FIMM High Throughput Biomedicine unit

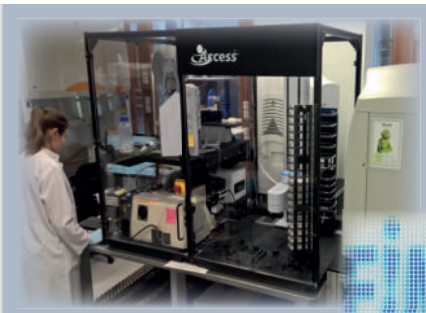
www.fimm.fi/en/services/technology-centre/high-throughput-biomedicine

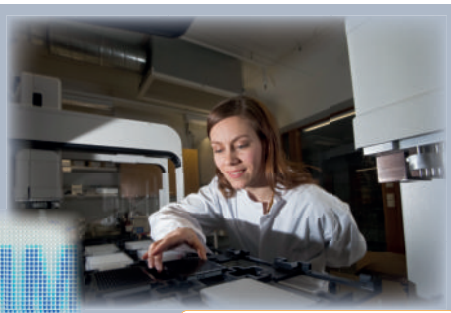
FINLAND

high-capacity screening site

HELSINKI

an official partner site of eu openscreen





THE PEOPLE

Jani Saarela
jani.saarela@helsinki.fi

Sergey Kuznetsov
sergey.kuznetsov@helsinki.fi

Laura Turunen
laura.turunen@helsinki.fi

Heidi Virtanen
heidi.virtanen@helsinki.fi

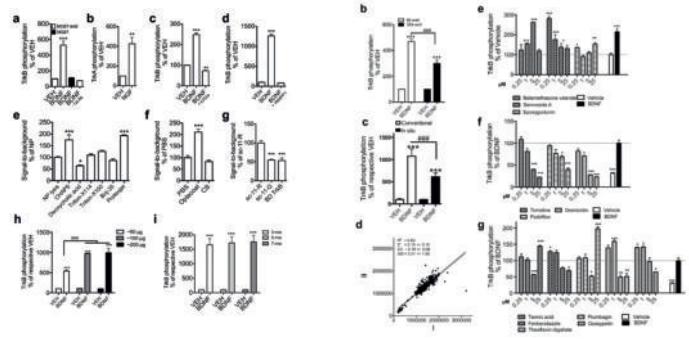
Päivi Tammela
paivi.tammela@helsinki.fi

THE PROJECTS

TrkB activator screening

Trk receptor tyrosine kinases regulate multiple important neuronal processes during development and in the adulthood. Small molecules activating Trk receptors could therefore serve as molecules promoting peripheral nerve regeneration. However, methods allowing simple and large-scale Trk phosphorylation analyses in cultured cells were previously lacking. To address this, we developed an in situ phospho-TrkB ELISA assay where cell culture, receptor stimulation and Trk phosphorylation analysis were all performed on the same multiwell plate. The whole assay was very complex (total assay time 120 h) and absolutely required the systematic assay handling by the FIMM HTB main robotic automation system for reproducible results. The assay readily and specifically detects TrkB phosphorylation in cells. A 100 000 compound screen was run with this method.

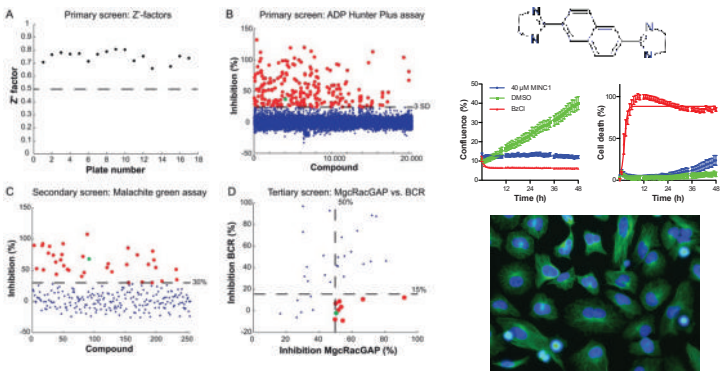
Reference: Antila et al. Journal of Neuroscience Methods, 2014, 222, 142–146.



Identification of MgcRacGAP inhibitors

MgcRacGAP, a Rho family GTPase activating protein involved in cytokinesis, is upregulated in many cancers and associated with poor clinical prognosis. Therefore, we designed and performed a biochemical and high-throughput screen of over 20 000 compounds in 1536-well format to identify small molecule inhibitors of MgcRacGAP. Through follow-up assays we finally identified the compound MINC1. Sequential cell-based assays showed that MINC1 induces an increased rate of cytokinetic failure and multinucleation in addition to other cell division defects.

Reference: van Adrichem et al., Comb Chem High Throughput Screen, 2015, 18, 3-17



THE HARDWARE

- *Labcyte Access robotic system (including Labcyte Echo 550 and 525 -acoustic dispensers, Nexus X-peel plate peeler and Agilent PlateLoc plate sealer and V-Spin centrifuge, Thermo Scientific Cytomat 10 -plate hotel, Labyte Deerac LX –bulk filler) to make assay ready compound plates*
- *HighRes Biosolutions ACell dynamic robotic system (including Agilent PlateLoc plate sealer and V-Spin centrifuge, BMG Pherastar FS plate reader, two ThermoFisherScientific Multidrop Combis, one Multidrop combi nl, Cytomat 24MPH plate hotel and Cytomat 10C plate incubator)*
- *Beckman Coulter Biomek FXp pipetting robot for running HTS assays*
- *Biotek EL406 plate washer/dispenser with plate stacker*
- *Stand alone BMG Pherastar FS -plate reader with plate stackers BioTek Cytation 5 -plate reader and microscope with plate stackers*
- *StoragePod chemical storage system*
- *Aushon Biosystems 2470 –Array printer*

THE EXPERTISE

- Absorbance
- Acoustic Dispensing
- AlphaScreen
- BSL II
- Fluorescence
- Fluorescence Polarization/anisotrophy
- FRET, BRET
- Luminescence
- Time-resolved fluorescence, TR-FRET
- Plate-based cytometry

High content imaging

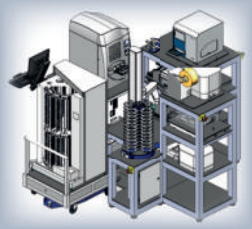
- Cell-based and biochemical screens using targeted or large chemically diverse libraries
- Molecular probe discovery
- Biological profiling using libraries of known bioactives
- Drug repositioning
- Personalized medicine screening (drug resistance and sensitivity) using approved and investigational drugs

THE SOFTWARE

Dotmatics Software
- Browser
- Studies
- Vortex
- Register
- Pinpoint
- Nucleus

Breeze - web-based in-house developed analysis, database and visualization software

SynergyFinder - web-based software for drug combination analyses



THE COMPOUNDS

>130 000 chemically diverse screening compounds (Specs, Chembridge, ChemDiv, Tripos)

>5 000 known bioactive and clinically investigated compounds (various sources)

THE OUTPUT

1. Kulesskiy E et al. 2016. Precision Cancer Medicine in the Acoustic Dispensing Era: Ex Vivo Primary Cell Drug Sensitivity Testing. Journal of Laboratory Automation, 21, p. 27-36
2. Pemovska, T., et al. 2015. Axitinib effectively inhibits BCR-ABL1(T315I) with a distinct binding conformation. Nature. 519, 7541, p. 102-225
3. Pemovska T. et al. 2013. Individualized Systems Medicine (ISM) strategy to tailor treatments for patients with chemorefractory acute myeloid leu kemia. Cancer Discovery. 3, p. 1416-29.
4. van Adrichem, A. J., et al. 2015. Discovery of MINC1, a GTPase-Activating Protein Small Molecule Inhibitor, Targeting MgcRacGAP. Combinatorial Chemistry & High Throughput Screening. 18, 1, p. 3-17

- 58 academic and 5 industrial (including SMEs) collaborations in 2017
- Member of:
  EU-LIFE,
  Nordic EMBL Partnership for Molecular Medicine
  Nordic Chemical Biology Consortium
  European Cell-based Assays Interest group

eulife

THE FUTURE

Adding high throughput flow cytometry screening capacity

Institute for Molecular Medicine Finland (FIMM), HiLIFE UNIT, University of Helsinki, Helsinki, Finland

FIMM UNIVERSITY OF HELSINKI HiLIFE