ANNUAL AEGIS NEWSLETTER 2017

About AEGIS

AEGIS is a Marie Skłodowska - Curie Innovative Training Network (ITN) for early stage researchers (ESR) funded by the European Commission under the H2020 Programme the EU framework programme for research and innovation.

The principal aim of the AEGIS ITN is to implement the first comprehensive, intersectoral cross-disciplinary and structured curriculum for doctoral students in the European Research Area by establishing a unique training platform for the next generation of European researchers in early drug discovery. A significant added value is provided through networking with key European pharmaceutical companies. A key research aim of AEGIS is improving the efficiency and success of early stage drug development by combining innovative methods and techniques to tackle difficult but promising targets (i.e. protein-protein interactions), as potentially valuable drug targets are often neglected due to the high risk associated with their validation.

The AEGIS Consortium

The AEGIS consortium consists of eleven Beneficiaries hosting fellows and is completed by sixteen associated Partner Organisations which provide support in training and in vitro and in vivo validation of the targets.

AEGIS Beneficiaries:

- Helmholtz Zentrum München
- Philipps-University Marburg
- University of Groningen
- University of Uppsala
- Institut Pasteur
- Jagiellonian University
- Swiss Federal Institute of Technology
- Ridgeview Instruments AB
- AstraZeneca AB
- Novartis Pharma AG
- Giotto Biotech Srl
AEGIS Partner Organisations:

- MPI für Biochemie (RH)
- University of Pittsburgh (UP)
- MPI für bio-physikalische Chemie (MPIBPC)
- Technische Universität München (TUM)
- Enamine (ENA)
- ASTEX (AST)
- Orphanet/INSERM (ORP)
- EURORDIS (EUR)
- Unternehmer-TUM (UNT)
- Patentanwalt Dietmar Forstmeyer (PAT)
- University of Firenze (UF)
- Ruhr-Universität Bochum (RUB)
- Eindhoven University of Technology (TUE)
- TelesisPharma (TP)
- University of Sao Paolo (USP)
- Carmolex (CAR)

The AEGIS Targets

For the AEGIS project distinct types of drug targets were selected that are representative of features posing particular challenges for drug discovery but that are of highest biomedical relevance for emerging threats to human health: Protein-protein interactions (PPI), oligomerisation control, flexible binding interfaces and allosteric inhibition of enzymes are in the focus of our research proposal.

The AEGIS project will focus on developing novel inhibitors for four targets that are involved in Trypanosomiasis, Tuberculosis, Malaria and Leishmaniasis.
The AEGIS Fellows

15 Early Stage Researchers from nine different countries are participating in the AEGIS program and working in cross-institutional and transnational groups with different methods on the AEGIS targets.

Charlotte Softley, Helmholtz Zentrum München  
Structural biology and detection of conformational dynamics and transient pockets in protein targets.

Roberto Fino, Helmholtz Zentrum München  
Combining fragment-based screening and MCR.

Francesca Magari, Philipps-University Marburg  
Fragment-based approaches to block protein functions at the example of Farnesyl-Pyrophosphate Synthase (FPPS) and other model proteases.

Engi Hassaan, Philipps-University Marburg  
Implementing Fragment-based drug design to tackle neglected infectious targets

Atilio Reyes Romero, University of Groningen  
Design, synthesis and in vitro screening of novel molecules to control the oligomeric state of malate dehydrogenase.

Giulia Opassi, Uppsala University  
Using binding kinetics for drug discovery
The AEGIS Events

After the Recruitment Meeting and the Kick-off Meeting at HMGU in Munich beginning 2016, the 1st AEGIS Training School was organized by University of Uppsala (Prof. Helena Danielson) in cooperation with Ridgeview Instruments AB (Dr. Karl Andersson) from Monday 3rd to Friday 7th November 2016. Besides the fellows also local students took the opportunity for participating.

Main topic was biophysical and biochemical assays in drug discovery. In addition to conventional lectures, the school included a “High urgency project exercise: HUPE” where students were split into teams and had to address the scenario of a rapidly emerging transformed strain of trypanosomiasis, threatening parts of southern Europe and being an Immediate threat to food supply across EU. The program was completed by lectures in the complementary skills “Project management for PhD students” and “Avoiding scientific
Misconduct – good scientific practice as a compass in research”.

Highlight of the training school was an excursion to the Nobel Museum in Stockholm:
The 2\textsuperscript{nd} AEGIS Training School was arranged by University of Groningen (Prof. Alex Dömling, Dr. Matthew Groves) from 8\textsuperscript{th} up to 12\textsuperscript{th} May 2017.

That time the main focus was Medicinal Chemistry and in particular an introduction to multicomponent reaction chemistry (MCR), covalent inhibitors, macrocycles, drugability, PK/PD properties, hit generation and hit-to-lead, virtual screening patents and biomarkers. Practical training included a computational project using the in-house software ANCHOR.QUERY. The fellows had to find a suitable anchor point, generate virtual hits, select, re-rank the hits and then rationalize their choice in a 10 minute presentation. The use of differential scanning fluorimetry (DSF) to screen compounds was also covered by a lecture and practical training. The program was completed with a lecture on complementary skills and entrepreneurship.
Selected Scientific Achievements

Even in their 1st year, the AEGIS fellows were already able to release some scientific publications and intermediate results were presented at conferences. In this newsletter we present 5 such papers, which demonstrate well the strong interdisciplinary nature of the research performed in the AEGIS network:


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