

ANNOTATION

OF RESEARCH TOPIC FOR POST-DOC POSITION

Repurposing of cardiotonics

Position available from: January 2019

Department: Department of Pharmacology and Toxicology, Faculty of Medicine in Pilsen, Charles University

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Input premise

Drug repositioning or drug repurposing, the application of an existing, and already approved, therapeutic to a new disease indication, holds the promise of rapid clinical impact at a lower cost than *de novo* drug development. To date there has not been a systematic effort to identify such opportunities, limited in part by the lack of a comprehensive library of clinical compounds suitable for testing¹. Drug repurposing is a promising strategy in pharmaceuticals. It considerably reduces the resources and shorten time needed for developing a known drug for new therapy and thus magnifies the probability that the drug reaches clinical phases and to market delivery for the new indication^{2,3}. Hence, it contributes to the use of new ways of EU economic thinking.

So far, there is limited, however promising and recent, knowledge about the utilisable activity of cardiotonics, as powerful ionic transport modulators, on cancer (cf. e.g.^{4,5,6,7}).

The project investigates in depth the apparent relation between the ionic transport on plasma membrane and cancer cells lifecycle and/or apoptosis/autophagy induction. For this purpose, classic cardiotonic steroids as well as some rare ones isolated from plants will be tested for their cytotoxic potency in cancer cells (non-small lung carcinoma), including multi-drug resistance cancer lines. To increase chemotherapeutic potential, the project will evaluate above-mentioned effects of cardiac steroids (cardenolides) with another lactone-type natural compounds, e.g. sesquiterpene lactones⁸. They target intracellular membranes and induce ionic flux and apoptosis. Recently, such compounds are under advanced level of clinical trials (thapsigargin-mipsagargin) for a treatment of solid tumours.

This project of based on long-lasting cooperation of two teams, biologists (team of doc. Kmonickova, Dept. Pharmacology and Toxicology, Faculty of Medicine in Pilsen, Charles University) and chemists (team of prof. Drasar, Department of Chemistry of Natural Compounds, University of Chemistry and Technology Prague). Position of post-doc fits well for Dept. Pharmacology and Toxicology, which is currently seeking for a person with readiness to transfer a chemical background skills into medical thinking and performing biological experiments.

Qualifications

- Ph.D. (or equivalent) degree recently graduated
- High motivation, ability to conduct collaborative research
- Knowledge: organic chemistry, medicinal chemistry, pharmacology, drug research and development, molecular modelling of compounds, biological screening of small-molecule compounds
- Previous participation in local and international projects, experience with preparing proposals
- Good English communication skills both in written and oral form
- Track record of publications in peer-reviewed journals: at least 5 publications in IF journals, two as a first author
- Traineeship in pharmaceutical company is an advantage

The applicants should submit

- [Letter of Reference](#)
- [Application for post-doc grant at Charles University](#)
- Curriculum vitae
- List of publications
- Copy of university diploma
- Brief description of prior research, skills and experiences

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- 1 Corsello S. M., Nat Med. 23(4), 405–408 (2017).
 - 2 Temesi G., Bolgár B., Arany A., Szalai C., Antal P., Mátyus P.: Future Med. Chem. 6, 563–575 (2014).
 - 3 Naveja J. J., Dueñas-González A., Medina-Franco J. L.: Epi-Informatics: Discovery and Development of Small Molecule Epigenetic Drugs and Probes, chap. 13, 327–357 pp. (2016).
 - 4 Xiao Y.J., Meng C., Lin J., Huang C.Q., Zhang X.L., Long Y.Y., Huang Y.D. Lin Y.: Oncol. Lett. 14, 6678–6684 (2017).
 - 5 Pereira D. G., Salgado M. A. R., Rocha S. C., Santos H. L., Villar J. A. F. P., Contreras R. G., Fontes C. F. L., Barbosa L. A., Cortes V. F.: J. Cell. Biochem. DOI:10.1002/jcb.26499, Published:2017-Nov-11.
 - 6 Yuan J.N., Zhou X.X., Cao W., Bi L.L., Zhang Y.F., Yang Q., Wang S.W.: Nanoscale Res. Lett. 12, Article Number: 585, DOI: 10.1186/s11671-017-2346-8 (2017).
 - 7 Li K., Feng J., Kuang Y., Song W., Zhang M., Ji S., Qiao X., Ye M.: Advan. Synth. Catal. 359, 3765–3772 (2017).
 - 8 Skorpilova L., Rimpelova S., Jurasek M., Budesinsky M., Lokajova J., Effenberg R., Slepicka P., Ruml T., Kmonickova E., Drasar P.B., Wimmer Z.: Beil. J. Org. Chem. 13, 1316–1324 (2017).