EFFECTS OF OLEUROPEIN ON COLON CANCER PROGRESSION *IN VITRO*. A PRELIMINARY REPORT

Carla Flandina[1], Marilena Crescimanno[1], Maria Vittoria Sepporta[2], Gaetano Leto[1]

[1]Dpt. PROMISE , School of Medicine, University of Palermo, Palermo - Italy, [2]Pediatric Unit, Department Women-Mother-Children, Pediatric Hematology-Oncology Research Laboratory,, Lausanne - Switzerland

Introduction: Accumulating evidence highlights that Oleuropein (OLE), one of the main bioactive phenolic compound present in olives, olive oil and olive leaves, appears to exert chemo-preventive effects against several human malignancies including gastrointestinal tumors. As the cellular mechanisms underlying this phenomenon are still not fully elucidated, we have undertaken some in vitro studies to examine the effects of OLE on the growth, adhesion and invasion of HCT116and SW480 human colon cancer cells and the influence of this molecule on the production of certain proteins that appear to be relevant to cancer progression namely, matrix metalloproteinase-2(MMP-2), matrix metalloproteinase-9(MMP-9) and transforming growth factor-β (TGF-β)

Methods: The effects of OLE on HCT116and SW480 colon cancer cells growth, adhesion and invasion were evaluated by i) the colorimetric MTT assay, ii) the fibronectin coated multi-well assay and iii) the Matrigel transwell invasion assay, respectively. The influence of OLE on the rate of MMP-2, MMP-9and TGF-β secretion by tumor cells during adhesion and invasion were determined by enzyme-linked immunosorbent assay.

Results:
1)Exposure of human HCT116and SW480 cancer cells for 24or 72h to different concentrations of OLE (10-500 μM) resulted in a dose- and time-dependent inhibition of cell proliferation. The calculated IC_{50} values were 323.1μM and 186.8μM at 24h and 72h respectively for HCT116tumor cells and 317.6μM at 24h and 226.8μM at 72h for SW480 tumor cells.
2) The adhesion of HCT116tumor cells exposed to non-cytotoxic concentrations of OLE (50-250 μM) up to 4h was reduced by 30% as compared to untreated cells while, a 72h continuous exposure to OLE (10-100 μM) decreased HCT116cell invasion by 40%. This molecule showed to inhibit also SW480 tumor cell adhesion (-25%) but only at the highest drug concentration (250 μM) while, its effects on SW480 invasion were negligible.
3) The secretion of MMP-2, MMP-9and TGF-β by OLE-treated HCT116cells during adhesion experiments was reduced (-39%,-19%,-48% respectively) as compared to unexposed cells while, in invasion experiments, the extracellular release of MMP-2and MMP-9resulted increased at 24h (+41% and +23%) and then decreased (~ -25%) after 72h. However, TGF-β secretion was not significantly influenced by drug treatments. Finally, in invasion experiments, MMP-9and TGF-β secretion by OLE-treated SW480 cells resulted impaired (-32% and-74% respectively) while, MMP-2levels were only slightly affected (-10%)

Conclusions: These data indicate that OLE might exert its chemo-preventive effects by interfering with some key steps of cancer progression, such as tumor cell proliferation, adhesion and invasion and by modulating the extracellular secretion of proteins that may foster these processes. Further studies to better assess the specific molecular mechanisms underlying these phenomena are warranted by these preliminary observations.