**Subject: Expertise of the NIC’s Department of Synthetic Biology and Immunology**

**National Institute of Chemistry (NIC) Ljubljana**, Slovenia has 350 employees. Of these, 250 are researchers in 9 departments and two infrastructure centers. Researchers are active in fields which are of long-term importance to both Slovenia and EU:

1) health, environmental protection, circular economy, sustainable energy, low carbon technology, climate change and analytics /

2) biotechnology, synthetic biology, environmental protection, structural and theoretical chemistry, analytical chemistry, materials research, and chemical engineering , through which the Institute is in line with the needs of the domestic and international mainly chemical and pharmaceutical industry.

**Department of Synthetic Biology and Immunology** focuseson the design of new biological structures and processes and deciphering molecular mechanisms of innate immunity and health applications.

Department strategic orientations:

1. **Synthetic biology** combines the engineering approach with biological systems, aiming to introduce new properties into biological or biomimetic systems including potential applications but also to understand the function of complex biological systems by the bottom-up construction. Our main directions in synthetic biology include

* Regulatory circuits based on modular building elements
* Design and characterisation of bionanostructures based on coiled-coil protein origami
* Advanced vaccines based on designed adjuvants and synthetic nanoparticles
* Synthetic biology approach to cancer immunotherapy and regulation of T cell activation

1. **Molecular mechanisms of recognition and activation of the innate immune system**

* Mechanism of activation of the inflammasome
* Transmission of signals by extracellular vesicles

**Representative publications:**

1. LEBAR, Tina, LAINŠČEK, Duško, MERLJAK, Estera, AUPIČ, Jana, JERALA, Roman. A tunable orthogonal coiled-coil interaction toolbox for engineering mammalian cells. **Nature Chemical Biology**, 2020, vol. 16, 513-519. link, doi: 10.1038/s41589-019-0443-y.
2. FINK, Tina, LONZARIĆ, Jan, PRAZNIK, Arne, PLAPER, Tjaša, MERLJAK, Estera, LEBEN, Katja, JERALA, Nina, LEBAR, Tina, STRMŠEK, Žiga, LAPENTA, Fabio, BENČINA, Mojca, JERALA, Roman. Design of fast proteolysis-based signaling and logic circuits in mammalian cells. **Nature Chemical Biology**. Feb. 2019, 15, 115-122. link, DOI: 10.1038/s41589-018-0181-6.
3. LJUBETIČ, Ajasja, LAPENTA, Fabio, GRADIŠAR, Helena, DROBNAK, Igor, AUPIČ, Jana, STRMŠEK, Žiga, LAINŠČEK, Duško, HAFNER BRATKOVIČ, Iva, MAJERLE, Andreja, KRIVEC, Nuša, BENČINA, Mojca, PISANSKI, Tomaž, ĆIRKOVIĆ-VELIČKOVIĆ, Tanja, ROUND, Adam, CARAZO, José María, MELERO, Roberto, JERALA, Roman. Design of coiled-coil protein-origami cages that self-assemble in vitro and in vivo. **Nature Biotechnology**. Nov. 2017, vol. 35, 1094-1101. link DOI: 10.1038/nbt.3994.
4. LEBAR, Tina, VERBIČ, Anže, LJUBETIČ, Ajasja, JERALA, Roman. Polarized displacement by transcription activator-like effectors for regulatory circuits. **Nature Chemical Biology**. 1 Jan. 2019, vol. 15, no. 1, str. 80-87, ilustr. ISSN 1552-4450. https://www.nature.com/articles/s41589-018-0163-8, DOI: 10.1038/s41589-018-0163-8.
5. HAFNER BRATKOVIČ, Iva, SUŠJAN, Petra, LAINŠČEK, Duško, TAPIA-ABELLÁN, Ana, CEROVIĆ, Kosta, KADUNC, Lucija, ANGOSTO-BAZARRA, Diego, PELEGRIN, Pablo, JERALA, Roman. NLRP3 lacking the leucine-rich repeat domain can be fully activated via the canonical inflammasome pathway. **Nature Communications**. 5 Dec. 2018, vol. 9, no. 5182, link DOI: 10.1038/s41467-018-07573-4.

**Our international projects:**

1. **MaCChines**: Molecular machines based on coiled-coil protein origami, ERC Advanced Grant 2017
2. **CCedit**: Coiled-coil mediated exonuclease tethering technology for the enhancement of CRISPR gene editing, ERC Proof of Concept, 2020
3. **VIROFIGHT**: General-purpose virusneutralizing engulfing shells with modular target-specificity, Horizon 2020 - FET Open, European Innovation Council, Pathfinder, 2020-2024
4. **MediSURF**: Designed nanostructured bioactive surfaces for precision medicines, M-ERA.NET 2015
5. **CC-LEGO:** Robust protein blocks to build cages and layers, Horizon 2020-MSCA-IF-2017

**Patents and patent applications**

* LAINŠČEK, Duško, JERALA, Roman. Coiled-coil mediated tethering of CRISPR-CAS and exonucleases for enhanced genome editing. European Patent Application EP19192490.1, 2019-08-20. München, European Patent Office, 2019. [COBISS.SI-ID 6691354].
* LAINŠČEK, Duško, LEBAR, Tina, JERALA,Roman. Engineered externally regulated artificial transcription regulatory system based on engineered NFAT. EP19150168.3, 2019-01-03. München, European Patent Office, 2019. [COBISS.SI-ID 6564378].
* LEGIŠA, Matic, LEŠNIK, Samo, KONC,Janez, ŠOLMAJER, Tomaž, KAVČIČ, Luka, VODOPIVEC,Tina, ČAMERNIK, Katja, POTOKAR,Urška Karolina. Small molecule-inhibitors of 6-phosphofructo-1-kinase for reducing lactate generation by cancer cells. PCT/EP2019/071059,2019-08-05. München, EPO, 2019. [COBISS.SI-ID 6452762].
* JERALA, Roman, BENČINA, Mojca, MAJERLE,Andreja, OBLAK, Alja, LEBAR, Tina,FORSTNERIČ, Vida, LOZNARIĆ, Jan, SMOLE,Anže, GABER, Rok, BEZELJAK, Urban, GOLOB, URBANC, Anja, KADUNC, Lucija, VUČKO, Dušan, STRAŽAR, Martin, PIRŠ, Boštjan, JERALA, Miha, ZUPANČIČ, Uroš, SOMRAK, Maja, LUŽNIK, Zala. Bistable genetic toggle switch comprising a pair of reciprocal repressors and a positive feedback loop based on DNA-binding proteins. European Patent Specification EP2898074 B1, 2019-01-02. München, European patent office, 2019. [COBISS.SI-ID 27822375].
* JERALA, Roman, GOLOB URBANC, Anja. Cepljeni superantigeni in njihova uporaba za imuniterapijo.Patent SI25475 A, 2019-01-31. Ljubljana,Urad RS za intelektualno lastnino, 2019. [COBISS.SI-ID 6563866] **.**

**Cooperation with industry**

* Janssen
* Hexal AG
* Lek d.d. Sandoz
* Krka tovarna zdravil
* MGC Pharmaceuticals

**Our infrastructure:**

* Department use a cutting edge of interdisciplinary instruments including biophysical techniques (DLS, MALS, CD, fluorescence, luminescence, flow cytometry, confocal fluorescence microscopy, FCS), molecular biology and biochemistry (DNA cloning, molecular modeling, protein design, CRISPR/Cas9) to animal experiments (in-house facility run by our department).
* Cryo electron microscope Glacios: CryoEM microscope Glacios enables: single-particle analysis, cryo-tomography and electron diffraction on microcrystals.
* Plater reader: detection of luminescence, fluorescence or absorbance of a larger number of samples.
* Microscope for spatial and temporal imaging of life cells Leica SP8: imaging of spatial and temporal changes in fluorescence-labelled molecules in cells.
* Lumi-Box: detection of luminescence.
* Centrifuge Beckman: centrifugation.
* HPLC chromatograph with manual injector and fraction collector: separation of proteins and peptides.
* Äkta chromatographic system for protein purification (2 systems): protein purification with programmable injector and fraction collector.
* IVC Techniplast Equipment: laboratory animal breeding and performing in vivo experiments
* Biorad Gene Pulser Xcell electroporator: used to facilitate entry of plasmid DNA into pro and eucariont cells.

**CONTACT**

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