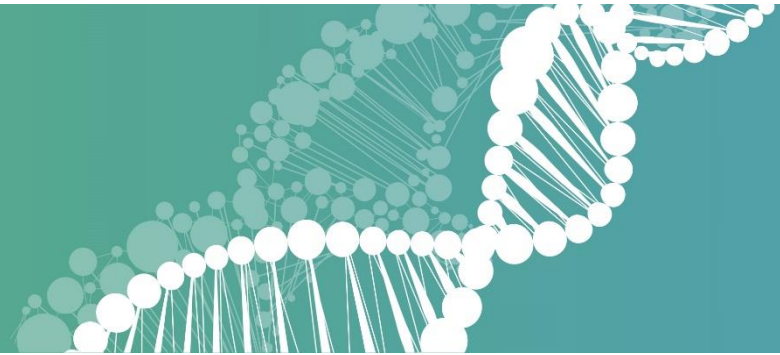




ERA CoBioTech

BIO TECH RESEARCH AND INNOVATION HACK 2021

Final seminar of the cofunded projects of ERA CoBioTech



**Title: Streamlined Streptomyces cell factories for industrial
production of valuable natural products**

Project acronym: **MISSION**

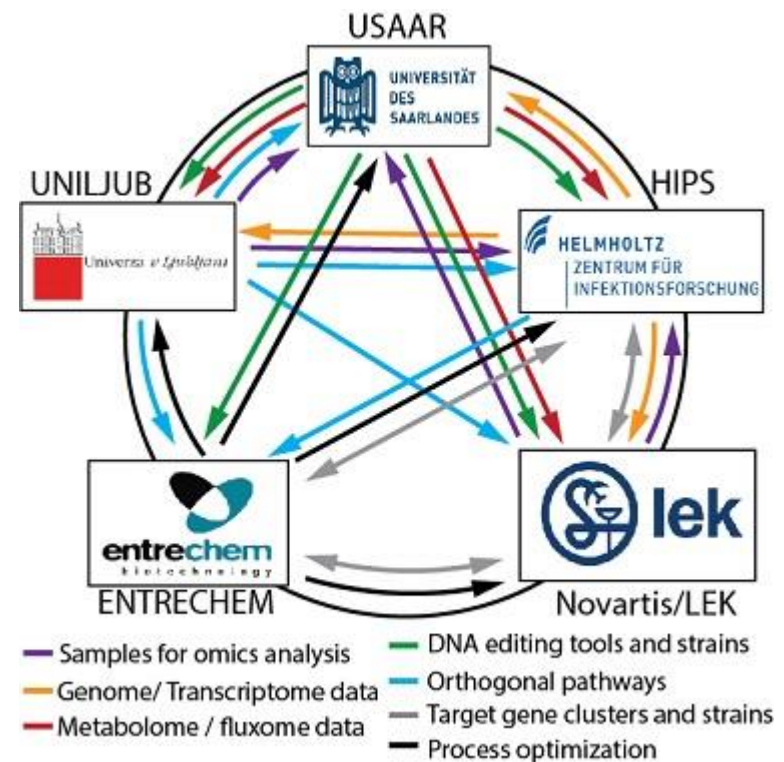
Name: Andriy Luzhetskyy, Saarland University



This project has received funding from the European Union's Horizon
2020 research and innovation programme under grant 722361

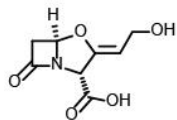
28.09.2021

- University of Saarland, Germany
- Helmholtz Institute of Pharmaceutical Research, Saarbrücken, Germany
- University of Ljubljana, Slovenia
- Novartis/LEK, Slovenia
- Entrechem, Spain
- Eurice, Saarbrücken, Germany
- Total project budget: 1.791.000 €
- Project start: 01 May 2018

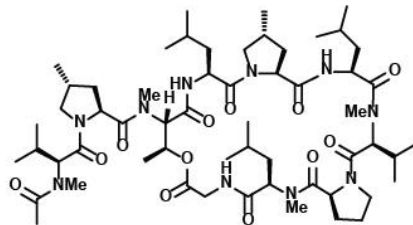


● Project Objectives: **Sustainable supply of anti-infectives and anti-cancer drug candidates**

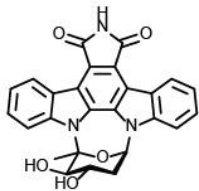
- ✓ **Synthetic biology and metabolic engineering** to create a chassis strain of *Streptomyces* with superior growth and robustness, and tuneable metabolic activities
- ✓ “Plug-in” of secondary biosynthetic pathways to derive streamlined cell factories for **novel anti-infectives and anti cancer drugs**



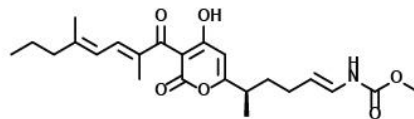
clavulanic acid



griselimycin



EC-70124

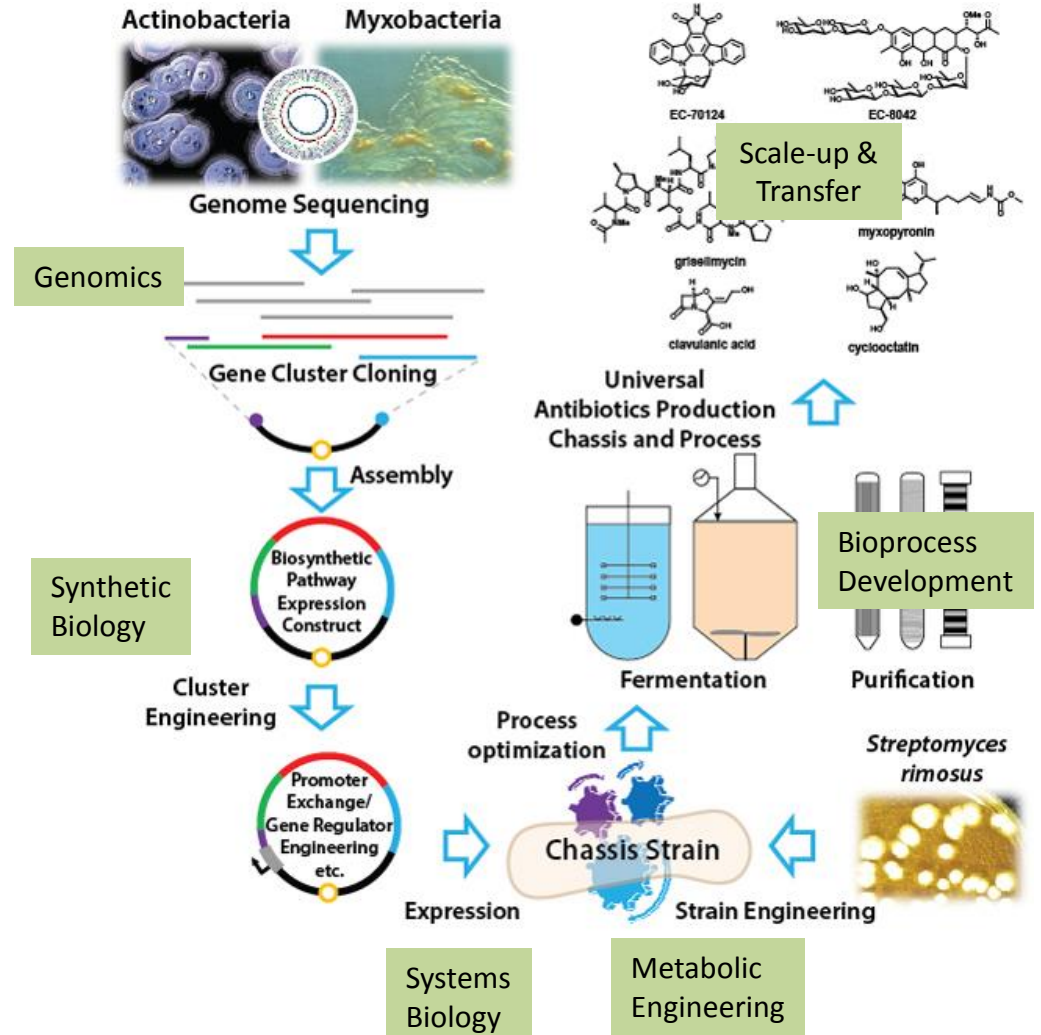


myxopyronin

***Streptomyces*: Two-time Noble Prize winner!**



- Scientific Approach: Interdisciplinary integration of systems and synthetic biology, metabolic engineering, process development
- Creation of an efficient value chain

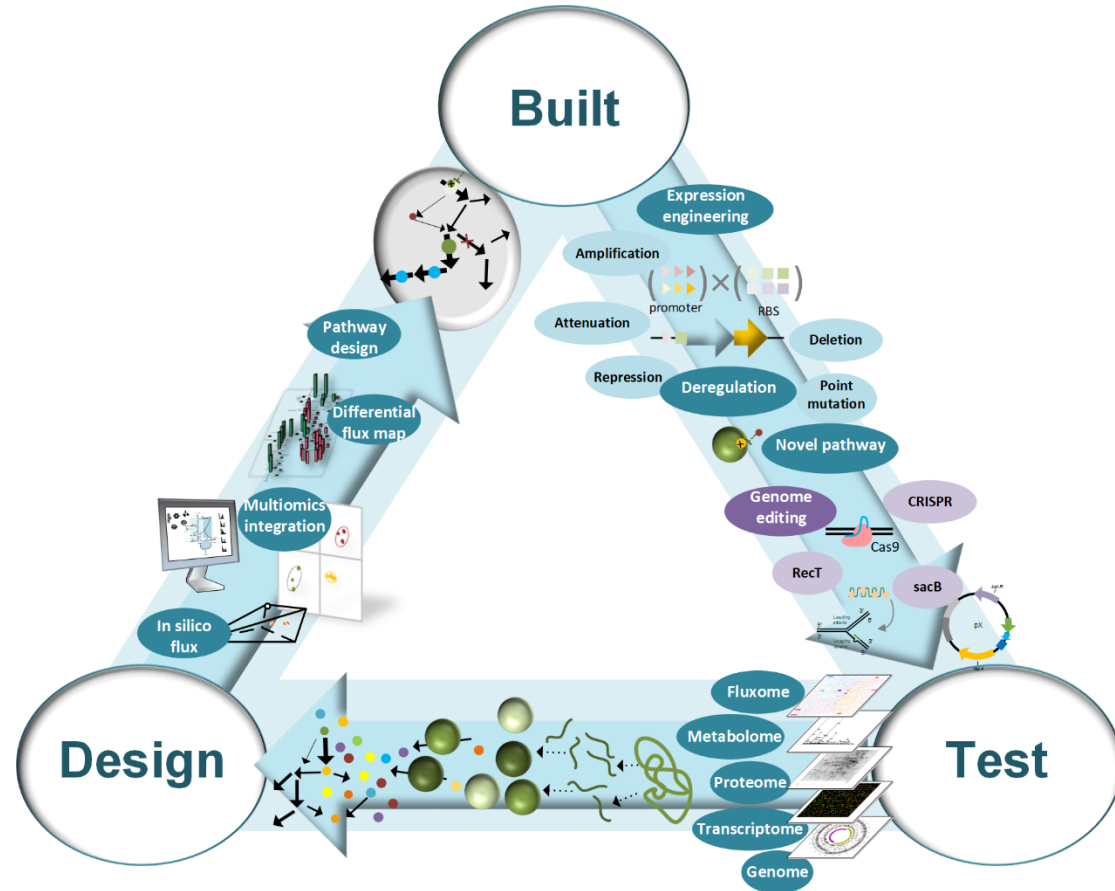


Objectives:

- ✓ Systems-wide profile of wild-type and industrial *S. rimosus*
- ✓ Analyze new strains created
- ✓ Integrate multi-omics data to understand cellular function and identify targets for metabolic engineering.
- ✓ GEM as premium knowledge and database.

Deliverables:

- ✓ Multi-omics data sets of initial and new strains
- ✓ Target identification for strain engineering
- ✓ Systems biology model

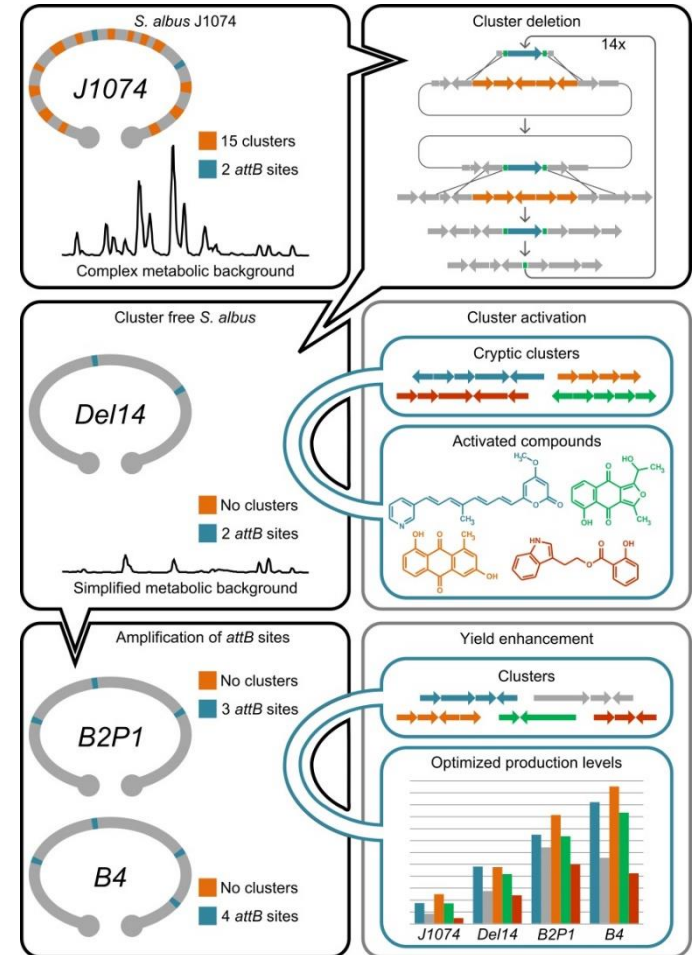


Objectives:

- ✓ To provide a standard operating procedure for streamlined genome engineering of industrial *S. rimosus* strains.
- ✓ To generate the *S. rimosus* chassis strain for optimized heterologous production of bioactive natural products.
- ✓ To reconstruct and verify synthetic promoters, RBSs and terminators in an industrial *S. rimosus* strain.

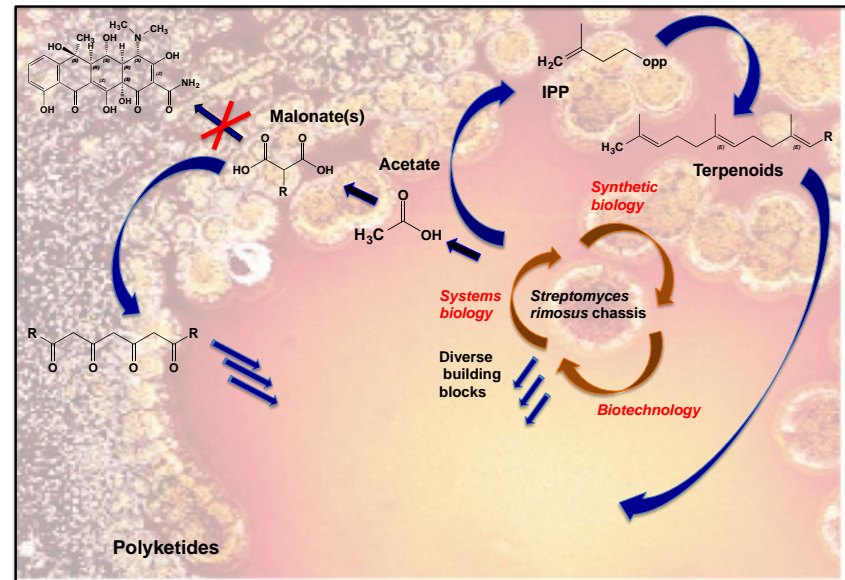
Deliverables:

- ✓ Technology platform for the efficient genome engineering of *S. rimosus*
- ✓ First-generation *S. rimosus* chassis strain
- ✓ Final collection of improved *S. rimosus* chassis strains and their genome sequences



Objectives:

- ✓ Optimize building block, redox and energy supply.
- ✓ Implement novel precursor pathways to enhance the chemical space
- ✓ Implement orthogonal pathways to drive the production of e.g. polyketides, isoprenoids and other compounds (with WP2).



Deliverables:

- ✓ Bioinformatic data set on *S. rimosus* metabolic potential
- ✓ Cloned target genes (enzymes) or metabolic pathways
- ✓ Hosts carrying the new pathways

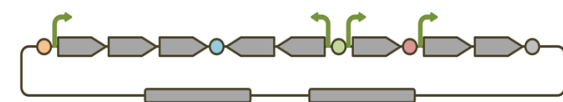
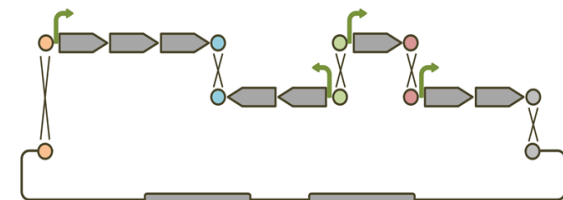
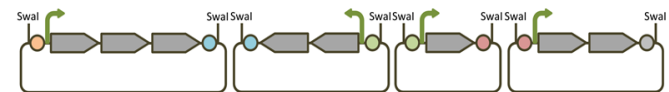
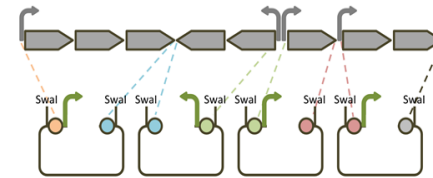
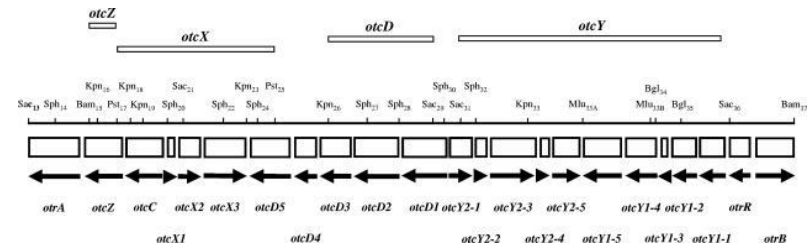


Objectives:

- ✓ Synthesize target gene clusters
- ✓ Re-engineer clusters via mini-plasmids
- ✓ Introduce clusters into suitable strains of *S. rimosus* and optimized versions (WP3).
- ✓ Evaluate the productivity at lab scale.

Deliverables:

- ✓ Gene clusters encoding biosynthesis of target compounds
- ✓ Engineered gene clusters containing suitable promoters and regulatory elements located on replicative or integrative vectors
- ✓ Ready-to-use *S. rimosus* transformants



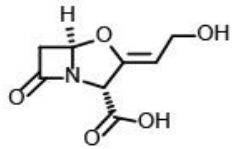
● Objectives:

- ✓ Re-adaptation of industrial media
- ✓ To scale down the process to lab-scale
- ✓ Strain testing at 5-L- and 20-L-fermenter scale.
- ✓ Down-stream processing.

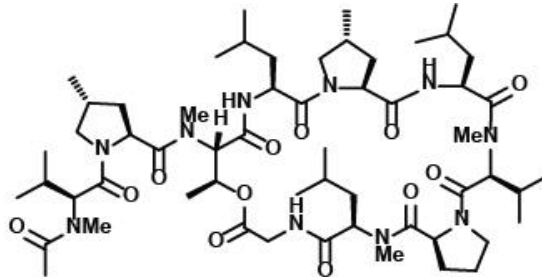
● Deliverables:

- ✓ Re-optimized media and fermentation procedures at lab, 5-L and 20-L-fermenter scale
- ✓ The best-performing strains tested and selected target compounds isolated

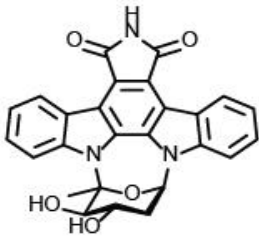




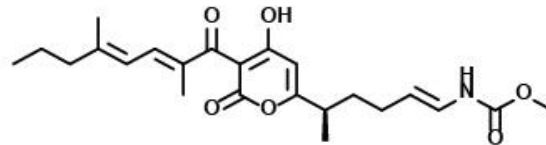
clavulanic acid



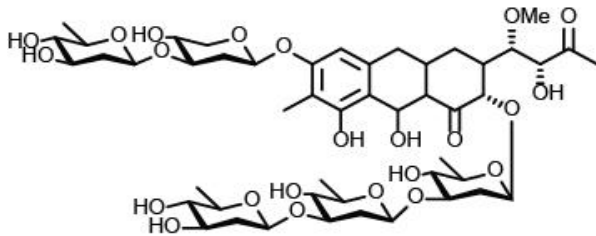
griselimycin



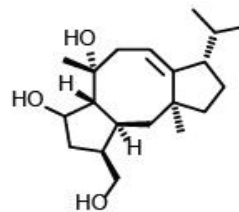
EC-70124



myxopyronin



EC-8042



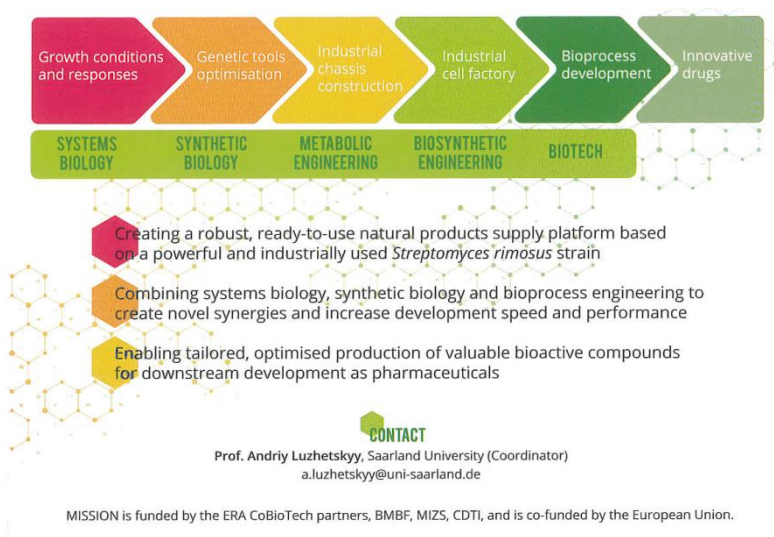
cyclooctatin

- Widely exploitable microbial hosts for the production of industrial goods
- High value anti-infectives and anti-cancer drugs in sufficient amount and quality for further commercial development

Round table and public event in Slovenia, Dornbirn, 25.09.2019 and in Germany, Saarbrücken, HIPS Symposium 27.06. 2019.

MISSION presentation in Piza, Genetics of Industrial Microorganisms International Symposium, 08-11.09.2019.

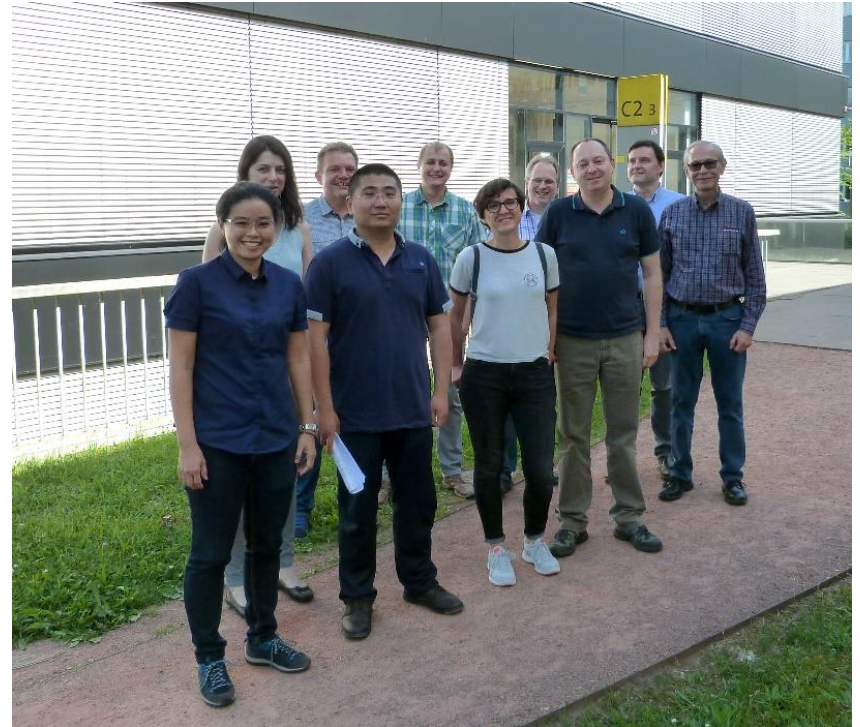
Flyers, webpage, posters etc.



Prof. Andriy Luzhetskyy
(MISSION Coordinator)

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Saarland University

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MISSION team at kick-off meeting in Saarbrücken, May 2018