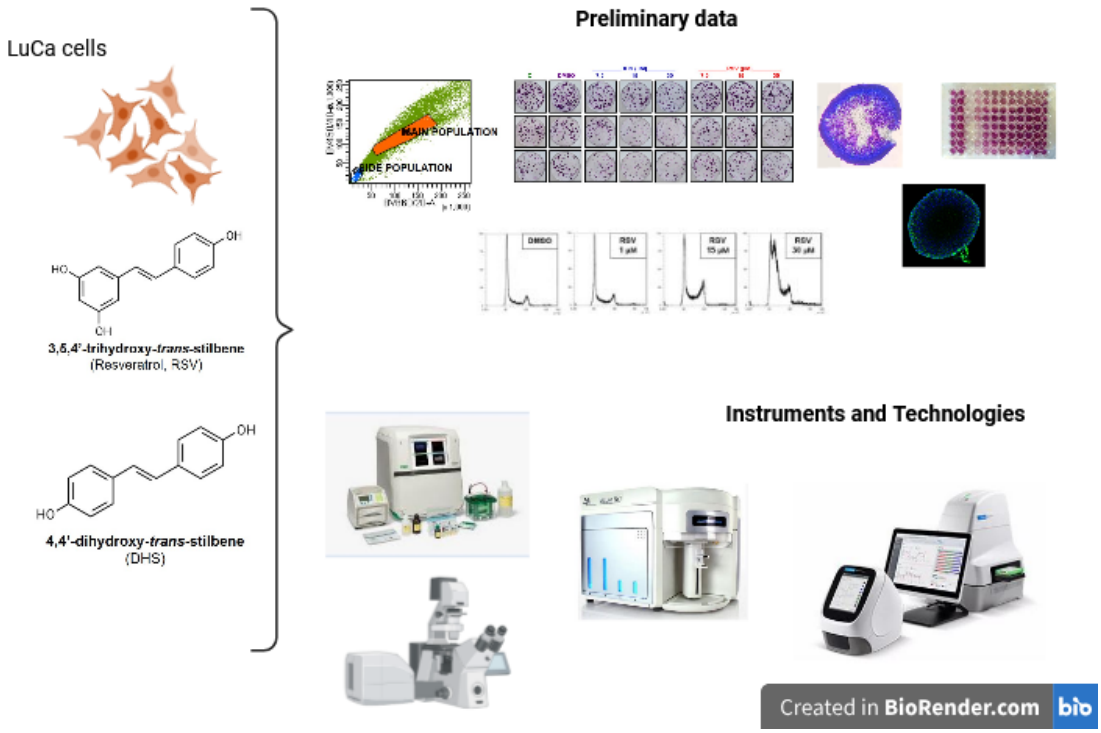
The Function of Natural Compounds in anti-Cancer Mechanisms.
PI: Monica Savio
Research Theme/Topic: Cellular and molecular mechanisms of resveratrol derivatives against cancer development.

Lung cancer (LuCa) is one of the most clinically relevant tumours, and its eradication remains an elusive clinical goal, largely because of the heterogeneous and peculiar nature of individual cancers, the onset of metastasis, and the inability to target therapies to neoplastic cells without damaging normal tissues. Growing evidence demonstrates that natural or synthetic derived compounds represent a fundamental source to reduce or delay the occurrence of malignancy or to synergise with traditional chemotherapeutic agents. In the last few decades, stilbene-based compounds have been widely investigated due to their multiple biological properties, and among these, the most studied has been resveratrol (3,4′,5-trihydroxy-*trans*-stilbene), especially for its cancer chemoprevention activity. We have synthesized and studied the anticancer activity of new hydroxylated and methoxylated resveratrol analogues, and in particular 4,4'-dihydroxy-*trans*-stilbene, which has shown a stronger inhibition of LuCa proliferation than resveratrol.

In order to identify the molecular mechanisms involved in tumour progression of lung cancer and evaluate new preclinical therapeutic strategies, the candidate in this PhD project will: 1) investigate the molecular mechanisms underlying the antitumor activity of 4,4'-dihydroxy-*trans*-stilbene, which appear to involve different signalling pathways from those activated by resveratrol; 2) study the impact on subpopulation of cancer stem cells (CSCs), identified and isolated with sorting strategy; 3) perform combined treatment approaches with the most bioactive derivatives together with traditional chemotherapeutic agents.
Techniques: Human and mouse cell cultures, Co-cultures, Spheroid formation, Immunofluorescence, Western Blotting, Flow Cytometry, Elisa, Immunochemistry, qPCR, RT-PCR, siRNA, Comet Assay, Adhesion and Migration assay (Boyden chamber), Transcriptome and Proteomic analysis, Real Time Cell Metabolic Analysis (Sea Horse).