

<b>Title</b>	<b>Novel anticancer strategies to fight drug resistance</b>
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**Project description:**

Targeted chemotherapy, one of the principal modes of treatment for cancer, has revolutionized cancer treatment. Nevertheless, its effectiveness is quite often offset by drug resistance, one of the most challenging problems facing cancer research today. A diverse range of molecular alterations has been implicated in drug resistance. These include increased rates of drug efflux, alterations in drug metabolism, changes in the tumor environment and mutation of drug targets, among others. Moreover, tumors are highly adaptable, and the activation of survival signaling pathways and the inactivation of downstream death signaling pathways can also lead to drug resistance. To complicate matters, many of these factors can be at play simultaneously in a single tumor. Thus, much effort is needed to design more effective drugs and/or strategies toward which resistance does not develop. An interesting strategy involves combining two active drugs functionalized with a lipophilic tail and a suitable linker into a single supramolecular structure (nanoparticle) that can interact with two relevant components of cancer process. A further approach is the design of dual ligands, i.e. single chemical entities acting on two biomolecular targets. The project aims at the biological evaluation of novel dual ligands and nanoparticles, allowing the selection of few leads endowed with an optimal antiproliferative activity on resistant cancer cells. The involved intracellular molecular target(s) will be also assessed. A full characterization of the molecular mechanism(s) of the selected most promising hits, leading to the cytotoxic effect on resistant cells, is the main goal of the research project. The PhD student will mainly focus on the field of cell and macromolecular biology. A wide range of techniques should be employed, ranging from cell manipulation to spectroscopic and electrophoretic methods, applied to molecular biology.

**Publications:**

**L. Dalla Via\***, M. Mejia, A. N. García-Argáez, A. Braga, A. Toninello, M. Martínez-Vázquez, Anti-inflammatory and antiproliferative evaluation of 4 $\beta$ -cinnamoyloxy,1 $\beta$ ,3 $\alpha$ -dihydroxyeudesm-7,8-ene from *Verbesina persicifolia* and derivatives *Bioorg. Med. Chem.* 23, 5816-5828 (2015). **L. Dalla Via\***, A. N. García-Argáez, E. Agostinelli, D. Belli Dell'Amico, L. Labella, S. Samaritani, New *trans* dichloro (triphenylphosphine)platinum(II) complexes containing N-(butyl),N-(arylmethyl)amino ligands: Synthesis, cytotoxicity and mechanism of action *Bioorg. Med. Chem.* 24, 2929-2937 (2016). G. Fumagalli, M. S. Christodoulou, B. Riva, I. Revuelta, C. Marucci, V. Collico, D. Prospero, S. Riva, D. Perdicchia, I. Bassanini, A. García-Argáez, **Lisa Dalla Via**, D. Passarella, Self-assembled 4-(1,2-diphenylbut-1-en-1-yl) aniline based nanoparticles: podophyllotoxin and aloin as building blocks *Org. Biomol. Chem.* 15, 1106-1109 (2017).

**Collaborations/Network:** National: Universities of Ferrara, Milano, Pisa, Palermo and Roma "La Sapienza". International: Universidad Nacional Autónoma de México (UNAM), Universidad de Colombia.