

## **Proposal for Dissertation Topic in the Doctoral Study Programme at the Faculty of Pharmacy, Masaryk University**

Study type (full-time/distant): full-time

Full name of the study programme: Medicinal chemistry

Department\*): Department of chemical drugs

Head of the Department: doc. PharmDr. Ing. Radka Opatřilová, Ph.D., MBA

Number of available stipends: 1

### Dissertation topic

Development of new chromatin modifying substances for anticancer therapy

### Summary

Epigenetic alterations are involved in every step of carcinogenesis. The development of chromatin modifiers has provided the ability to fight tumors by reversing these changes. Six chromatin-modifying agents have recently been approved for the treatment of cancer: two DNA demethylating agents and four histone deacetylase inhibitors (HDACi). Many promising chromatin modifiers are currently being clinically evaluated in several types of tumors. Besides, already approved drugs from this group are still under clinical investigation to improve their efficacy and extend their use to various types of cancer. Combination therapy with chromatin modifiers is already considered a promising strategy to improve clinical effects and reduce side effects. The aim of the dissertation will be the design and synthesis of new compounds capable of modifying chromatin with a potential effect on tumor growth. The work will build on the previous promising results of our group in the development of histone deacetylase inhibitors.

### Preliminary aims

(1) Development of methodology for the preparation of substances capable of chelating zinc in HDAC enzyme (this also includes the design of suitable structures, design of their synthesis, synthesis itself, physicochemical characterization of prepared compounds, etc.) (2) Preliminary evaluation of their effect (cytotoxicity, inhibition of proliferation, etc.) to various strains of tumor cells in cooperation with the Department of Pharmacology and Toxicology, Faculty of Pharmacy MU. (3) Modification of

structures with regard to their preliminary evaluation and their synthesis. (4) Determination of the activity of selected most active substances on individual HDAC isoforms in cooperation with a foreign workplace.

## Grant funding

- Information about associated grant(s): The application for grant support was submitted this year (AZV).
- Information about the availability of employment or project funding above the framework of the MU-awarded stipend:

## Brief requirements according to the Subject Area Board (SAB)

- Publication activities: Experience with publishing scientific papers and previous active participation in conferences are welcome. Prior to study completion, the student must be an author of at least two papers in journals with impact factor (first author in at least one of these).
- Information about a compulsory scientific stay abroad: Participation in foreign internships at the Medical Faculty of Martin Luther University in Halle, Germany is expected.
- The student's involvement in teaching activities at the faculty: The student will be involved in teaching organic and medicinal chemistry.
- English language knowledge (specify the requirements): Knowledge of English by word and in writing is a must (the students must be able of understanding the scientific literature).

## Information about the supervisor

Name, surname, titles: doc. Ing. Pavel Bobál, CSc.

- Publication activity of the supervisor: Number of publications in Web of Science: 40, h-index: 13
- Success in grant project submission (grant projects awarded): Internal Grant Agency MUNI: MUNI/A/1510/2020, MUNI/A/1682/2020; GACR 16-07193S (2016-2019); Internal grant agency UVPS Brno: 315/2019/FaF, 320/2018/FaF, 323/2017/FaF, 327/2016/FaF, 50/2014/FaF, 108/2013/FaF, 91/2013/FaF, 80/2012/FaF, 49/2011/FaF, 51/2011/FaF, 63/2011/FaF; Interní vzdělávací agentura VFU Brno: 2019FaF/3150/83, 2018FaF/3150/78, 2015FaF/3150/89, 2014FaF/3150/62, 2014FaF/3150/64; University Development Fund: 162/2013/G6, 1131/2012/F3/a.

- International cooperation (potentially with the possibility of student's stay): prof. Reinhard Neier, University of Neuchatel, Switzerland; prof. David Lightner, University of Nevada Reno, USA; Dr. Július Brtko, Institute of experimental endocrinology, Biomedical Research Center SAS, Slovak republic.
- Number of current doctoral students led by the supervisor: 4
- Number of successful PhD graduates led by the supervisor and their further career: 1 (assistant professor, Dept. Chem. Drugs, Faculty of Pharmacy MU)

## Information about the Consultant

Name, surname, titles:

- Publication activity of the supervisor: Number of publications in Web of Science: , h-index:
- Success in grant project submission (grant projects awarded): Klikněte nebo klepněte sem a zadejte text.
- International cooperation (potentially with the possibility of student's stay): Klikněte nebo klepněte sem a zadejte text.
- Number of current doctoral students led by the supervisor: Klikněte nebo klepněte sem a zadejte text.
- Number of successful PhD graduates led by the supervisor and their further career: Klikněte nebo klepněte sem a zadejte text.