# Core Facility for High Throughput Cell Based Screens

*Biotech Research and Innovation Center (BRIC), Faculty of Health and Medical Sciences*
*Copenhagen University*

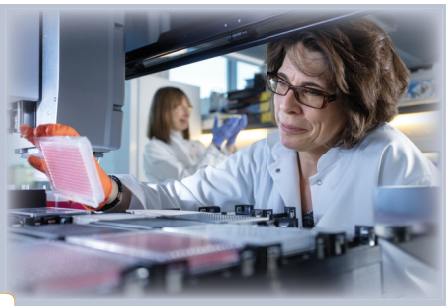
https://www.bric.ku.dk/core-facilities/ht-cell-based-screens/

DENMARK

specialist screening site

COPENHAGEN

a nominated partner site of eu openscreen



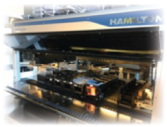
## THE PEOPLE

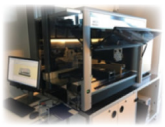
*Krister Wennerberg, Prof*
*Cornelia Steinhauer, PhD*
*Elin Pietras, PhD*
*Henning Gram Hansen, PhD*

## THE HARDWARE

### HTS screening systems

Automated liquid handling is primarily performed on a STAR and STARlet liquid handling station (Hamilton) equipped with a 96well and 384well head respectively and plate handling capacities. Low volumes and more flexible liquid transfer are performed on an Echo 550 acoustic dispenser (Labcyte).
In addition, the facility has access to an Echo525 (Labcyte), MultiFlo FX dispenser (Biotek), ELX 405 washer (Biotek) and Mantis Microfluidic Liquid Handler (Formulatrix).

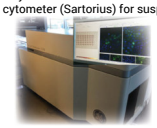


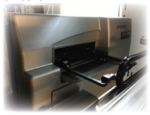


| | Microlab STAR | Microlab STARlet | Echo 550 |
|---|---|---|---|
| **Instrument** | | | |
| **Manufacturer** | Hamilton | Hamilton | Labcyte |
| **Capabilities** | Liquid transfer using disposable pipettips (Hamilton); 96well head and individual channels; vacuum manifold; shaker; plate handling; barcode reader | Liquid transfer using disposable pipettips (Hamilton); 384well head; plate handling | Liquid transfer using acoustic dispensing; 2.5nl any-well-to-any-well transfer |
| **Applications** | HT 96well transfections/treatments; minipreg; library replating | HT 384well transfections/treatments; HT-QPCR; library handling | HT 384well compound transfer; library cherry pick |
| **Plate format** | 96- and 384-well | 384-well | 384-well |
| **Transfer volume** | 2-1000µl | 2-50µl | 2.5nl-2µl |

### Readouts/ Screening technologies

Phenotypic cell-based readouts are primarily performed on an IN Cell Analyzer 2200 high content microscope (GE Healthcare). Life imaging can be followed on either our ZOOM or S3 Incucyte systems (Sartorius). For absorbance or luminescence based assays we use a Synergy HTX Multi-Mode Reader (Biotek).
In addition, the facility has access to an ENSIGHT plate reader with imaging capacity (PerkinElmer) and an iQue Screener Plus flow cytometer (Sartorius) for suspension cells.



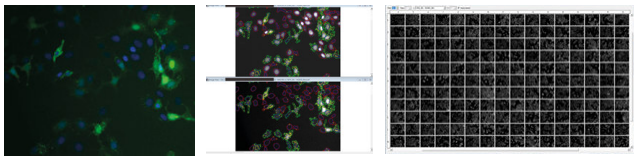


| | IN Cell Analyzer 2200 | Synergy HTX Multi-Mode Reader |
|---|---|---|
| **Instrument** | | |
| **Manufacturer** | GE Healthcare Life Sciences | BioTek |
| **Capabilities** | Fast, sensitive, and flexible automated cell imaging using 4x, 10x, 20x and 40x objectives and filters for imaging DAPI, FITC, Cy3, TxRed, Cy5, CFP and YFP; non-confocal but with advanced 3D deconvolution software | Flexible and sensitive plate reader with monochromator based absorbance and filter based fluorescence/luminescence |
| **Applications** | Broad range of high-content assays, 2D and 3D | Broad range of absorbance or lumiscent based biological readouts; DNA measurement |
| **Plate format** | slide to 384-well | 96- and 384-well |

## THE SOFTWARE

### Data analysis tools

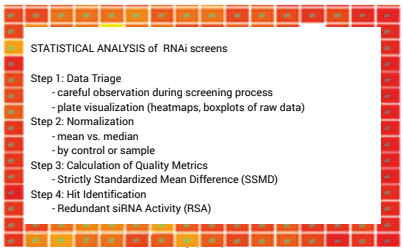
The Core Facility for HT Cell Based Screens at BRIC offers cell-based assay development and high content screening services utilizing phenotypic image-based analysis as primary readout.
The facilities IN Cell Analyzer 2200 automated high content microscope (GE Healthcare) is a non-confocal system with advanced 3D deconvolution software. It allows for fast, sensitive, and flexible automated cell imaging using 4x, 10x, 20x and 40x objectives and filters for imaging DAPI, FITC, Cy3, TxRed, Cy5, CFP and YFP. The proprietary IN Cell Investigator and INCarta software provides sophisticated image analysis on various user levels. In addition, we utilize Volocity (PerkinElmer) and Cell Profiler Analyst (Broad Institute) for advanced image analysis.

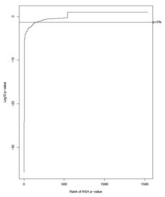


*Images courtesy of Roland Baumgartner and Alison Louw*

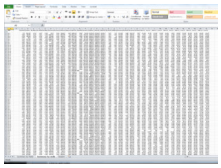
### Software tools

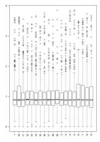
The facility has developed their own R-based statistical pipeline and data analysis workflow utilizing RSA analysis as hit picking algorithm (2).
Data visualization and further statistical analyses are performed using Spotfire High Content Profiler (PerkinElmer) and JMP (SAS).



*Birmingham et al. Nat Methods 2009; 6(8): 569-575*





## THE OUTPUT

1. *eIF5A is required for autophagy by mediating ATG3 translation. Lubas M, Harder LM, Kumsta C, Tiessen I, Hansen M, Andersen JS, Lund AH, Frankel LB. EMBO Rep. 2018 Jun;19(6). pii: e46072. doi: 10.15252/embr.201846072. Epub 2018 Apr 30.*
2. *High-throughput siRNA screening applied to the ubiquitin-proteasome system. Poulsen EG, Nielsen SV, Pietras EJ, Johansen JV, Steinhauer C and Hartmann-Petersen R Methods in Molecular Biology: Proteostasis 2016; 1449:421-39*
3. *miR-339-5p regulates the p53 tumor-suppressor pathway by targeting MDM2. Jansson MD, Damas ND, Lees M, Jacobsen A, Lund AH. Oncogene. 2014 Jun 2. doi: 10.1038/onc.2014.130.*
4. *A Screen Identifies the Oncogenic Micro-RNA miR-378a-5p as a Negative Regulator of Oncogene-Induced Senescence. Kooistra SM, Nørgaard LC, Lees MJ, Steinhauer C, Johansen JV, Helin K. PLoS One. 2014 Mar 20;9(3):e91034. doi: 10.1371/journal.pone.0091034. eCollection 2014*
5. *Histone acetyltransferase PCAF is required for Hedgehog-Gli-dependent transcription and cancer cell proliferation. Malatesta M, Steinhauer C, Mohammad F, Pandey DP, Squartrito M, Helin K. (2013) Cancer Res. 2013 Aug 13. [Epub ahead of print]*

### Collaborations:

The Core Facility for HT Cell Based Screens works in close collaboration with the High Throughput Translational Hematology (HTTH) Laboratory under the lead of Krister Wennerberg and Cornelia Steinhauer. This enables additional access to state-of-the-art automation technology and data analysis tools.

## THE FUTURE

The facility has an open application to expand in terms of screening content, imaging capacity (confocal microscopy), plate handling and bioinformatic data analysis.

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