

Efficient identification and validation of disease-specific targets

Overview

As part of BioFocus DPI's suite of target-to-drug discovery services, we offer a proprietary technology platform that enables the efficient discovery of fully validated targets. Human primary cell assays that model the disease of interest are the basis for this platform. We apply arrayed knock-in and knock-down libraries to over-express or silence human genes. The libraries cover drugable as well as antibody targets.

Focusing on the drugable genome

Our full length-cDNA (**FLeXSelect**) and shRNA (**SilenceSelect**) collections of arrayed adenoviruses are very effective to knock-in or knock-down human genes in primary cells. The libraries focus on targets deemed drugable by the pharmaceutical industry, i.e. small molecule tractable. This greatly increases the chance to yield clinically beneficial compounds. In addition, we have expanded the knock-down library with antibody targets to enable the identification of targets for antibody drugs.

Modeling diseases in human primary cells

Human primary cellular assays are the best systems to model human diseases *in vitro*. Human primary cells closely mimic human *in vivo* physiology in contrast to animal or tumorigenic cell lines. Our adenoviral system has some distinct advantages over conventional transfection technologies:

USP's of our adenoviral platform

Transduction of a broad range of human primary cells, including cells from patient material

Efficient introduction of cDNA and shRNA constructs (>70%)

Expression during > 10 days, allowing a window for complex assays

The platform has a track record across a broad range of human primary cell types:

Primary cell types successfully used in our target discovery programs

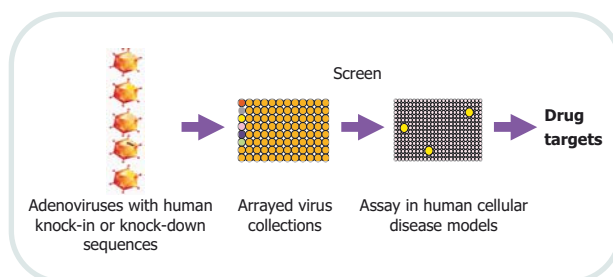
mast cells	osteoblasts
dendritic cells	macrophages
endothelial cells	keratinocytes
chondrocytes	synovial fibroblasts

A versatile platform

High-throughput screening: Assays can be run in a high-throughput (96- or 384-well) format, supported by our bioinformatics tools and multiplex and high content image analysis.

Long-term studies: In contrast with synthetic siRNA, adenoviral-mediated transfer of shRNA induces long term (> 10 days) knock-down, allowing efficient silencing of the gene of interest. Furthermore, this feature allows the implementation of complex biological assays such as cellular differentiation assays.

In vivo studies: Adenoviral technology can also be applied to validate targets *in vivo*: constructs identified as hits in target discovery can be used directly in animal models to demonstrate the effect on the disease.





Broad range of disease areas

We are at the forefront of using human primary cellular assays to model human diseases. By combining our disease-biology expertise with our technology platform, we can accelerate target discovery in any disease area. This expertise is reflected by our successful target discovery programs in:

- Allergic rhinitis
- Alzheimer's Disease
- Asthma
- Atherosclerosis
- Cancer
- Cystic fibrosis
- Diabetes
- Huntington Disease
- Microbial/viral infections
- Obesity
- Osteoarthritis
- Osteoporosis
- Psoriasis
- Rheumatoid arthritis

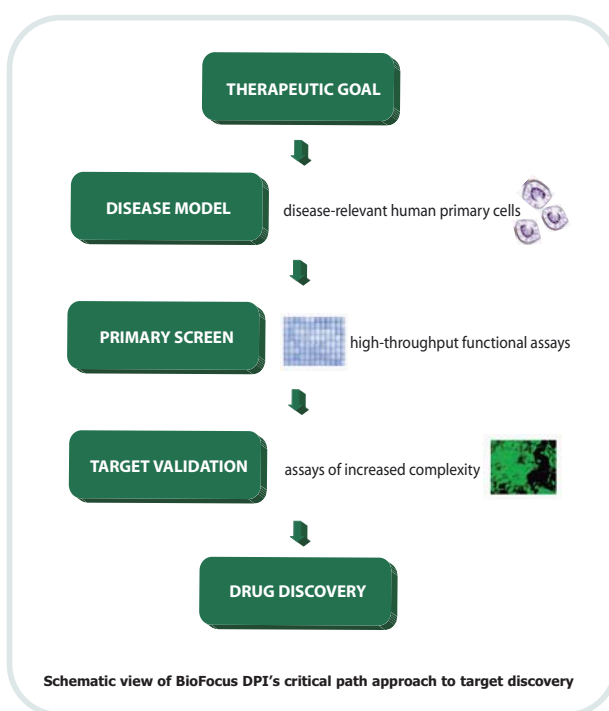
Unique critical path approach

Our methodology is fundamentally different from conventional genomics technologies. We apply a "critical path" approach to deliver validated drug targets into compound screening. For each disease program, our libraries are functionally screened in human primary cell disease models to identify hits that regulate the disease phenotype. These hits are then passed through increasing complex validation assays, establishing the biological relevance of the targets. The primary human cell as the basis for the target discovery process increases the chances of translating an observed therapeutic effect into man.

Partnerships

All target discovery programs are set up according to our critical path approach, formed by a joint steering committee of BioFocus DPI scientists and the partner.

We are proud to be the target discovery partner of choice for a wide range of pharmaceutical, biotech and patient organizations.



Contact

To learn more about our target screening platform and assay expertise, contact us at biofocusdpi@glpg.com



biofocusdpi.com

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