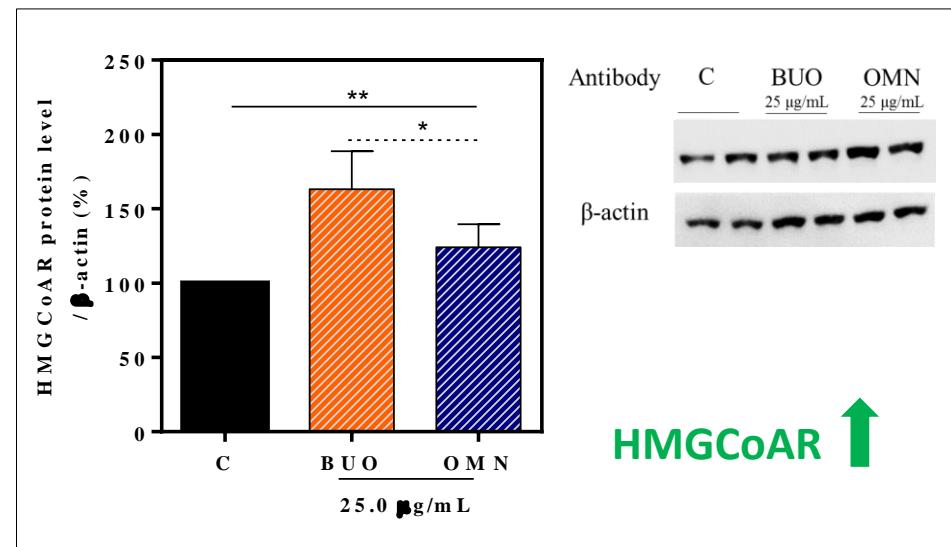
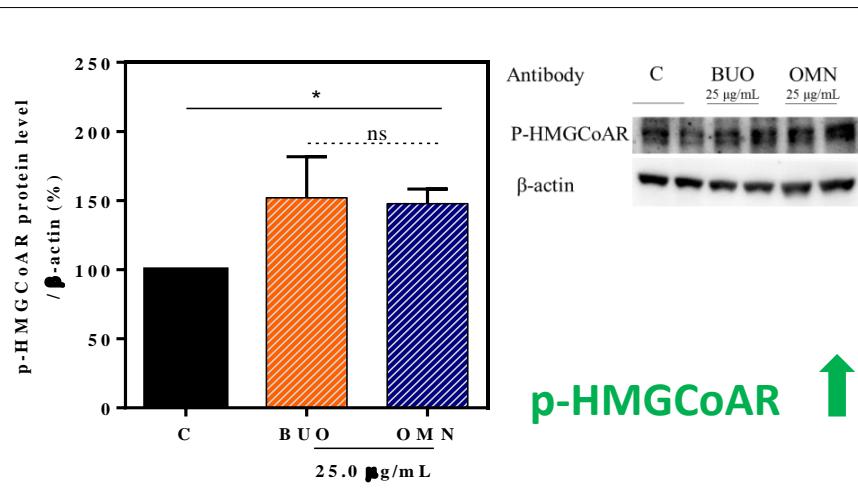
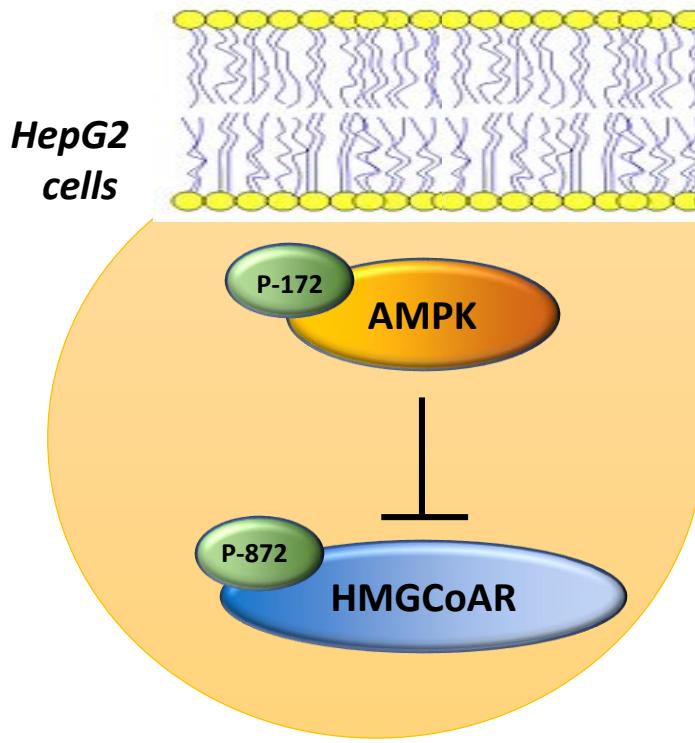


LDLR ↑

Effect of BUO and OMN extracts on the LDLR Pathway



Effect of BUO and OMN extracts on the LDLR Pathway



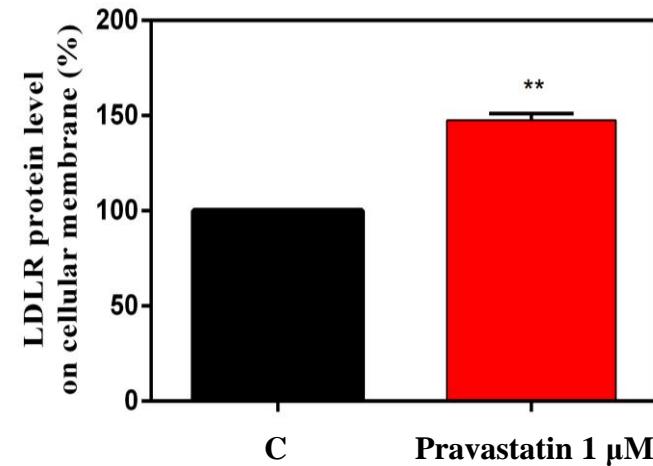
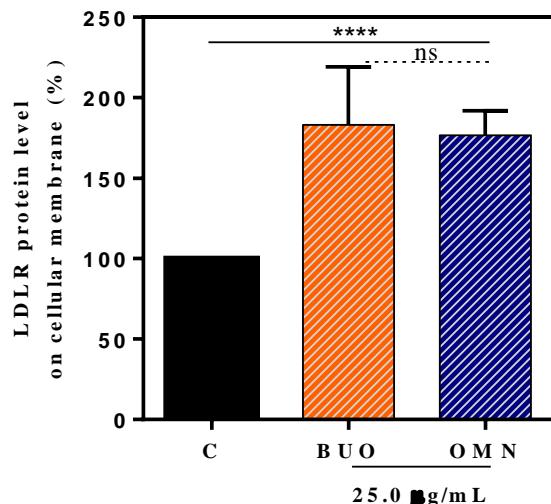
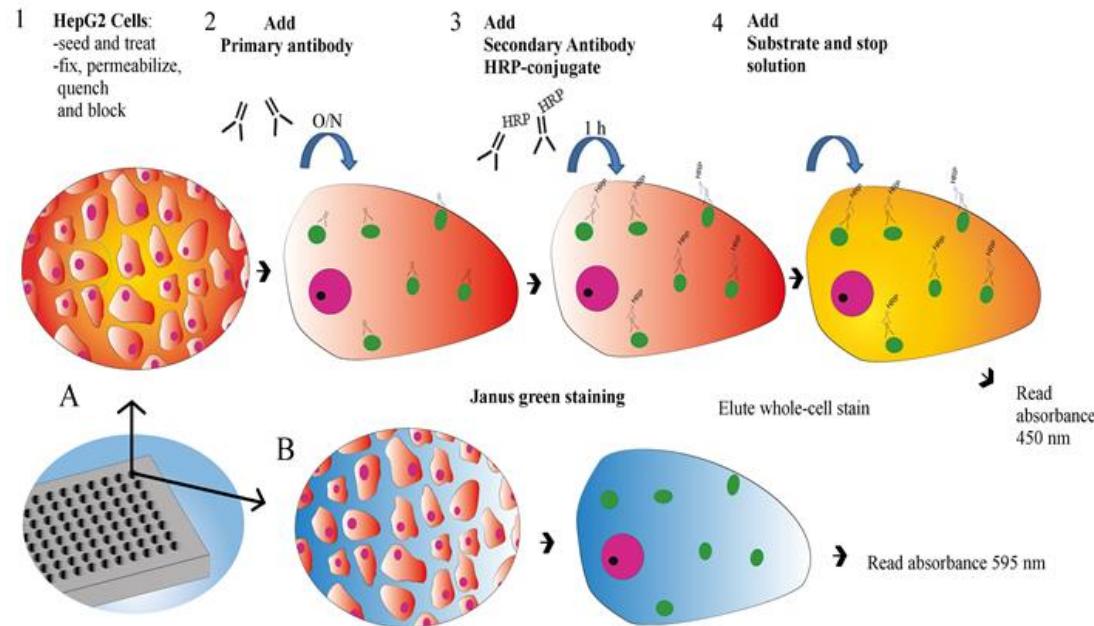
Effect of BUO and OMN extracts on the LDLR Pathway

In-cell Western assay

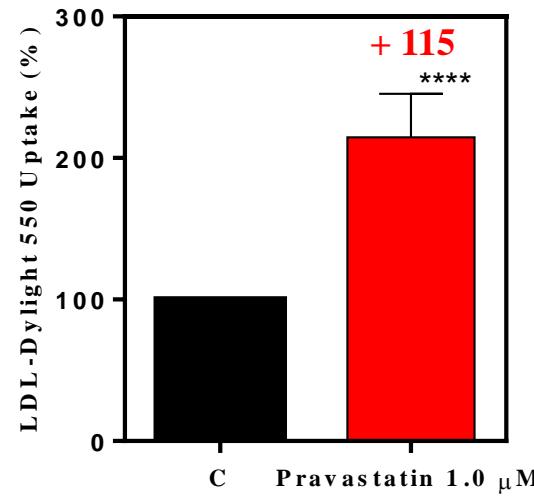
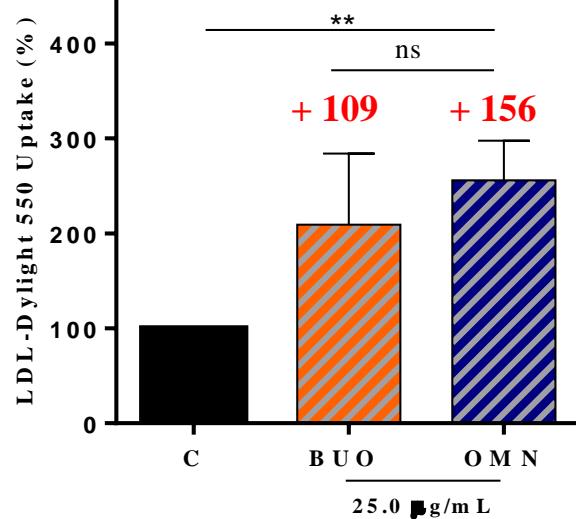
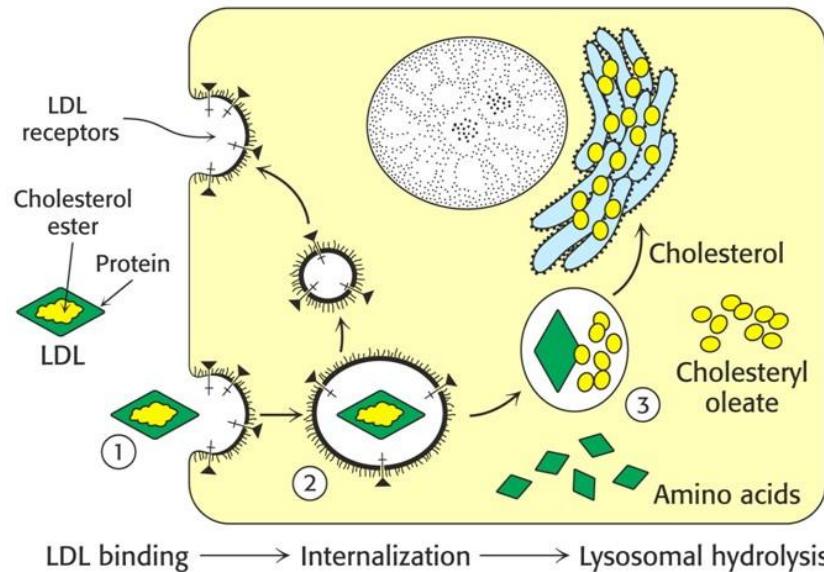
Carmen Lammi, Chiara Zanoni, Anna Arnoldi (2015) A simple and high-throughput in-cell Western assay using HepG2 cell line for investigating the potential hypocholesterolemic effects of food components and nutraceuticals. Food chemistry, DOI:10.1016/j.foodchem.2014.07.133

Giovanni Grazioso, Carlotta Bollati, Jacopo Sgrignani, Anna Arnoldi, Carmen Lammi (2018) First Food-Derived Peptide Inhibitor of the Protein–Protein Interaction between Gain-of-Function PCSK9D374Y and the Low-Density Lipoprotein Receptor. J. Agric. Food Chem. https://doi.org/10.1021/acs.jafc.8b03233

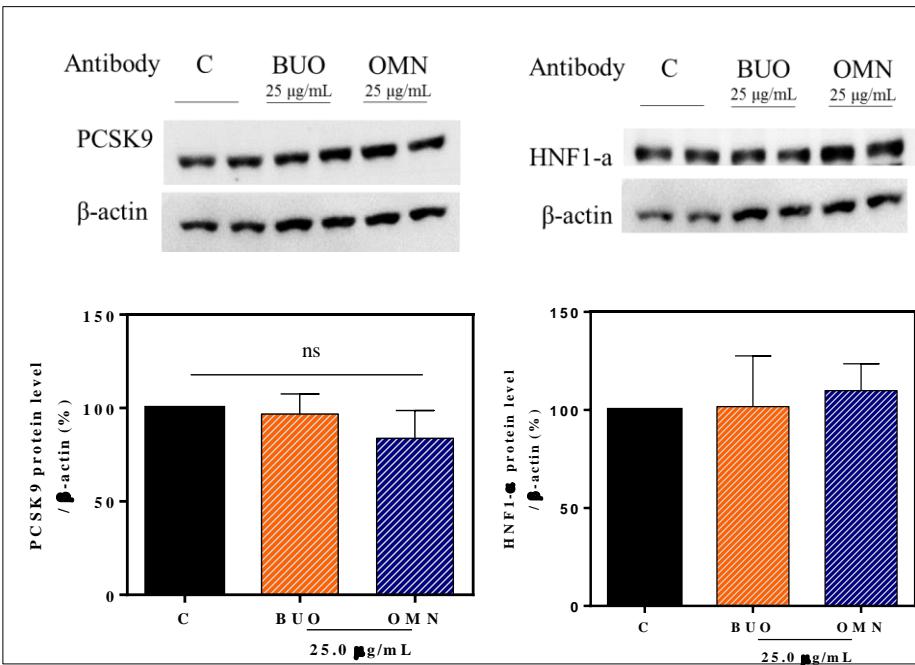
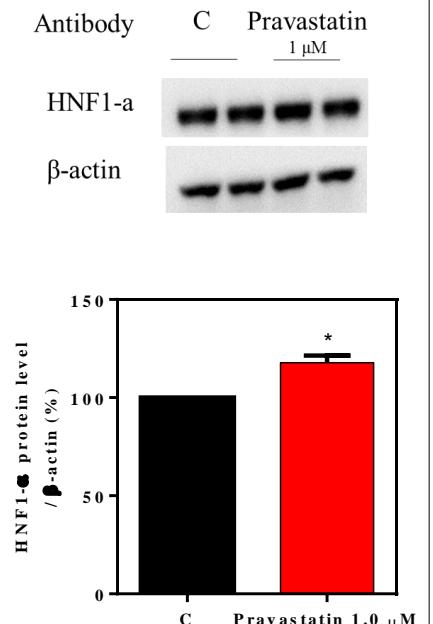
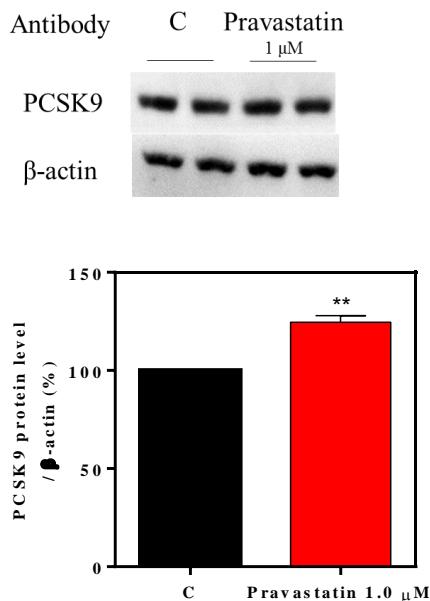
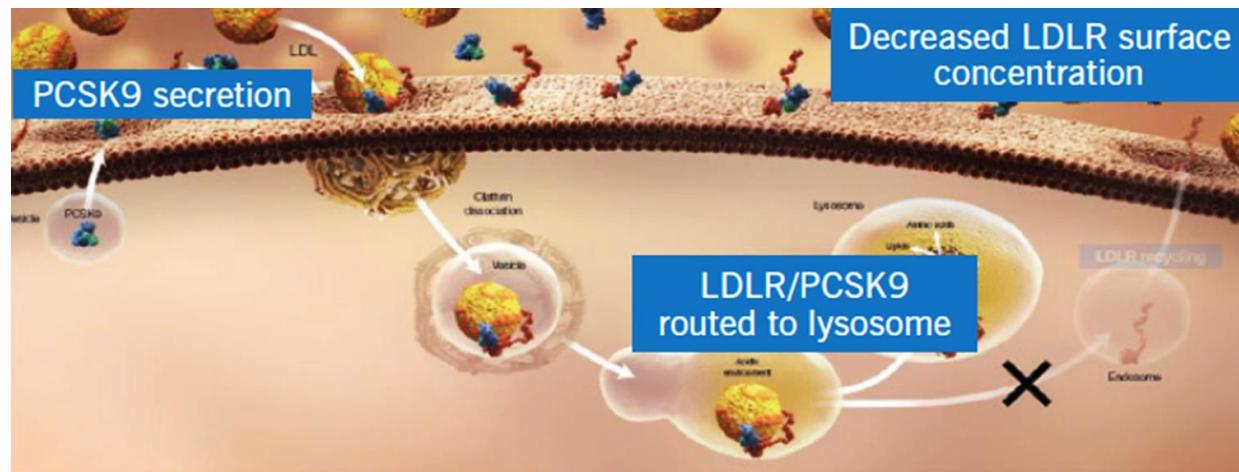
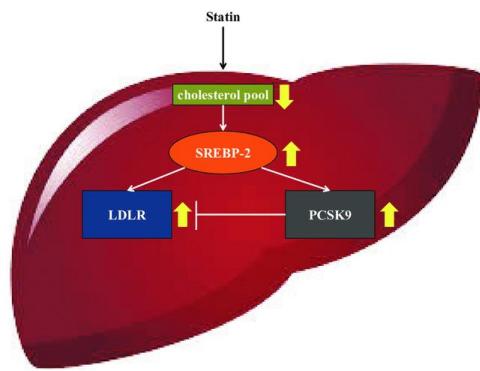
Carmen Lammi, Jacopo Sgrignani, Anna Arnoldi & Giovanni Grazioso (2019) Biological Characterization of Computationally Designed Analogs of peptide TVFTSWEELYLDWV (Pep2-8) with Increased PCSK9 Antagonistic Activity. Sci.Rep.



BUO and OMN improve the functional ability of Hepg2 cells to uptake LDL

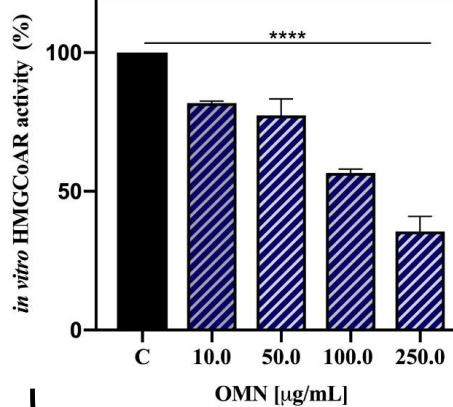
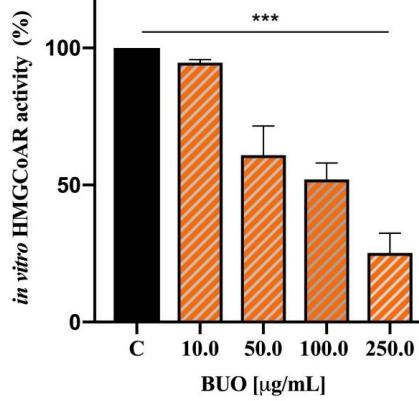


Effect of BUO and OMN extracts on the PCSK9 Pathway

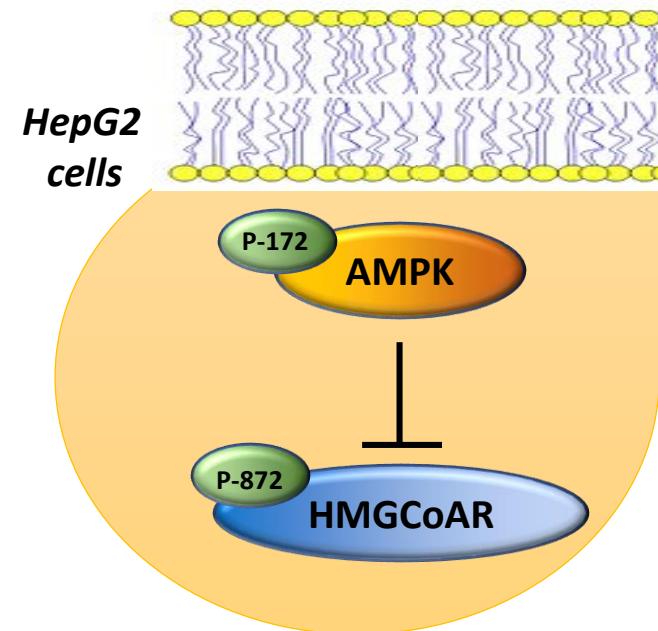


BUO and OMN extracts

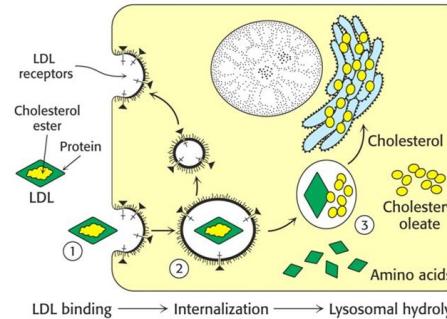
ENZYMIC INACTIVATION



INTRACELLULAR REGULATION

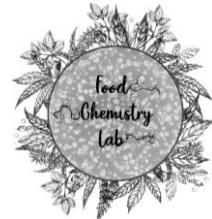


↑
LDLR LEVEL
and
LDL UPTAKE



Acknowledgment

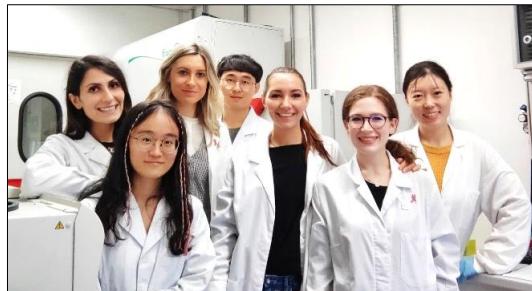
Thank for your kind attention



UNIVERSITÀ DEGLI STUDI
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Prof. Anna Arnoldi

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