ÚOCHB AV ČR
IOCB PRAGUE

Meeting with Group Leaders

Zdenek Hostomsky | Jan. 15, 2018

Agenda

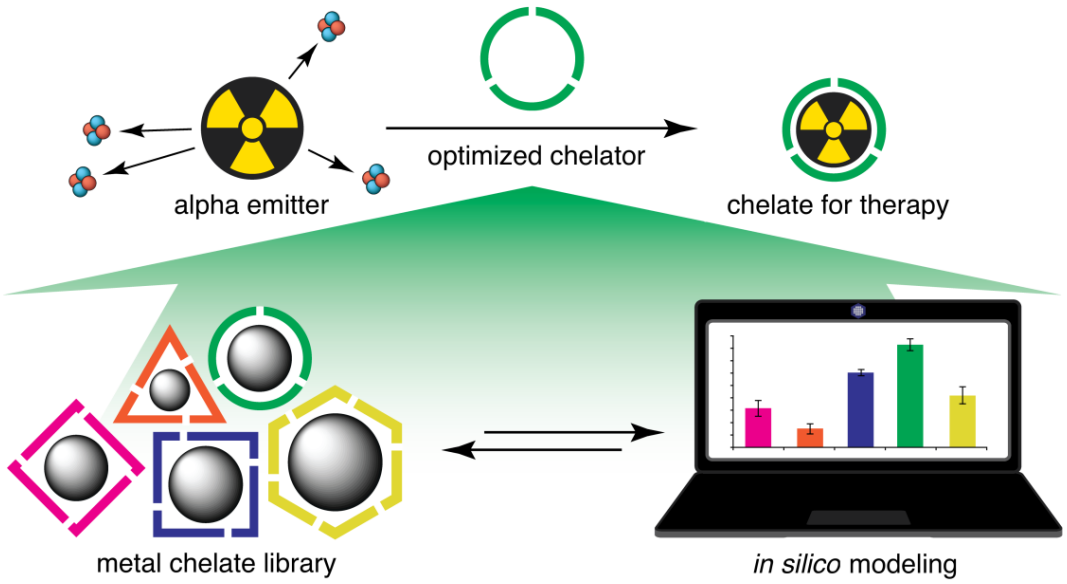
- IOCB interdisciplinary grants winners
- Bridging support
- Miscellanea

IOCB interdisciplinary grants

- Mechanism to support interdisciplinary collaborations within IOCB
- 5 applications received by the deadline
- Decisions at the Dec 19, 2017 mtg of the Evaluation Committee
- Start on Jan. 1, 2018

Alpha for Life

Miloslav Polášek PI
Michal Straka co-PI



Program Synopsis

Radioactivity is deadly but it can be made deadly in a smart way. When selectively delivered to cancer with targeted molecules, it can efficiently kill cancer cells. The concept of **targeted radiotherapy** can utilize various radionuclides and is rapidly finding its way to clinical practice.

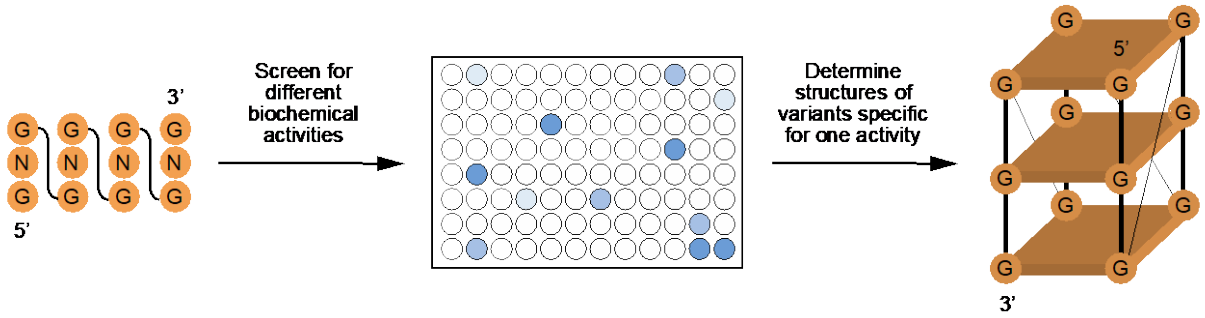
However, the most potent **alpha emitters** 223Ra and 225Ac still elude this application because there are no suitable **chelators** for stable linkage of these radionuclides to targeting molecules. In this project **we want to develop chelators for radium and actinium** to allow this. We will first develop a **computational model** for testing **kinetic inertness** of metal chelates *in silico*, which will enable us to pre-screen new chelator designs suitable for 223Ra and 225Ac. The model will be validated on our extensive collection of **experimental data** for more than 1300 metal chelates already synthesized at IOCB. Most promising 223Ra and 225Ac chelators will be synthesized and tested with real radionuclides. Enabling stable chelation of 223Ra and 225Ac will have **high impact on targeted radiotherapy of cancer**.

Structural basis of G-quadruplex biochemical specificity

Edward Curtis PI
Václav Veverka co-PI

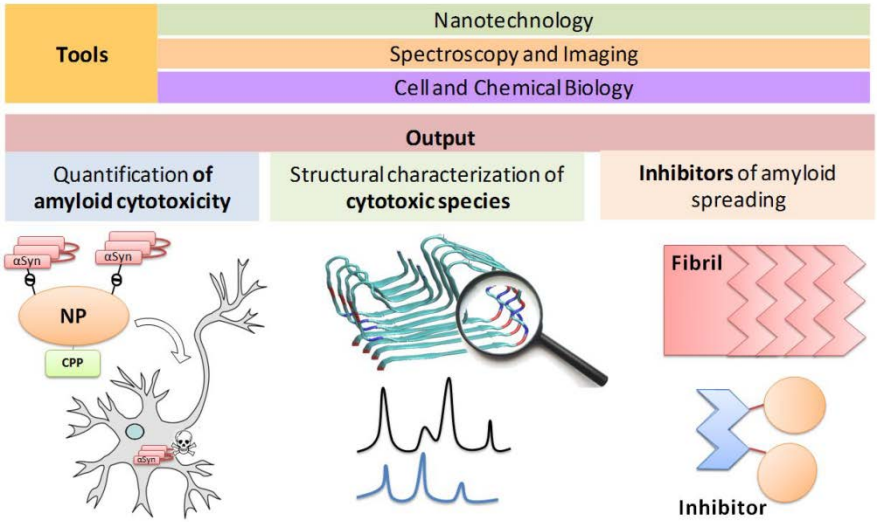
Program Synopsis

G-quadruplexes are four-stranded nucleic acid structures thought to play widespread biological roles. Although computational methods have been developed to identify G-quadruplex forming sequences in genomes, these approaches cannot typically distinguish G-quadruplexes with different biochemical activities. To address this limitation, here we propose using a combination of biochemical and structural methods to identify and characterize mutations that alter the biochemical specificity of G-quadruplexes. These experiments should provide a wealth of information about factors that influence the biochemical specificity of G-quadruplexes, and in the long-term we anticipate that they will facilitate analysis of these structures in sequenced genomes.



Uncovering Structure-Cytotoxicity Relationship of α-Synuclein Aggregates

Dmytro A. Yushchenko PI
Petr Bouř co-PI
Petr Cígler co-PI



Program Synopsis

Protein misfolding and aggregation are omnipresent in many diseases including Alzheimer's, Parkinson's, and prion–related neurodegenerations. Typically, they lead to appearance of amyloid fibrils as pathological hallmarks. However, the exact structure of the fibrils, mechanisms of their formation and involvement in neuronal toxicity remain unclear. In particular, obstacles in determination and characterization of cytotoxic aggregates are related to challenges in investigation and manipulation of the protein aggregates in the living cells. On the other hand, flexibility in *in vitro* experiments enables preparation of distinct aggregates with very different structures and morphologies. Within this project, we will combine both approaches to develop methodologies for determination of the structure and behavior of various species of amyloidogenic protein α-synuclein with the emphasis on the origin of their cytotoxicity. Our approach will be based on controlled nanoparticles-mediated delivery of model amyloid species into cells accompanied by spectroscopic characterization, modeling of protein conformational changes and cellular toxicity tests. Based on resultant structure-toxicity correlations we aim to design and synthesize inhibitors of amyloid growth. The methodologies developed for α-synuclein will be applicable to other amyloidogenic proteins. This work will be possible owing to the collaboration between three groups experienced in the fields of nanoparticles, spectroscopy and amyloid biochemistry.

Bridging support

Who qualifies:

- Excellent rating of a grant application but no money awarded
- No other running grant funding in the group

How much:

- Support for 1 year in the amount of 80% of the first year request in the grant application

Deadline: Jan 31, 2018

- So far, 1 qualifying application received

IOCB Research Output Evaluation

- Quantitative group output – scientometric
- Cumulative 2015, 2016, 2017
- The library will deliver the publications for the 3 year period. Please forward the edited list to director‘s office by February 28, 2018
- Proportional distribution of 2.5 M CZK to the groups (another 2.5 M will be distributed for the winning most significant publications).

Miscellanea

IOCB TTO renamed to IOCB TECH in 2018

IOCB Development Center

- Welcome new management:

- Michal Lebl
- Ondřej Pačes

General assembly of IOCB employees

- Friday Feb 9, Balling Hall, NTK
- Language question

It was announced that the Assembly will be conducted in English – simulataneous Czech translation will be provided via earphones. Several protests were received.

Important Reminders

- GLs Annual reports due

  Jan 15, 2018 **Today!**

- Work safety instruction
  before **Feb. 16, 2018**

- **Assembly of IOCB employees**
  Feb. 9, 2018

- Next meeting with Group Leaders
  Monday, Feb 19, 2018 **10:00 a.m.**

- Start assembling your Most significant publications for 2017

Mtgs w GLs - 2018 Schedule

- January 15
- February 19
- March 19
- April 23
- May 21
- June 25
- September 10
- October 15
- November 12
- December 17

Always on Mondays at 10:00 am in the Director‘s Boardroom

Institute of Organic Chemistry and Biochemistry

of the Czech Academy of Sciences