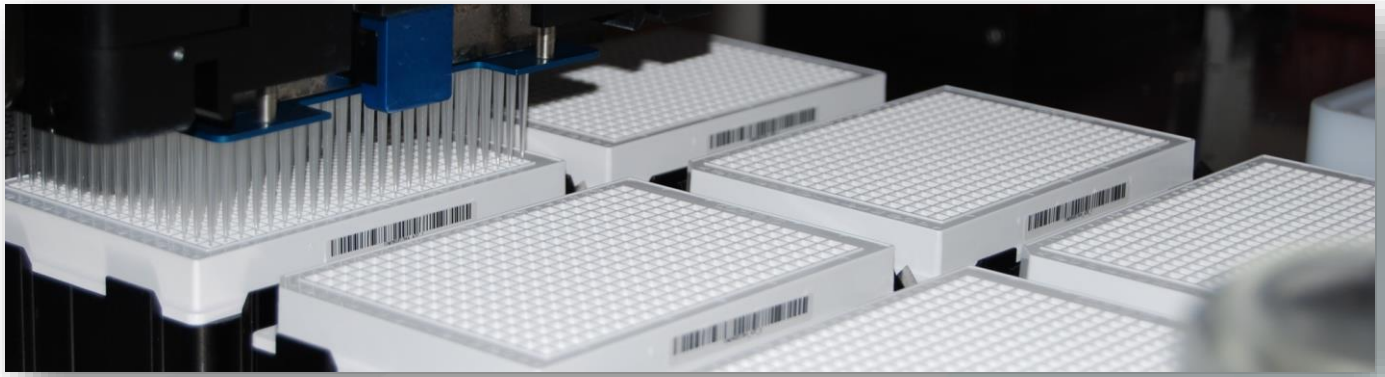
The Target Discovery Institute
Cellular High Throughput Screening



NUFFIELD DEPARTMENT of MEDICINE

TARGET DISCOVERY INSTITUTE

Daniel Ebner
HIDI
October 1st, 2018

TDI Cellular Screening Facility & CRISPR Screening

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3.

1. TDI Cellular HTS Screening

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Target Discovery Institute – TDI
Nuffield Department of Medicine

University of Oxford

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Chemical Biology | Mass Spectrometry | Medicinal Chemistry | Epigenetics | Cellular HTS | Quantitative Imaging | Pharmacogenomics
ARUK Oxford Drug Discovery Institute | Biophysics and Biochemical Screening

Libraries and Reagents

Libraries

The Target Discovery Institute holds expansive RNAi libraries encompassing **siRNA, shRNA** and **miRNA**; in addition to diverse set and FDA approved **Small Compound Libraries**.

Our screening libraries are available as **Mouse** or **Human** species specific targets and are arrayed into targeted subsets (e.g. Oncology Drug Sets, Protein Kinase Inhibitors etc.) for efficient, target driven screening.

All libraries are available in **96** or **384** well format, suitable to your screening platform.

All reagents and libraries within these pages are available to any investigators interested in running screens.Our primary **On-Target Plus** siRNA libraries are supplied by **ThermoFisher** as pooled whole genome siRNA's and custom designed "druggable" siRNA libraries.

Reagents

In addition to our RNAi libraries we have access to a large number of Transfection Reagents suitable for RNAi screening applications.

For High Content Imaging we have access to wide range of stains and protocols. Click for more information on High Content Imaging and the range of stains available.

For further information about any of the TDI libraries, Transfection Reagents, High Content Imaging and Stains; or for more information about any aspect of Screening, please contact Daniel Ebner.

Cellular HTS

- High Throughput Screening
- CRISPR Pooled Screening
- HTS Equipment
- HTS Readouts
- Libraries/Reagents
  - siRNA Libraries
  - shRNA Libraries
  - Small Compound Libraries
  - cDNA Libraries
  - Transfection Reagent Panel
- Group Members
- Application and Fees
- BHF Cardiovascular Target Discovery
- News and Publications
- Contact

Athena SWAN Silver Award

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Medical Sciences Division | Oxford University

Nuffield Department of Medicine ...fostering your career in science

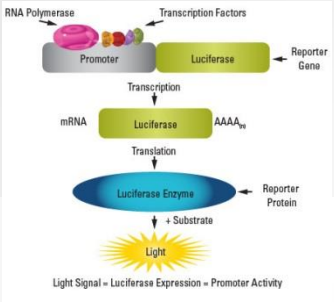
Libraries/Reagents
- siRNA Libraries
- shRNA Libraries
- Small Compound Libraries
- cDNA Libraries
- Transfection Reagent Panel

http://www.tdi.ox.ac.uk/high-throughput-screening

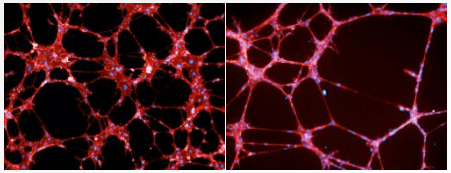
If you are interested in initiating a screen, just send me an email:

daniel.ebner@ ndm.ox.ac.uk

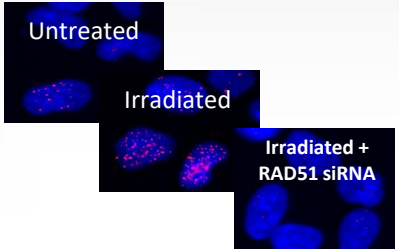
Snapshot of TDI Cellular HTS Outputs



"Negative autoregulation of BMP dependent transcription by SIN3B splicing reveals a role for RBM39." Faherty et al., Bhattachary - RDM

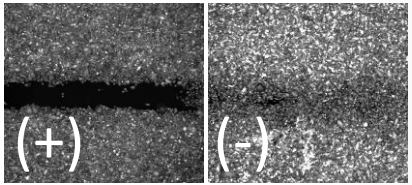


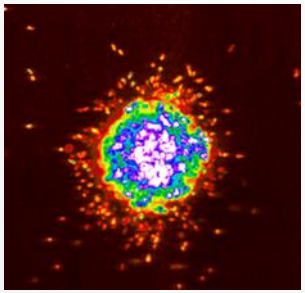
"The retinoid agonist Tazarotene promotes angiogenesis and wound regeneration" ZEN - RDM



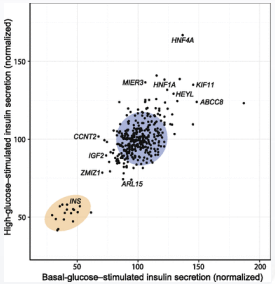
"A genome-wide IR-induced RAD51 foci RNAi screen identifies CDC73 involved in chromatin remodeling for DNA repair" Helleday – Oncology

"Functional HTS to identify microRNAs regulating EMT in prostate cancer" Edwards / Rao - NDS

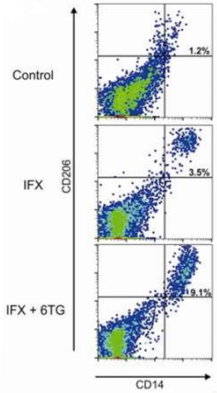




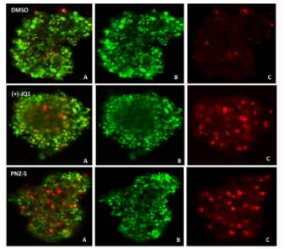
"Neuroblast Spheroid Migrartion" Ducker, Millar



"Systematic Functional Characterization of Candidate Causal Genes for Type 2 Diabetes Risk Variants" Thomsen, Ceroni,

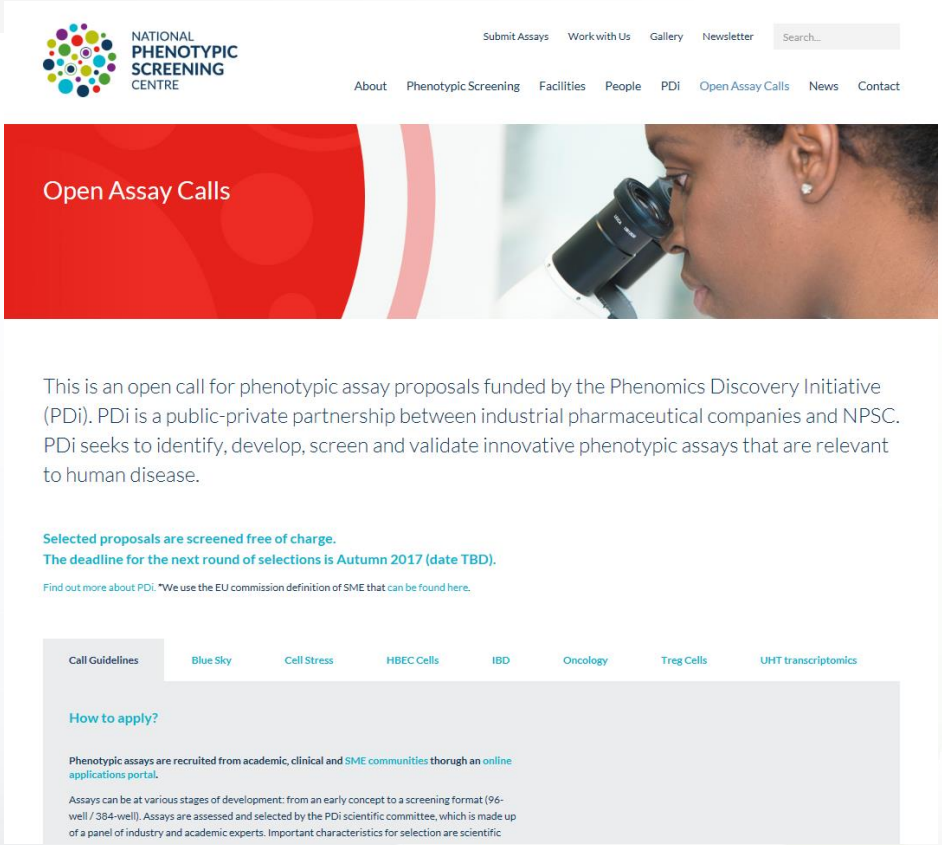


"Benzimidazoles promote anti-TNF induced regulatory macrophage formation and potentiate therapeutic effect in vivo model of IBD" Wildenberg - Academic Medical Center, Amsterdam



"BET inhibition as a new strategy for the treatment of gastric cancer" Montenegro et al. Müller – TDI/SGC

2. NPSC / PDi Drug Discovery Initiative



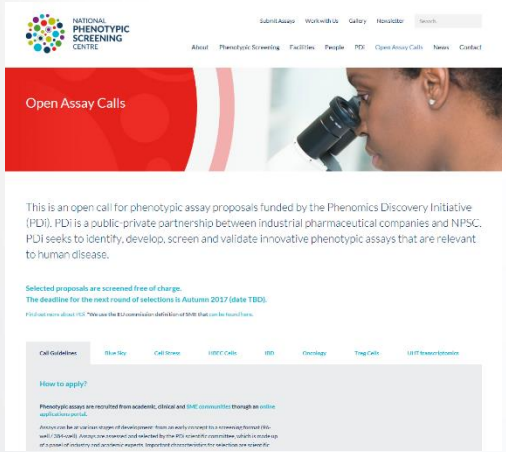
http://npsc.ac.uk/

NATIONAL PHENOTYPIC SCREENING CENTRE

THE UNIVERSITY OF EDINBURGH
UNIVERSITY OF DUNDEE
SULSA Scottish Universities Life Sciences Alliance

PDi PHENOMICS DISCOVERY INITIATIVE

Immuno-oncology open call, Oct 31st



http://npsc.ac.uk/open-assay-calls

- Phenotypic assays that accurately ***model the complexity of the tumour microenvironment***. These should allow screening to be carried out in more relevant immune contexts, and be more representative of the pathophysiology of the disease.
- Novel assays for intracellular (or even extracellular) ***immune-regulatory mechanisms*** that cannot be targeted by current monoclonal antibody-based approaches. These assays should help broaden the potential mechanisms that can be targeted by new therapies.
- Assays that allow the discovery of small molecules that ***synergise with known therapeutics*** (biologics or CAR-T) to extend their scope and efficacy.
- Models for immunologically ***"warming" up "cold" tumours***, including ones involving infiltration of 3D tumour spheroids by T cells. It is expected that these models will be complex in order to accurately represent the disease model.
- Models that can explore novel ways of ***activating exhausted intra-tumoral T cells***.
- Models involving the manipulation of immunosuppressive Treg cells and/or key cytokines.
- Assays that involve other ***immunosuppressive cell types*** (for example, MDSCs, dendritic cells and TAMs).
- Models that could uncover new targets in ***innate immune system*** cell types (eg. NK cells, dendritic cells and macrophages).

PDi
PHENOMICS
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3. Oxford CRISPR/Cas9 Screening Facility

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CRISPR/Cas 9 Cell Screening Facility

Introduction

CRISPR/Cas9 technology is ideally suited for genome-wide screening applications due to the ease of generating guide RNAs (gRNAs) and the versatility of Cas9 or Cas9 derivatives to knockout, repress, or activate expression of target genes. Several pooled lentiviral CRISPR libraries have been developed and are now publicly available. Here at the TDI we have Pooled Lentiviral CRISPR genome knockout and CRIPSR gain of function libraries.

Daniel Ebner, Elena Navarro Guerrero and Dylan Jones

Cellular HTS

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- CRISPR Pooled Screening
  - CRISPR loss of function screening
  - CRISPR gain of function screening
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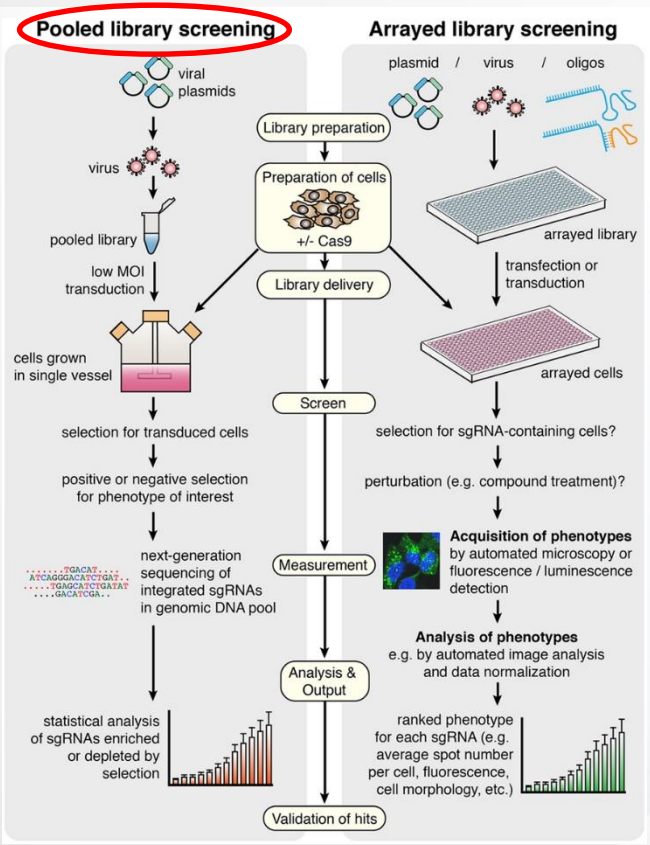
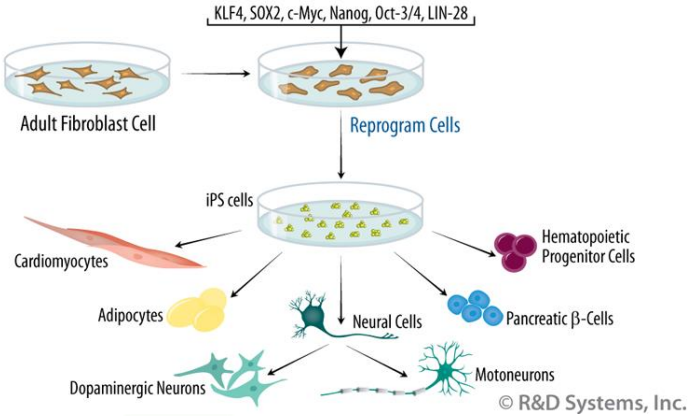
- Toronto KnockOut (TKO) CRISPR Library - Version 3 (Pooled Library #90294)
- Human CRISPR Knockout Pooled Library (GeCKO v2) (Pooled Library #1000000048, #1000000049)
- Human Genome-wide CRISPRi-v2 Libraries (Pooled Libraries #83969, #1000000090)
- Mouse CRISPR Activation Library (SAM - 3 plasmid system) (Pooled Library #1000000075)
- Mouse Genome-wide CRISPRa-v2 Libraries (Pooled Libraries #83996, #1000000093)

A quick review of CRISPR/Cas9 Screening and iPSCs:



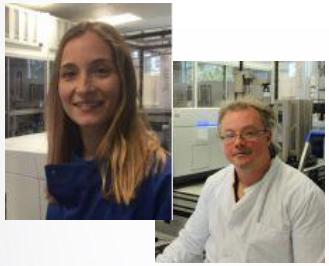


iPSCs are derived by reprogramming somatic cells of patient donors to obtain stem cell lines that retain the genetic background of the donor and have a normal karyotype, yet can replicate indefinitely and be instructed to differentiate into a wide variety of cell types.

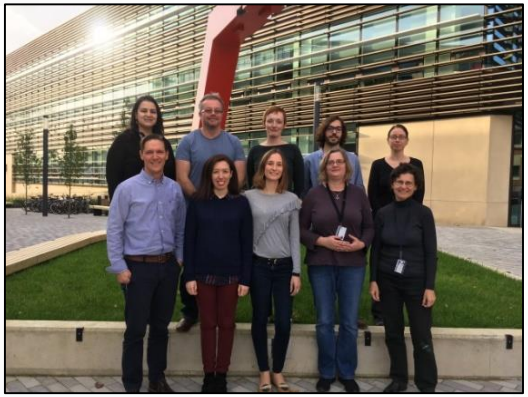
Target Discovery Institute Cell Screening Facility Personnel

Nuffield Department of Medicine

CRISPR Cas9 Screening Facility



CRISPR/Cas9 LOF and GOF Screening
Arrayed CRISPR Screening Development



TDI Cellular Screening Facility

Oncology Screening

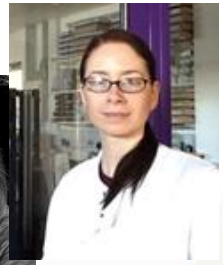
ODDI Neurodegeneration Assay Development Platform

Students/Visiting Fellows

Co-supervised Student – RDM/OCDEM
Functional Genomics of T2D

Junior Research Fellow – 3D Oncology

NPSC/PDi



Cellular HTS
PDi Image Analysis Specialist