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# Development of prohibitin ligands to treat cancers, cardiac and immunological disorders

Laurent Désaubry

Laboratory of Cardio-oncology and Medicinal Chemistry, CNRS, University of Strasbourg, France & Sino-French Joint Lab of Food Nutrition/Safety and Medicinal Chemistry, Tianjin University of Science and Technology, China

***Abstract***

Over the last three decades, the scaffold proteins prohibitins-1 and -2 (PHB1/2) have emerged as key signaling proteins regulating a myriad of signaling pathways in health and diseases. Small molecules targeting PHBs display promising effects against several disease. With our collaborators we developed analogues of natural products belonging to the class of flavaglines that block the interaction between PHBs and C-RAF and, thereby, inhibit C-RAF-MEK-ERK signalling, which is critical to survival and proliferation of cancer cells.

We also demonstrated that these compounds protect the hear from the adverse effects of cancer chemotherapies involving anthracyclines. We showed that this cardioprotection i mediated by the activation of the mitochondrial PHB-STAT complex.

In addition to these lines of research, we also developed new PHB ligands belonging to the classes of spiro-oxindoles and triazines that respectively promote cardioprotection and modulate the biosynthesis of melanin in melanocytes. The structure-activity relationships of these new drugs and their detailed mechanism of action will also be presented.

***Biography:***

Laurent Désaubry is a CNRS research director in the University of Strasbourg in France (website: http://desaubry.u-strasbg.fr/) and adjunct professor at Tianjin University of Science and Technology (TUST) in China. After a Ph.D. degree in medicinal chemistry at Strasbourg University and postdoctoral internership at SUNY at Stony Brook, USA and he Strasbourg he got a CNRS Research Senior Scientist at CNRS. He was promoted CNRS research director (corresponds to full professor) in 2014, and became also adjunct professor at TUST in 2015. He has published more than 90 publications and has been serving as an editorial board member of Frontiers in Chemistry, Medicinal Chemistry, Current Chinese Chemistry and The Open Medicinal Chemistry Journal.

***Speaker Publications:***

1. Flavaglines as natural products targeting eIF4A and prohibitins: From traditional Chinese medicine to antiviral activity against coronaviruses; Eur J Med Chem, . 2020 Jul 15;203:112653.
2. A subset of flavaglines inhibits KRAS nanoclustering and activation; Journal of Cell Science, 24 Jun 2020, 133(12)
3. The prohibitin-binding compound fluorizoline affects multiple components of the translational machinery and inhibits protein synthesis; J Biol Chem, 2020 Jul 17;295(29):9855-9867
4. Recent advances in the synthesis of 2,3-dihydropyrroles; Chem Commun (Camb), 2020 May 27;56(42):5584-5592

5th Pharmaceutical Chemistry Conference; Webinar, - April27-28, 2020.

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