



# Research Group for Molecular Biology and Nanomedicine

Department of Chemistry and Biochemistry

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RGL: Assoc. prof. Zbynek Heger

## Who we are:

The research group for Molecular Biology and Nanomedicine (RGMBN) focuses on interdisciplinary research spanning:

- i) Engineering of smart protein-based nanovehicles for drug delivery
- ii) Design and formulation of smart responsive lipid-based nanoparticles for drug delivery and vaccination, focusing on the functional delivery of siRNA, mRNA payloads
- iii) Design and formulation of theranostic lipid-based nanoparticles for image-guided, precision therapeutic approaches for cancer treatment
- iv) High-throughput *in silico* development of targeting ligands for active drug delivery

To achieve the above, RGMBN has broad expertise in a broad spectrum of synthetic chemistry skills, formulation, molecular, physico-chemical, analytical and cellular methodologies, plus *in silico* capabilities. RGMBN also operates a fully equipped facility for work with small rodents.

## What we offer:

- i) Experience in the design, formulation and testing of nanomaterials (*in vitro/in vivo*) with a special emphasis on delivery efficiency, biodistribution, bio- and immunocompatibility.
- ii) Capabilities for the production of smart responsive lipid-based nanoparticles that mimic viral cell entry and intracellular release of a payload. These nanoparticles exhibit excellent physico-chemical and biological properties for use in drug delivery or vaccination applications.
- iii) Expertise in delineation of nanotoxicological aspects of novel materials or for description of mechanisms of action of nanomedicines.
- iv) Broad experience with *in silico* design (mostly based on receptor homo-/hetero-oligomerization) of targeting ligands for active delivery, and on protein-protein interaction models
- v) Animal model facility with workers experienced at immunology and biochemistry for any medium-scaled preclinical testing.

## What we are searching for:

- strong partners/consortia with specific activities including the development of specific types of short nucleic acids for therapeutic or vaccination purposes, targeted delivery of interesting bioactive compounds with poor bioavailability/dissolubility/high non-target toxicity, or interesting nanoscaled modalities with low tissue selectivity for which targeting ligands could be developed. This includes domains for blood-brain barrier transcytosis, *etc*
- strong partners/consortia with novel nanomaterials under development with unknown biological activities
- strong partners/consortia who will find aspects of our expertise fitting their activities

## Established and available methodologies/techniques:

- ✓ Rational *in silico* design/molecular cloning/production of recombinant proteins,

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- ✓ Broad experiences with siRNA-mediated knock-downs and transient knock-ins,
- ✓ CRISPR/Cas9, nucleofection,
- ✓ Flow cytometry, single-cell sorting,
- ✓ cDNA microarrays, qPCR,
- ✓ Formulation of lipid nanoparticles (high-pressure extrusion),
- ✓ An array of physico-chemical methodologies (DLS, TEM, cryo-SEM, AFM, AAS, FT-IR, XPS, PXRD, NMR, UV/Vis spectrofluorimetry, *etc.*),
- ✓ Several GPUs for efficient *in silico* analyses (GROMACS, AMBER, *etc.*),
- ✓ Facility for synthesis (f-moc solid state), purification and characterization of short peptides (up to 40 amino acids), synthetic organic chemistry suite
- ✓ Microscopic facility (high-resolution CLSM, epifluorescence, holotomography),
- ✓ Long-term experiences with testing of nanoscaled materials at *in vitro* level including functional testing of mechanisms of action,
- ✓ Established chick-chorioallantoic membrane (CAM) assay to determine the cellular intravasation/extravasation potential, fluorescence angiography,
- ✓ Small rodents' facility with *in vivo* imager and histopathological facility.

#### **Selected projects:**

- 2022-2025, The Czech Science Foundation, Biodistribution and real-time monitoring of free or apoferritin-encapsulated charged cholinesterase reactivators,
- 2021-2024, The Czech Health Council, Ferritins as tools for enzyme-directed prodrug activation,
- League against Cancer Prague (annually from 2014),
- 2019-2021, The Czech Science Foundation, Encapsulation of cholinesterase reactivators using apoferritin for enhanced bioavailability in central nervous system,
- 2019-2021, The Czech Science Foundation, Zinc-dependent signaling and expression of metallothionein sub/isoforms in breast cancer: Implications for prognostic and therapeutic purposes,
- 2018-2020, The Czech Science Foundation, Comprehensive insight into the mechanisms of action and metabolism of tyrosine kinase inhibitors and a study of ways increasing their antitumor efficiency,
- 2018-2022, Towards the Understanding a Metal-Tumor Metabolism, ERC Starting Grant, ERC-2017-STG,
- 2017-2022, The Czech Ministry of Education, Youth and Sports, OPVVV Project FIT (Pharmacology, Immunotherapy, nanoToxicology) CZ.02.1.01/0.0/0.0/15\_003/0000495
- 2017-2019, The Czech Science Foundation, Construction of modified apoferritin nanoparticles with anticancer agents and study of mechanisms potentiating their effects in chemotherapy,
- 2017-2018, H2020 – 763685 Back for the Future (Back4Future),
- 2015-2016, H2020-JTI-IMI2-2014-02-single, Ultra-Fast Molecular Filovirus Diagnostics „FILODIAG“, IMI2-2014-02-05.

### Selected publications:

- 1) Ressnerova A., Novotny F., Michalkova H., Pumera M., Adam V., Heger Z. (2020) Efficient Protein Transfection by Swarms of Self-Propelled Plasmon Virus-sized Nanorobots. *ACS Nano*, *in press*. **IF 15.881**
- 2) Tesarova B., Dostalova S., Smidova V., Goliasova Z., Skubalova Z., Michalkova H., Hynek D., Michalek P., Polanska H., Vaculovicova M., Hacek J., Eckschlager T., Stiborova M., Pires A. S., Neves A. R. M., Abrantes A. M., Rodrigues T., Matafome P., Botelho M. F., Teixeira P., Mendes F., Heger Z. (2020) Surface-PASylation of ferritin to form stealth nanovehicles enhances *in vivo* therapeutic performance of encapsulated ellipticine. *Appl. Mater. Today*, vol. 18, art. no. 100501, **IF 10.041**
- 3) Michalkova H., Skubalova Z., Sopha H., Strmiska V., Tesarova B., Dostalova S., Svec P., Hromadko L., Motola M., Macak J. M., Adam V., Heger Z. (2020) Complex cytotoxicity mechanism of bundles formed from self-organised 1-D anodic TiO<sub>2</sub> nanotubes layers. *J. Hazard. Mater.* 388, art. no. 122054. **IF 10.588**
- 4) Beladi-Mousavi S. M., Khezri B., Krejcová L., Heger Z., Sofer Z., Fisher A. C., Pumera M. (2019) Recoverable bismuth-based microrobots: Capture, transport, and on-demand release of heavy metals and an anticancer drug in confined spaces. *ACS Appl. Mater. Interfaces*. 11, 13359-13369. **IF 9.229**
- 5) Peskova M., Ilkovic L., Hynek D., Dostalova S., Sanchez-Carnerero E. M., Remes M., Heger Z., Pekarik V. (2019) Detergent-modified catalytic and enzymomimetic activity of silver and palladium nanoparticles biotemplated by *Pyrococcus furiosus* ferritin. *J. Colloid. Interface Sci.* 537, 20-27. **IF 8.128**
- 6) Khezri B., Mousavi S. M. B., Krejcová L., Heger Z., Sofer Z., Pumera M. (2019) Ultrafast electrochemical trigger drug delivery mechanism for nanographene micromachines. *Adv. Funct. Mater.* 24, art. no. 1806696. **IF 18.808**
- 7) Villa K., Krejcová L., Novotny F., Heger Z., Sofer Z., Pumera M. (2018) Cooperative multifunctional self-propelled paramagnetic microrobots with chemical handles for cell manipulation and drug delivery. *Adv. Funct. Mater.* 28, art. no. 1804343. **IF 18.808**
- 9) Dostalova S., Cerna T., Hynek D., Koudelkova Z., Vaculovic T., Kopel P., Hrabeta J., Heger Z., Vaculovicova M., Eckschlager T., Stiborova M., Adam V. (2016) Site-directed conjugation of antibodies to apoferritin nanocarrier for targeted drug delivery to prostate cancer cells. *ACS Applied Materials & Interfaces*. 8, 14430-14441. **IF 9.229**
- 10) Smidova V., Michalek P., Goliasova Z., Eckschlager T., Hodek P., Adam V., Heger Z. (2021) Nanomedicine of tyrosine kinase inhibitors. *Theranostics*. 11(4), 1546-1567. **IF 11.556**
- 11) Tesarova B., Musilek K., Rex S., Heger Z. (2020) Taking advantage of cellular uptake of ferritin nanocages for targeted drug delivery. *J. Control. Release*. 325, 176-190. **IF 9.776**
- 12) Haddad Y., Charousova M., Zivotska H., Splichal Z., Rodrigo M. A. M., Michalkova H., Krizkova S., Tesarova B., Richtera L., Vitek P., Stokowa-Soltys K., Hynek D., Milosavljevic V., Rex S., Heger Z. (2020) Norepinephrine transporter-derived homing peptides enable rapid endocytosis of drug delivery nanovehicles into neuroblastoma cells. *J. Nanobiotechnol.* 18(1), art. no. 95. **IF 10.435**
- 13) Buchtelova H., Strmiska V., Skubalova Z., Dostalova S., Michalek P., Krizkova S., Hynek D., Kalina L., Richtera L., Moulick A., Adam V., Heger Z. (2018) Improving cytocompatibility of CdTe quantum dots by Schiff-base-coordinated lanthanides surface doping. *J. Nanobiotechnol.* 16, art. no. 43. **IF 10.435**