Title	**Dual kinase/HDAC inhibitors for cancer treatment**
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Project description:

The research on anti-cancer drugs is constantly moving towards the targeted therapy, that relies on inhibiting specific biomolecules fundamental for cancer growth. Ideal biological targets are the tyrosine kinases (TKs) and the histone deacetylases (HDACs). Recent findings have highlighted the importance of a multi-target approach: the simultaneous blockade of different pathways involved in the cancer growth leads to a more effective therapy, with reduced drug resistance phenomena onset. The co-administration of a TK inhibitor and of an HDAC inhibitor is largely more effective than the administration of a single drug. The multi-target approach can be pursued also through a single agent endowed with multiple potency (*i.e.* a single compound able to inhibit more targets), leading to higher potency and lower side effects when compared with the co-administration of different target-selective agents. The present project relies on the synthesis and the biological evaluation of novel anticancer multi-target compounds able to inhibit: 1) at least one tyrosine kinase and 2) one of the HDAC isoforms. The expected results of the project will be: 1) the development of novel compounds of pharmaceutical interest; 2) the improvement of the knowledge on dual inhibitors; 3) the improvement of the knowledge regarding the intercommunication between the TKs-mediated pathways and the HDACs-mediated pathways. The PhD student will deal with both classical and advanced organic synthesis techniques. Once new lead compound(s) will be identified, small libraries of analogues will be prepared by using the late stage functionalization techniques recently developed for the fast identification of pharmaceutically promising compounds characterized by improved solubility and catabolic stability.

Publications:

- Carbajales C., et al., *ACS Comb Sci*, 19, 153-160, **2017**
- Marzaro G., et al., *Eur J Med Chem*, 115, 416-425, **2016**
- Gandin V., et al., *Sci Rep*, 5, 16750, **2015**
- Marzaro G., et al., *J Med Chem*, 57, 4598-4605, **2014**
- Conconi M.T., et al., *Eur J Med Chem*, 67, 373-383, **2013**

Collaborations/Network:

Internal collaborators: Prof. Adriana Chilin (DSF); Dr. Valentina Gandin (DSF); Dr. Andrea Mattarei (DSF). External collaborators: Prof. Matthew B. Soellner (University of Michigan, USA; pharmacy.umich.edu/people/soellner); Prof. Ke Ding (Guangzhou University, China; english.gibh.cas.cn/iocb/rp/DingKe/); Prof. Alberto Coelho Coton (University of Santiago de Compostela, Spain; www.researchgate.net/profile/Alberto_Coelho)

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