

HIGH CONTENT SCREENING

Assay Development and Screening



OUR CAPABILITIES, SKILLS, EXPERTISE AND APPLICATIONS

HIT IDENTIFICATION

Key applications and benefits

- Generate novel hits for targets that are difficult to screen biochemically such as membrane receptors, transcription factors and protein:protein interactions
- Carry out pathway and phenotypic screens to identify disease-relevant compounds early, using cell lines, primary cells and stem cells
- Substantially reduce false positive rates by using read-out multiplexing and sophisticated data analysis

Assay principles

- Dye, antibody or GFP-based assay readouts
- Translocation assays applied, for example, to kinases, GPCRs, transporters and transcription factors
- Phosphorylation
- Protein aggregation

- Ligand binding
- Cell morphology and phenotype

SCREENING LIBRARY

- High quality library consisting of 250,000 compounds for HTS, selected for diversity and containing over 80,000 non-commercially available compounds synthesised by Evotec

HIT AND LEAD OPTIMISATION

Key applications and benefits

- Hit profiling after high throughput screening and support of medicinal chemistry programmes
- Profiling of compounds by monitoring complex cellular functions in great detail. Evaluation of cell-based efficacy, off-target effects and pathway profiling
- Sophisticated data to prioritise com-

By turning complex cellular events into statistically and pharmacologically relevant information, Evotec's high content screening (HCS) platform will add significant value to your hit identification, hit and lead optimisation programmes. Based on the world class Opera™ platform, pathway and phenotypic screening become possible and thus enables a powerful approach to cell-based drug discovery and cell systems biology. Furthermore, multi-colour, multi-parameter fluorescence imaging will eliminate false positives and allow the capture of parallel information on multiple targets and cellular events earlier in the drug discovery process. Consequently, this will help to drive your program with increased efficiency and effectiveness. Finally, Evotec's unique small molecule screening collection will provide the best chances of finding high quality hits.

— pound series: Link cellular signatures in multiplexing assays to chemical structure

Assay principles

- Dye, antibody or GFP-based assay readouts
- Target induction
- Cell signalling: Target translocation and / or phosphorylation
- Cell stress: Cytotoxicity, cell viability, apoptosis, necrosis and mitochondrial potential
- Cell proliferation, cell cycle analysis
- Cell morphology and phenotype
- Neurite outgrowth and network formation
- Readout multiplexing

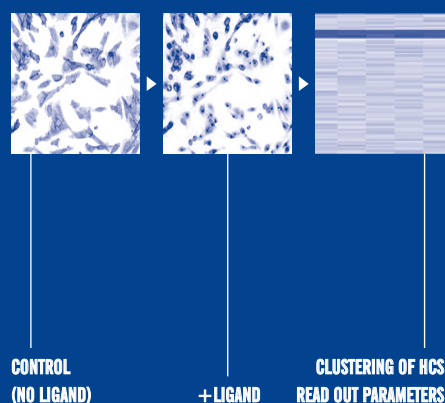
Used as primary and / or secondary screening, Evotec's state-of-the-art HCS platform will accelerate your drug discovery programme by addressing functional targets in their (patho)physiological background, thereby allowing more relevant and predictive in vitro results to be generated early in the discovery process

Case study: High throughput, high content screening campaign yields novel antagonist series

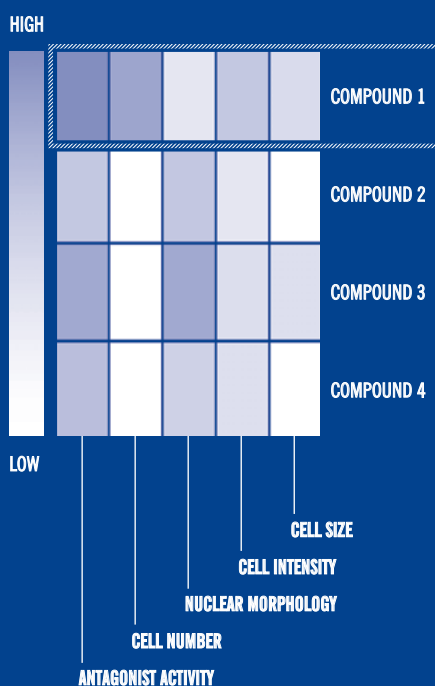
ENDOTHELIN A RECEPTOR

— Evotec carried out a high throughput, high content hit identification campaign to identify GPCR antagonists following receptor internalisation as a readout
 — Novel antagonist series, free of toxic properties, were identified

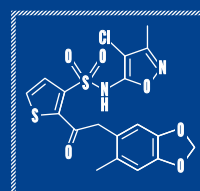
HIGH THROUGHPUT SCREEN



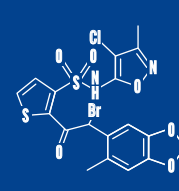
DATA ANALYSIS



RESULT (EXAMPLES)



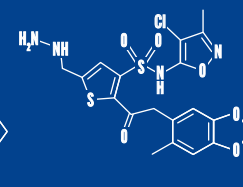
COMPOUND 1
 high antagonistic activity
 low toxicity



COMPOUND 2
 high antagonistic activity
 high toxicity



COMPOUND 3
 high antagonistic activity
 high toxicity



COMPOUND 4
 high antagonistic activity
 high toxicity

Case study: Turning complex cellular events into statistically and pharmacologically relevant information

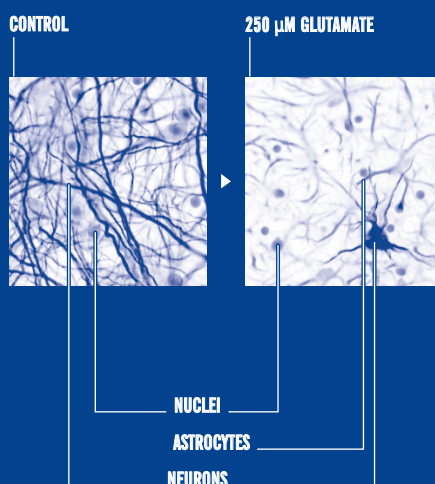
COMPOUND PROFILING USING PRIMARY NEURONAL CELLS

— Evotec has successfully undertaken the characterisation of compounds acting on the central nervous system, using primary neuronal cells
 — Neurite outgrowth, network formation, neuroprotection and toxicity were measured in a complex *in vitro* cellular system

READOUTS

- Cell type identifier
- Neurite outgrowth
- Neurite branching
- Network formation
- Cell viability
- Apoptosis

EXPERIMENT



RESULT (EXAMPLES)

— In this example, neuronal cell death was investigated

