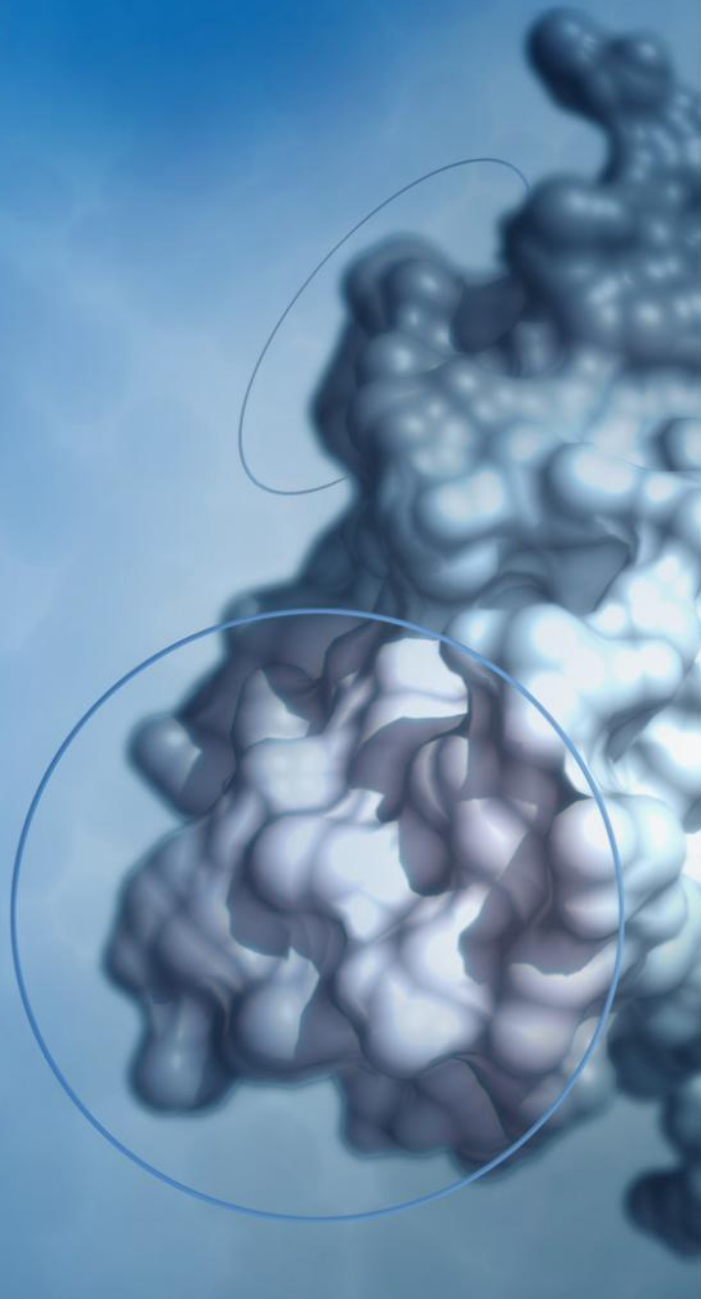
Open Targets:

An Innovative Public-Private Partnership

https://www.opentargets.org/

Philippe Sanseau
GSK, Target Sciences
20th June 2017



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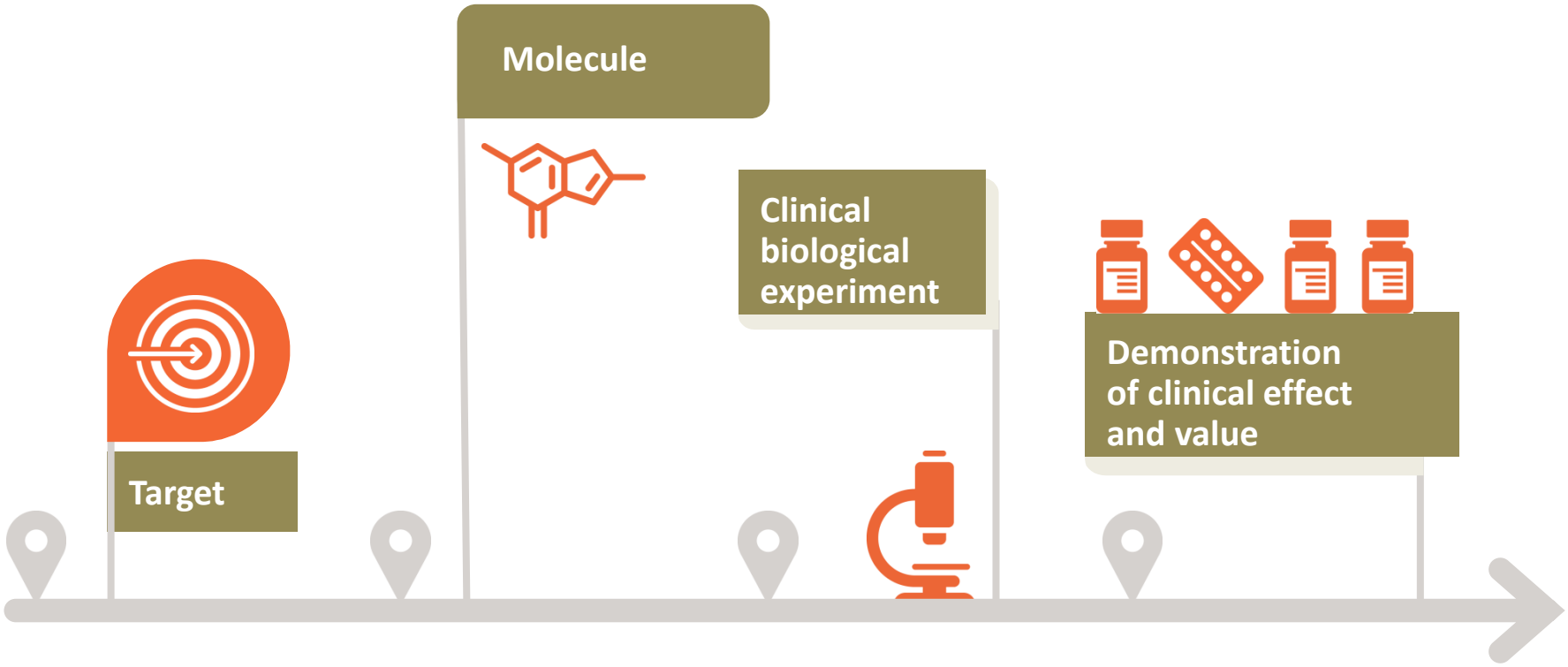
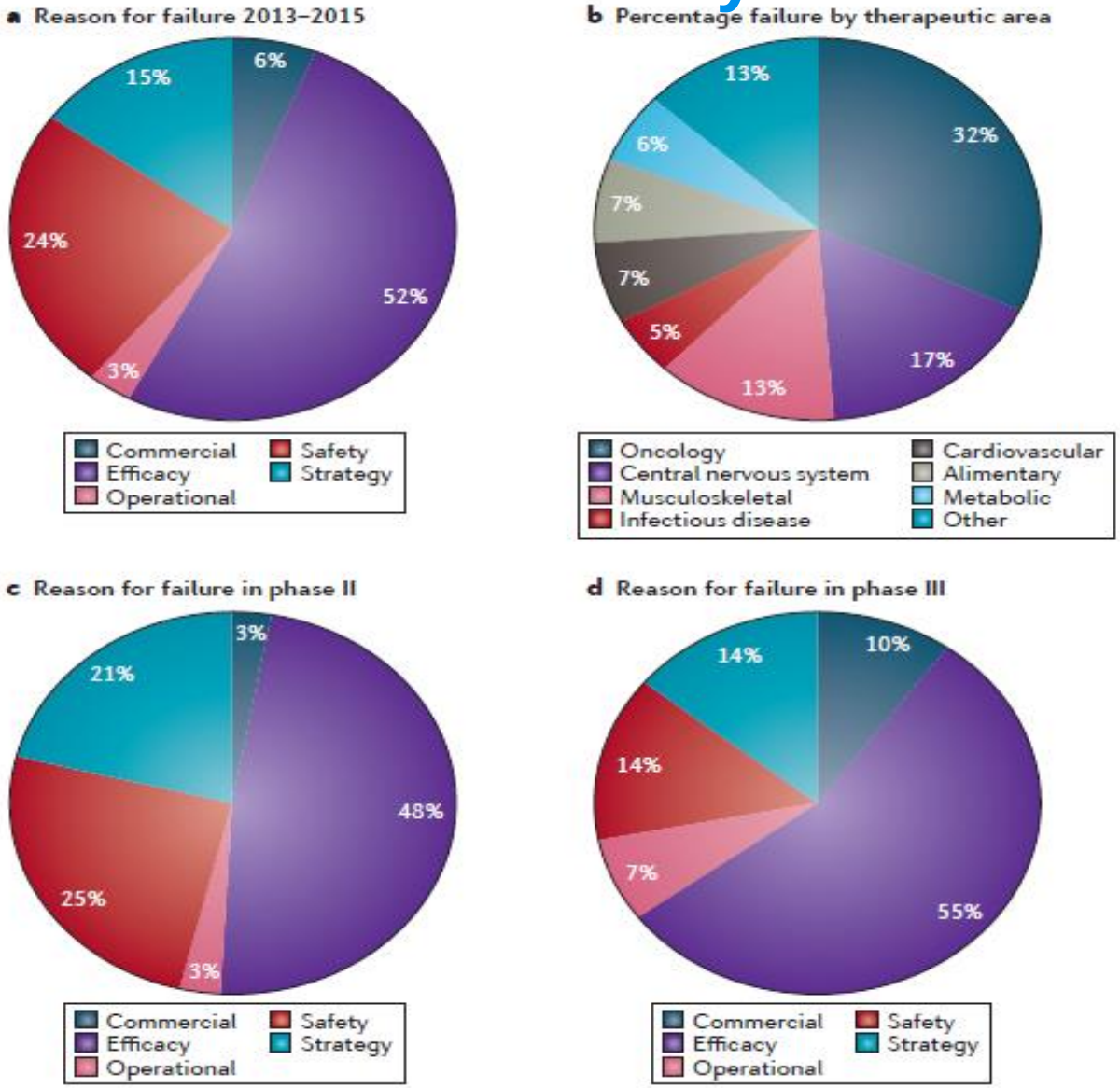
There are four big decisions in making medicines



.....and it costs over $1bn and more than a decade

Open Targets

Clinical failures are costly



Nat. Rev. Drug Disc. Dec 2016, 817-818

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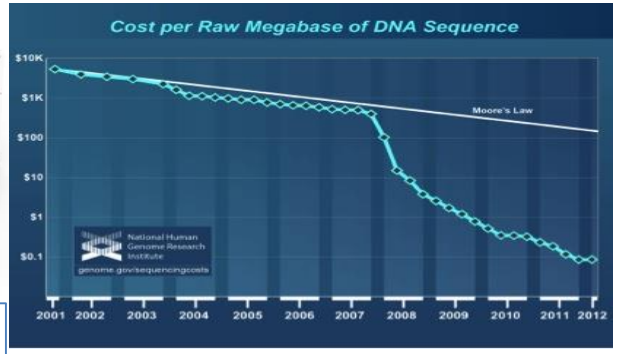
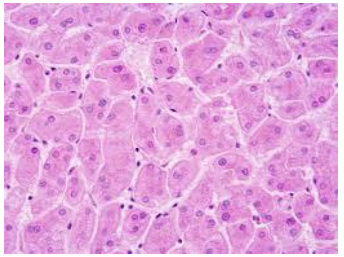
The right time?

Technology

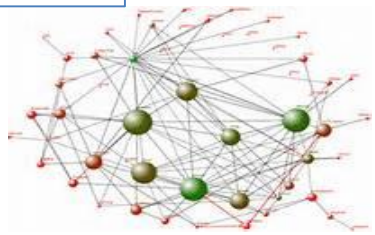


Gene editing

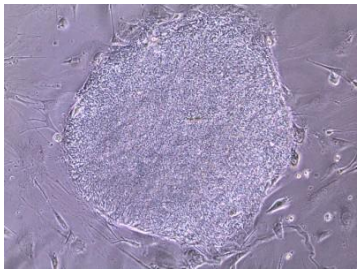


Human tissues

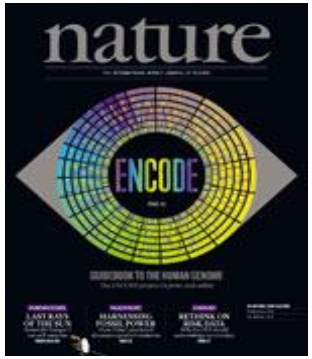
Genetic associations



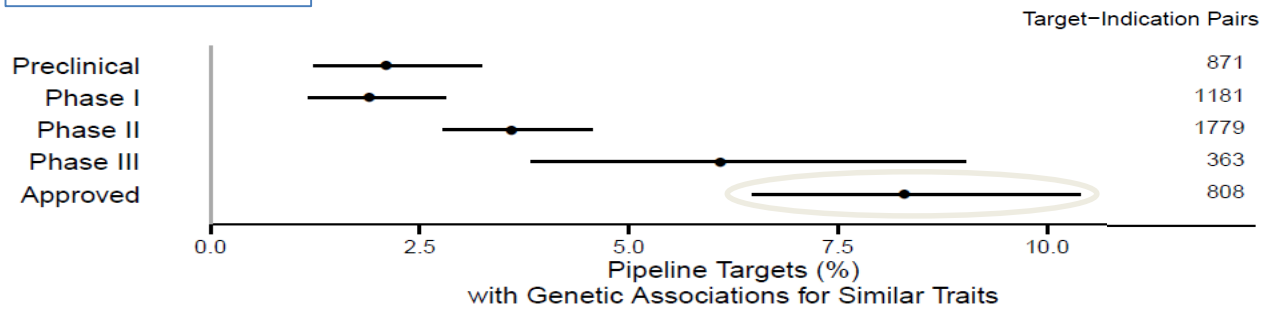
Informatics



iPS cells



ENCODE data & genomics technologies



Nelson, Nat Genet, 2015

Open Targets

The Vision

A public-private initiative to transform drug discovery by enabling the systematic identification and prioritisation of targets

Professor Dame Janet Thornton
former Director, EMBL-EBI

Patrick Vallance, President Pharmaceuticals R&D GlaxoSmithKline

Professor Sir Mike Stratton
Director, Sanger Institute

Core Principles

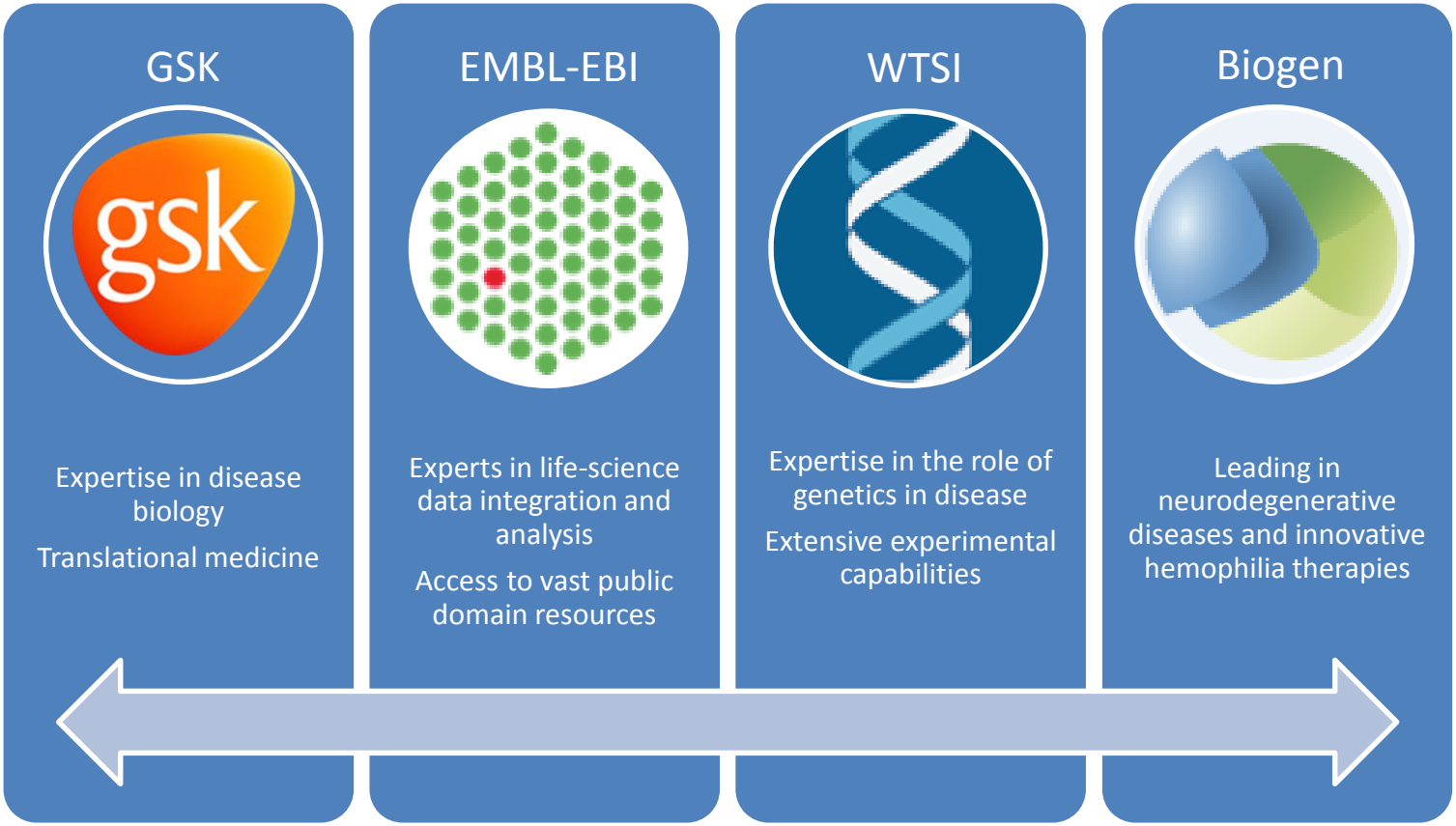
We are focused on **pre-competitive research** that will enable the systematic identification and prioritisation of targets.

We are committed to **rapid publication** and making data, methods and results **publically available** as soon as possible.

We believe in non-exclusive **partnerships** that foster the free exchange of ideas and expertise.

Open Targets

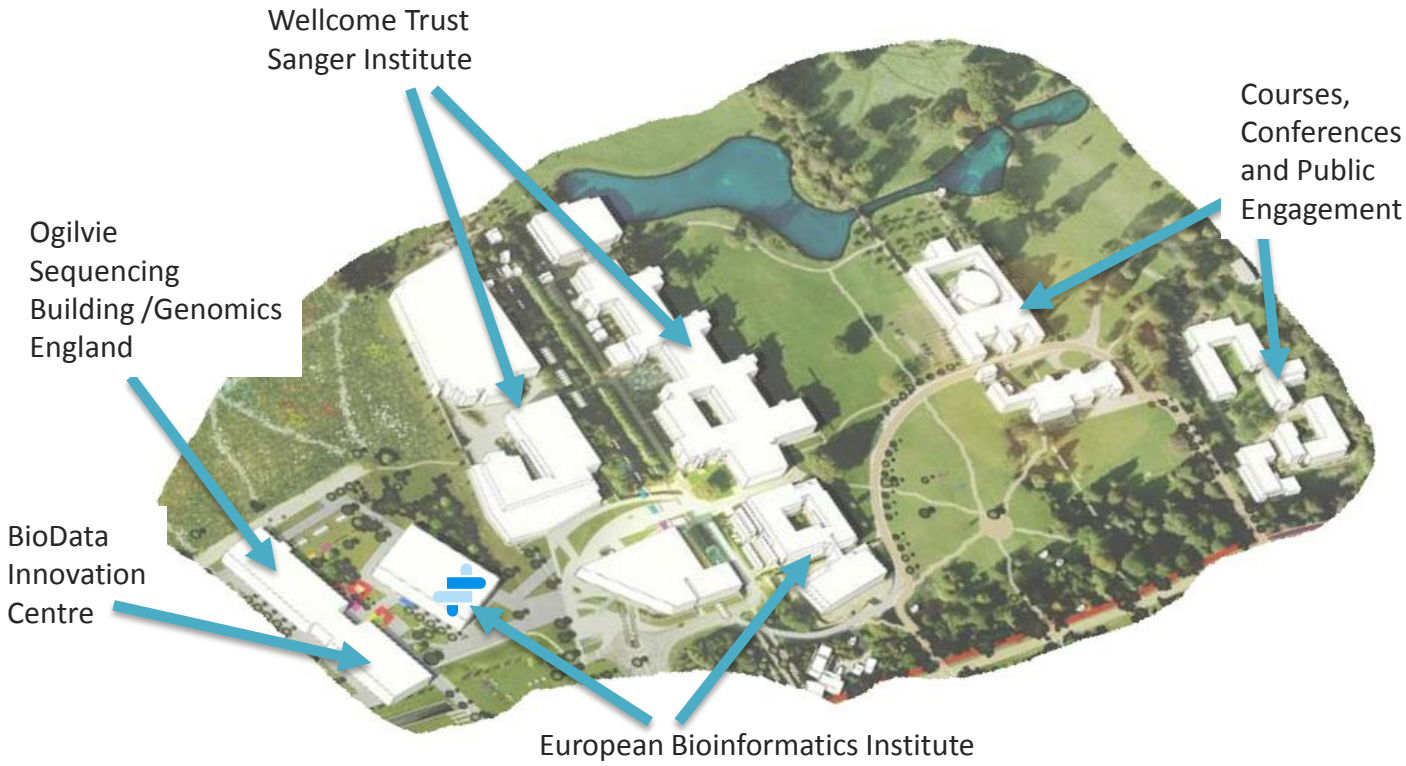
The Partners



The partners shared the idea that target validation could be improved but that one institute could not necessarily do it alone.

Open Targets

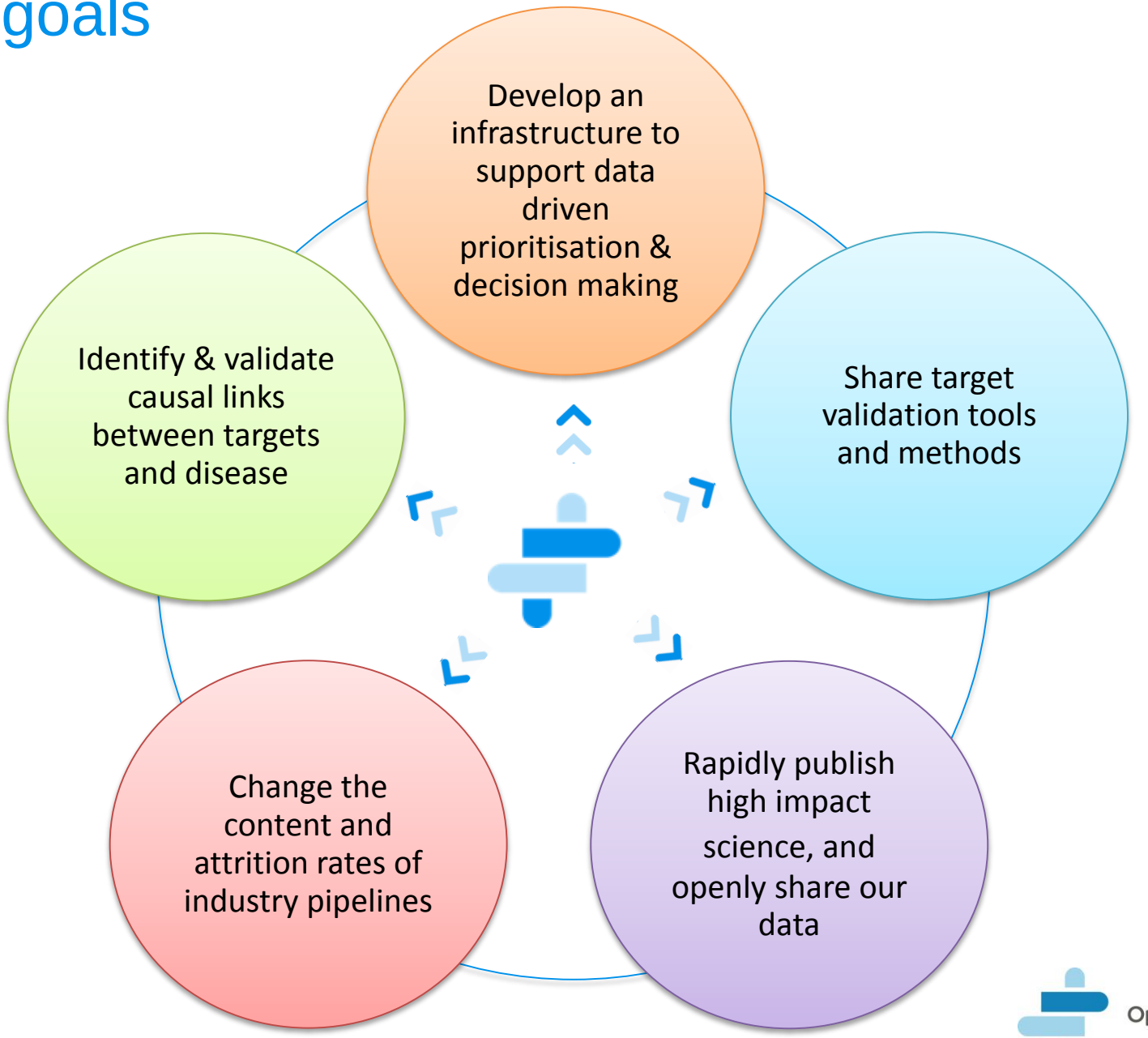
Based on the Wellcome Genome Campus



- The Campus - one of the world's largest genomic research centres (home to over 2000 genomic scientists; hosts of major international conferences; situated within one of the world's top innovation districts (Cambridge, UK)
- Location enables close collaboration and leverages existing campus expertise and synergies - integrating scientists specialising in genomics, drug discovery and bioinformatics in one centre to focus on major challenges in target validation.

Open Targets

Our goals



Open Targets

Target Validation Knowledge Cycle

Public Databases and Pipelines

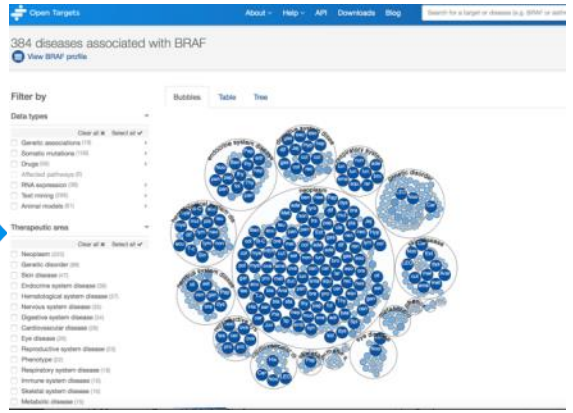
ChEMBL UniProt Europe PMC REACTOME IntAct intOgen Integrative Onco Genomics G2P

New experimental data
Physiologically relevant and at scale

Oncology Immunity Neuro Cross-Disease

Open Targets Platform

www.targetvalidation.org



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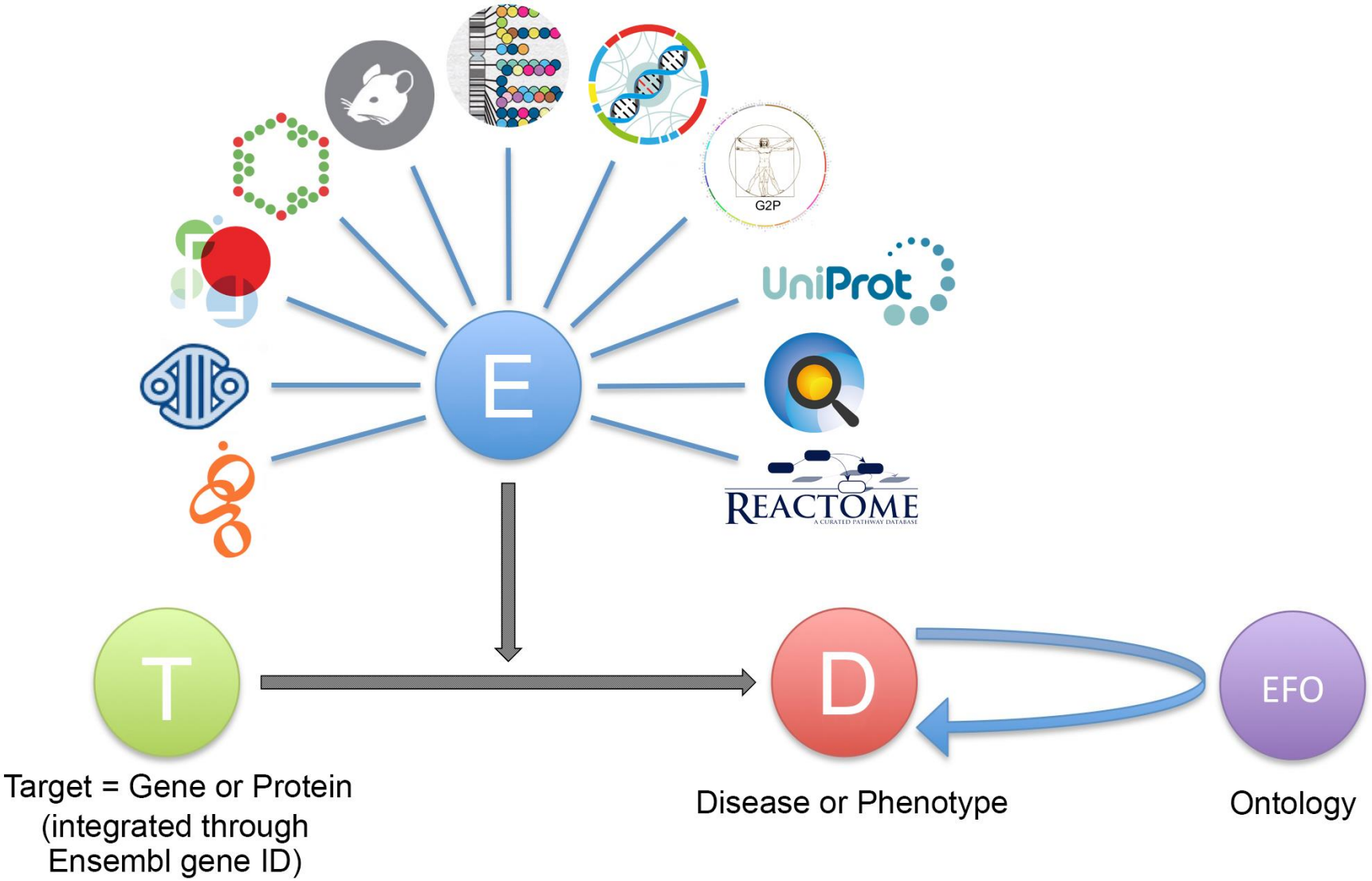
The Evidence Model



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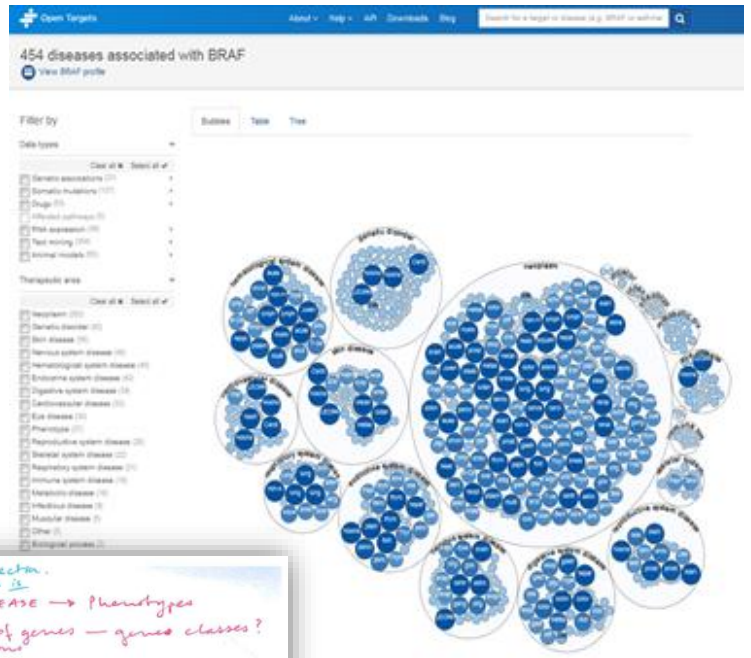
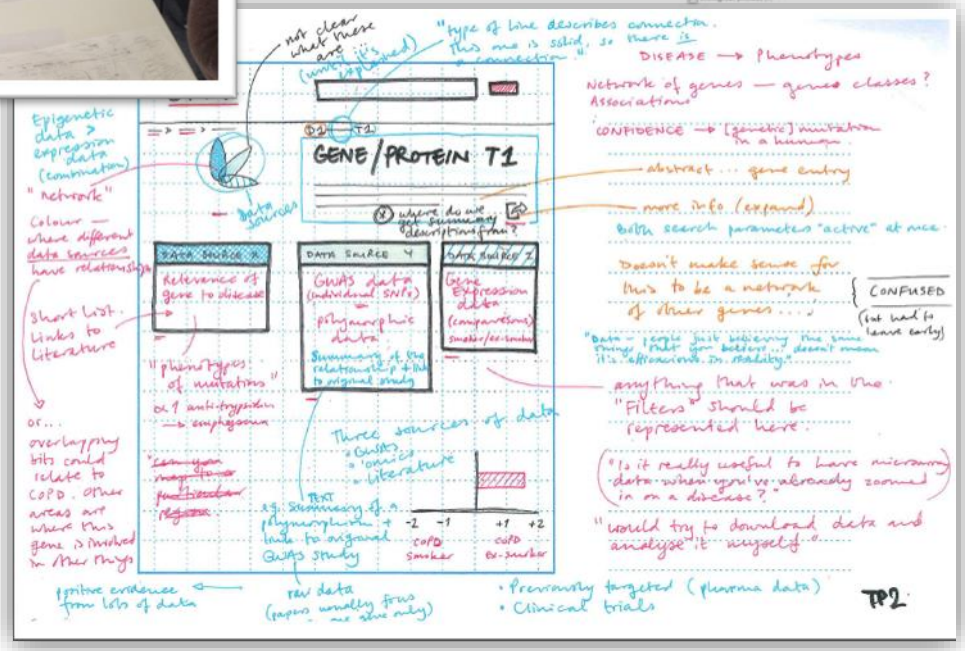
Using a User Experience Approach

Putting the User first





Facilitating decision-making

A) Which targets are associated with a disease?

B) What evidence supports this target-disease association?

C) Are there drugs for this association in clinical trials?

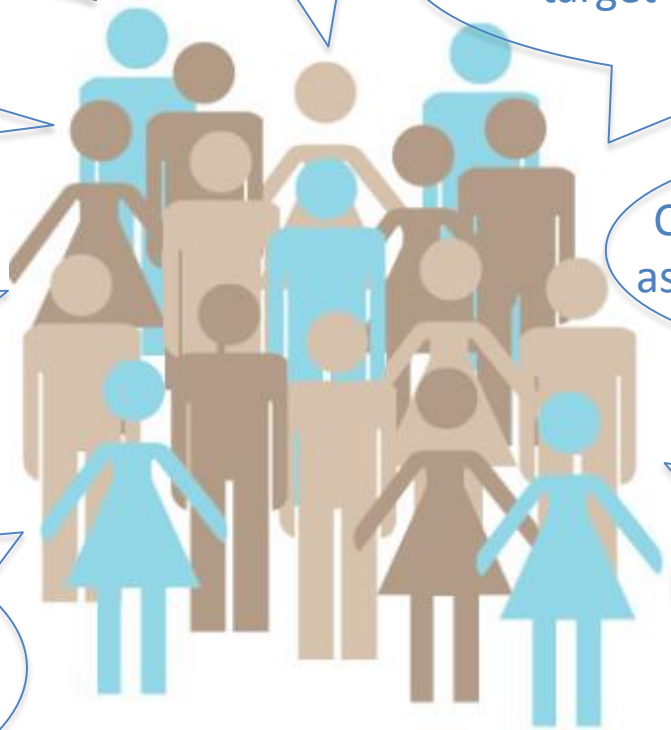
D) For a given target, are there other diseases associated with it?

E) Can I find the association focusing on two (or more) different therapeutic areas?

F) What else can I find out about my drug target?

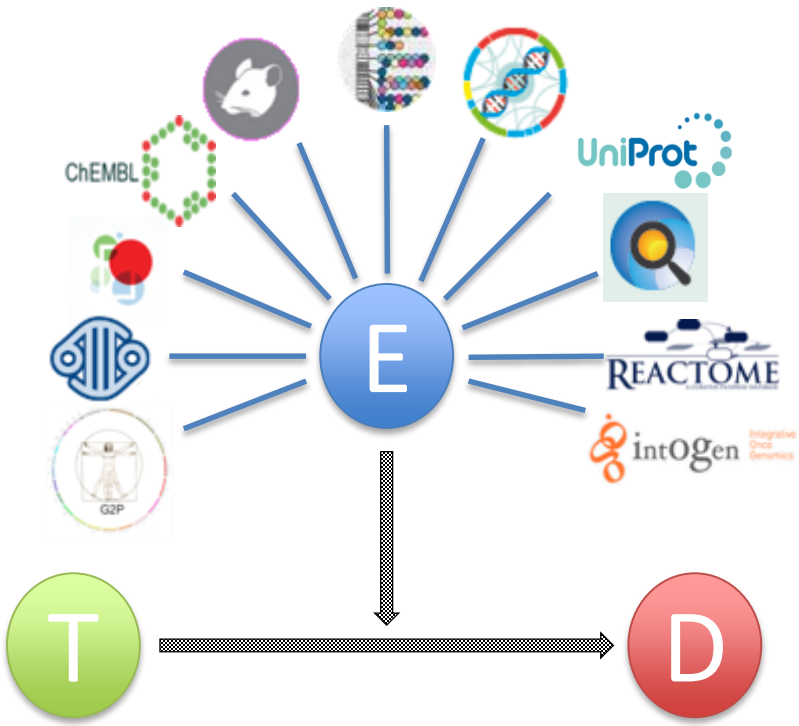
G) What else can I find out about my disease?

H) Can I look at multiple targets at a time?



Open Targets

Current status



Releases

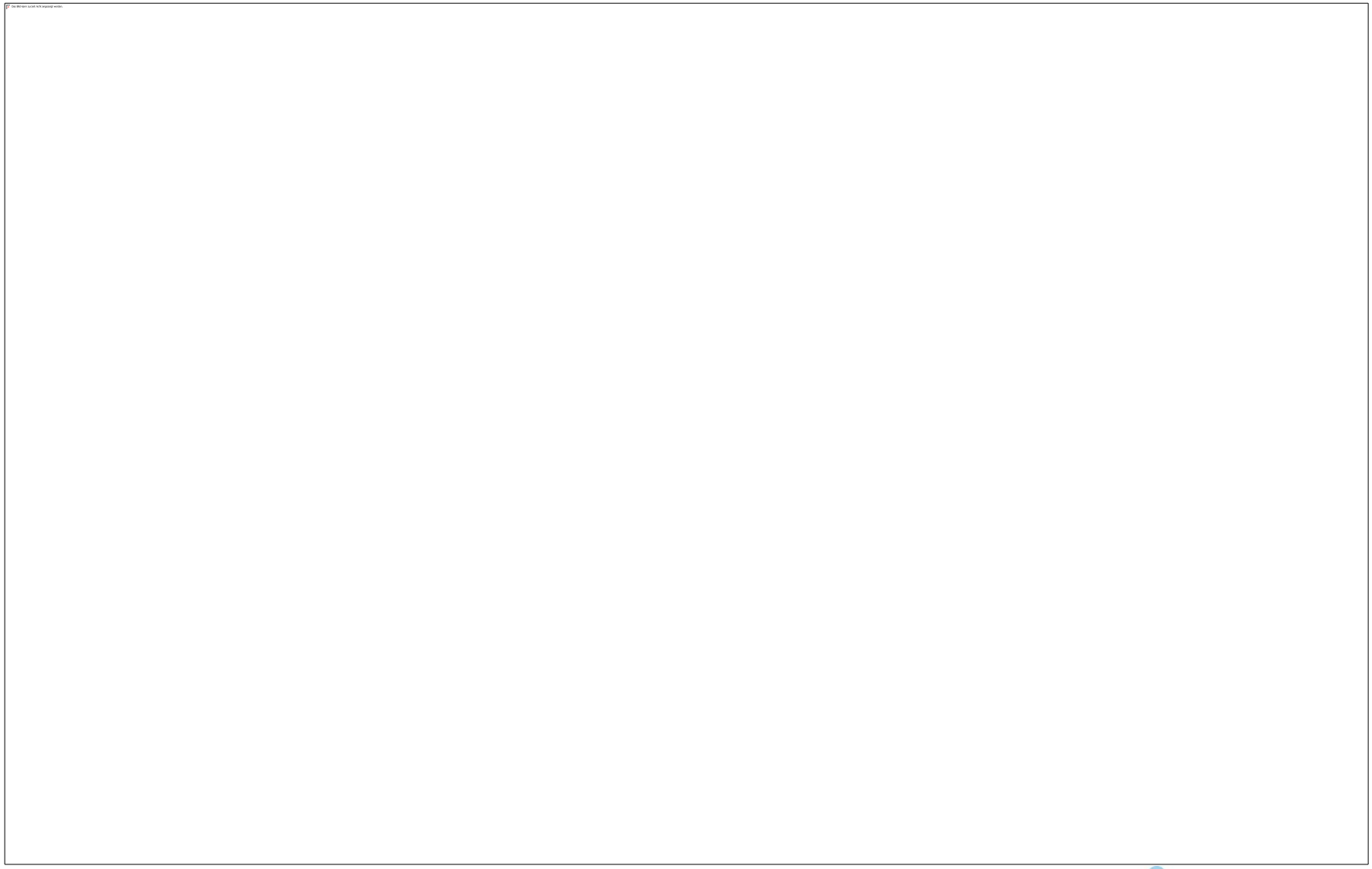
Dec 2015
Apr 2016
Aug 2016
Dec 2016
Mar 2017

Evidence Type	Source	Target-Disease Association Objects
Marketed drugs	ChEMBL	120,520
Affected pathways	Reactome	6,143
Somatic mutations	Cancer Gene Census	23,440
Proteins with disease roles	Uniprot	21,870
Genetic for rare diseases	Gene2Phenotype	975
Rare genetic mutations	European Variation Archive	28,050
Complex disease	GWAS Catalog	32,363
Cancer driver mutations	IntOGen	2,377
Mouse models	Phenodigm	395,622
RNA expression	ArrayAtlas	529,084
Text mining	EuropePMC	3,678,967

Koscielny et al. Open Targets: a platform for therapeutic target identification and validation published online 29 November 2016. doi: 10.1093/nar/gkw1055

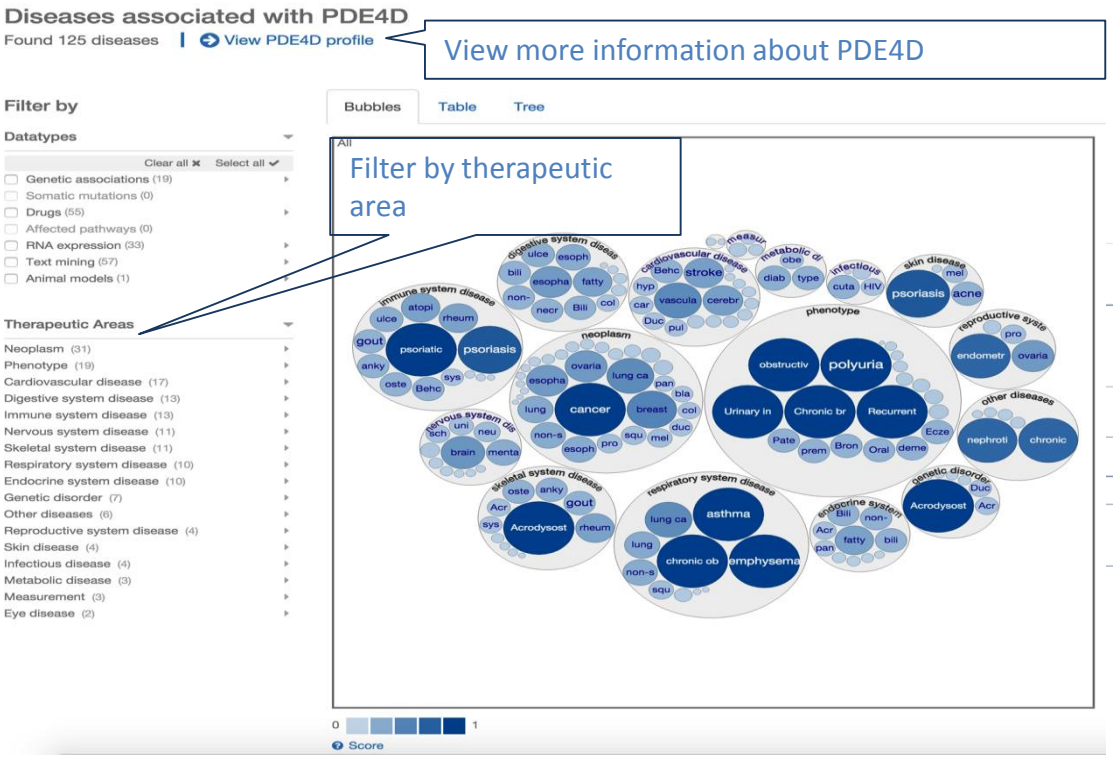
Open Targets

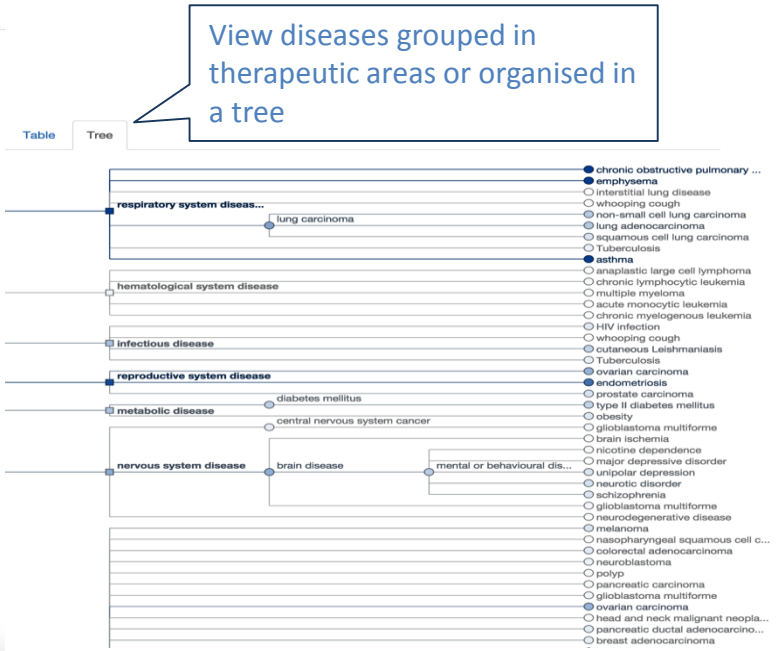
The Open Targets Platform



Open Targets

Which other diseases are associated with PDE4D?





Open Targets

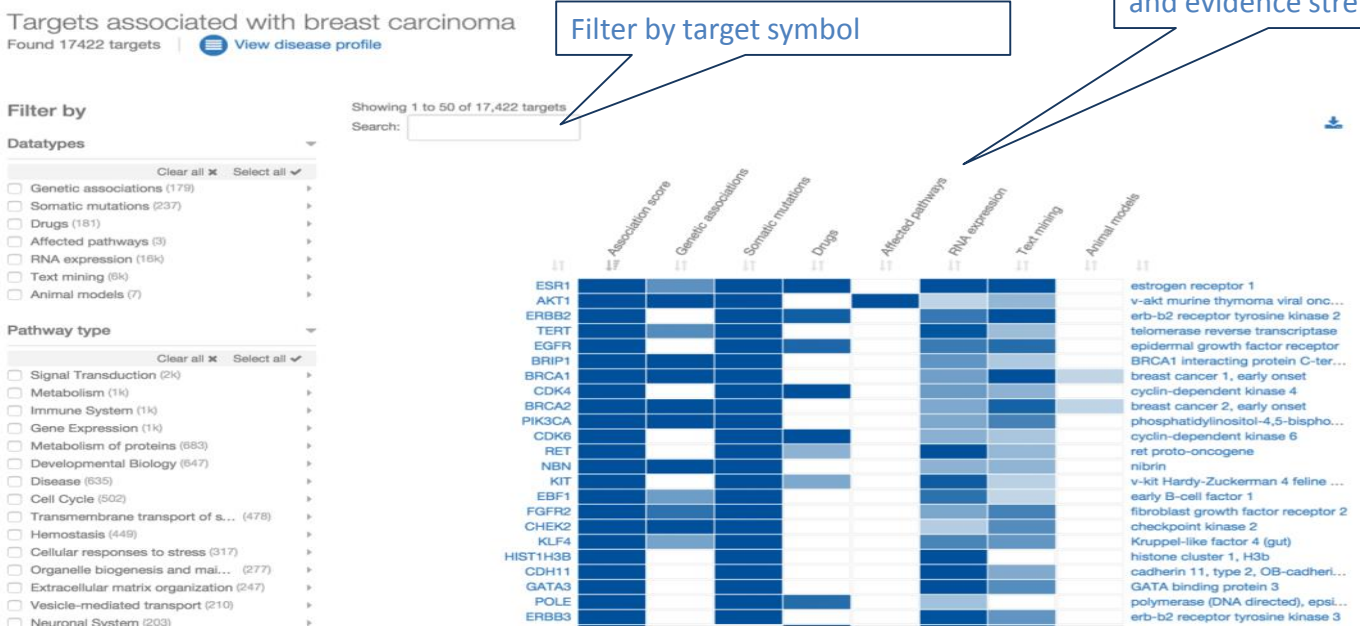
Which targets are associated with breast carcinoma?

Filter by evidence type: e.g. 237 targets are supported by somatic mutations

Filter by pathway type and particular pathways

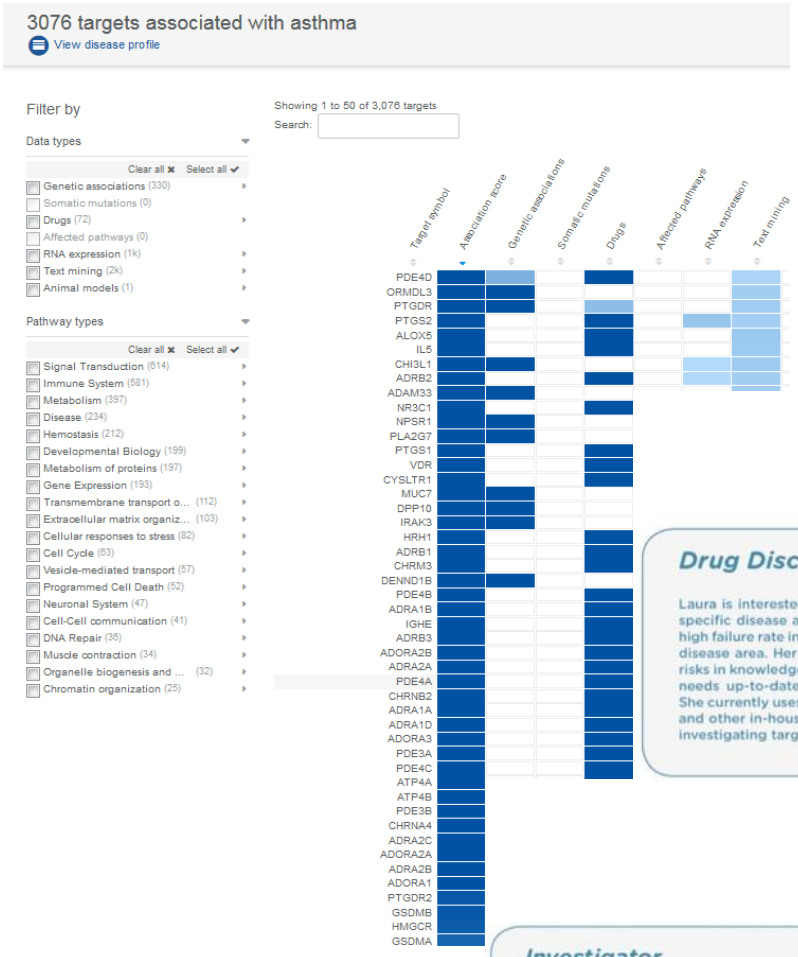
Filter by target symbol

Order by evidence type and evidence strength



Open Targets

A comprehensive and intuitive resource



Nick

Drug Discovery Head

Nick is a business decision maker.
He is concerned about the attrition rate prior to Phase III & believes correct target selection could be a key factor in addressing this. He would like to have more concrete target-disease evidence to include in his 3-year business plan; more evidence means less risk and increased confidence in target-disease associations.

Pulls lots of information together in an intuitive interface!

Laura

Drug Discovery Manager

Laura is interested in finding the best target for a specific disease area. She is concerned about the high failure rate in identifying targets for her team's disease area. Her team aims to investigate gaps & risks in knowledge about a particular target. Laura needs up-to-date information on several targets. She currently uses PubMed, some public databases and other in-house analysis pipelines and tools for investigating targets.

Powerful resource, clear links and easy to use without training, especially for a non-bioinformatician!

Derek

Investigator

Derek explores target space to find out what is already known about a target's role in his disease area of interest. Derek works in a matrix (multidisciplinary) team with scientists from genetics, computational biology, disease experts and clinical. He likes to work on a case-by-case examples of specific targets. It is not a large-scale approach, but rather detailed and focussed. Typically he accesses information by PubMed and uses Excel spreadsheets to analyse the data he collects. Derek occasionally uses bioinformatics database websites such as OMIM, UniProt, ChEMBL and Orphanet.

Lots of data in one place so saves time going to different websites. It's easy to go into more depth if needed as the data is all there!

Open Targets

Platform Development Acknowledgements

GWAS Catalog

Atlas

Phenodigm

Web production

Development

EBI Embassy Cloud

EBI Database Admin

Statistical Integration
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Jenny Cham, Francis Rowland Bren Vaughan

Jeff Barrett, Ewan Birney, Philippe Sanseau, Jessica Vamathevan, David Hulcoop, Holly Foster

100 GSK beta testers

Core platform development team


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ChuangKee Ong


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Eliseo Papa


Gareth Peat


Gautier Koscielny


Ian Dunham


Luca Fumis


Miguel Carmona


Miguel Pignatelli

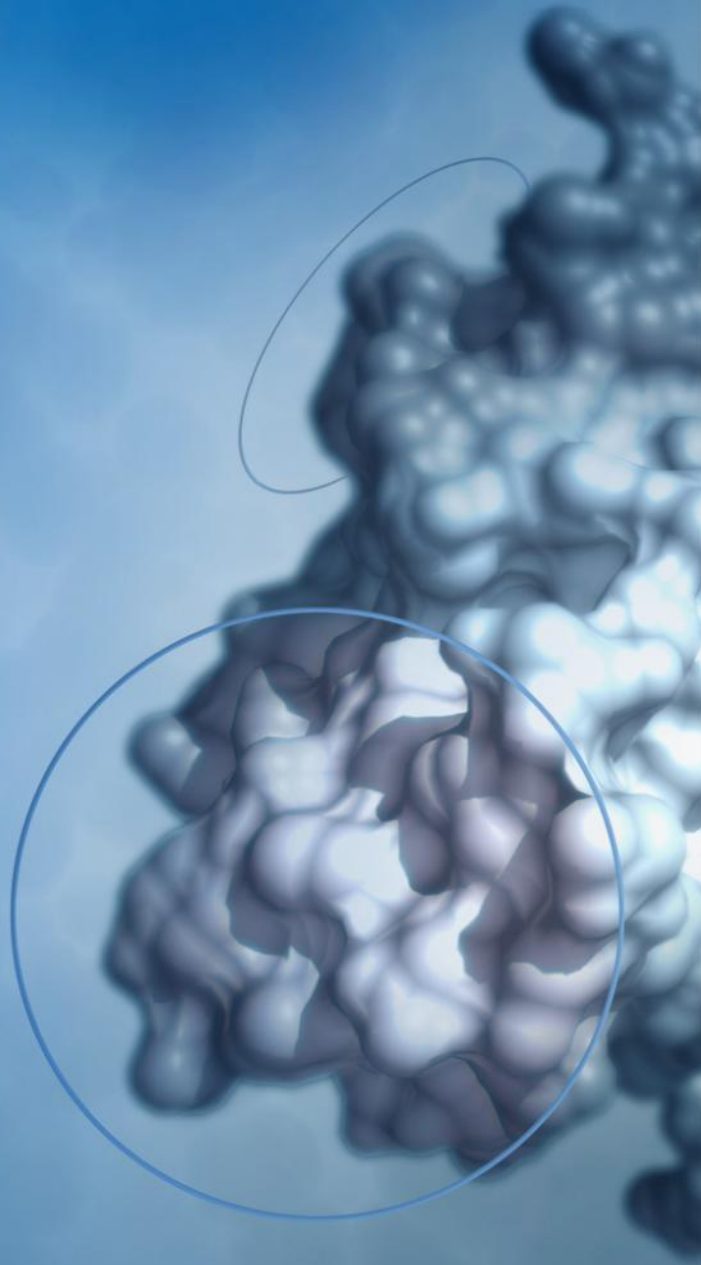

Naveen Kumar


Niki Karamanis


Priyanka Wankar


William Newell

Thank you



Open Targets

Nucleic Acids Research Database 2017

Open targets: a platform for therapeutic target identification and validation, NAR Database 2017, In Press

Open targets: a platform for therapeutic target identification and validation

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ABSTRACT

We have designed and developed a data integration and visualization platform that provides evidence about the association of known and potential drug targets with diseases. The platform is designed to support identification and prioritization of biological targets for follow-up. Each drug target is linked to a disease using integrated genome-wide data from a broad range of data sources. The platform provides either a target-centric workflow to identify diseases that may be associated with a specific target, or a disease-centric workflow to identify targets that may be associated with a specific disease. Users can easily transition between these target- and disease-centric workflows. The Open Targets Validation Platform is accessible at https://www.targetvalidation.org

INTRODUCTION

The fundamental tenet of pharmacology is that a drug (small molecule or biological) can be identified that specifically interacts with a target molecule (usually a protein) to modulate a physiological process and thus alter the course of a disease (1,2). The pharmaceutical industry has developed powerful approaches to discover and optimize drug molecules that affect the function of a target. There are also complex strategies in practice to deal with drug efficacy, dosing and safety issues that accompany getting a drug into humans and finally to market. However, analysis of progress through development pipelines has highlighted that lack of efficacy is a major cause of failure, particularly in the later, more expensive, clinical stages (3,4). The implication is that

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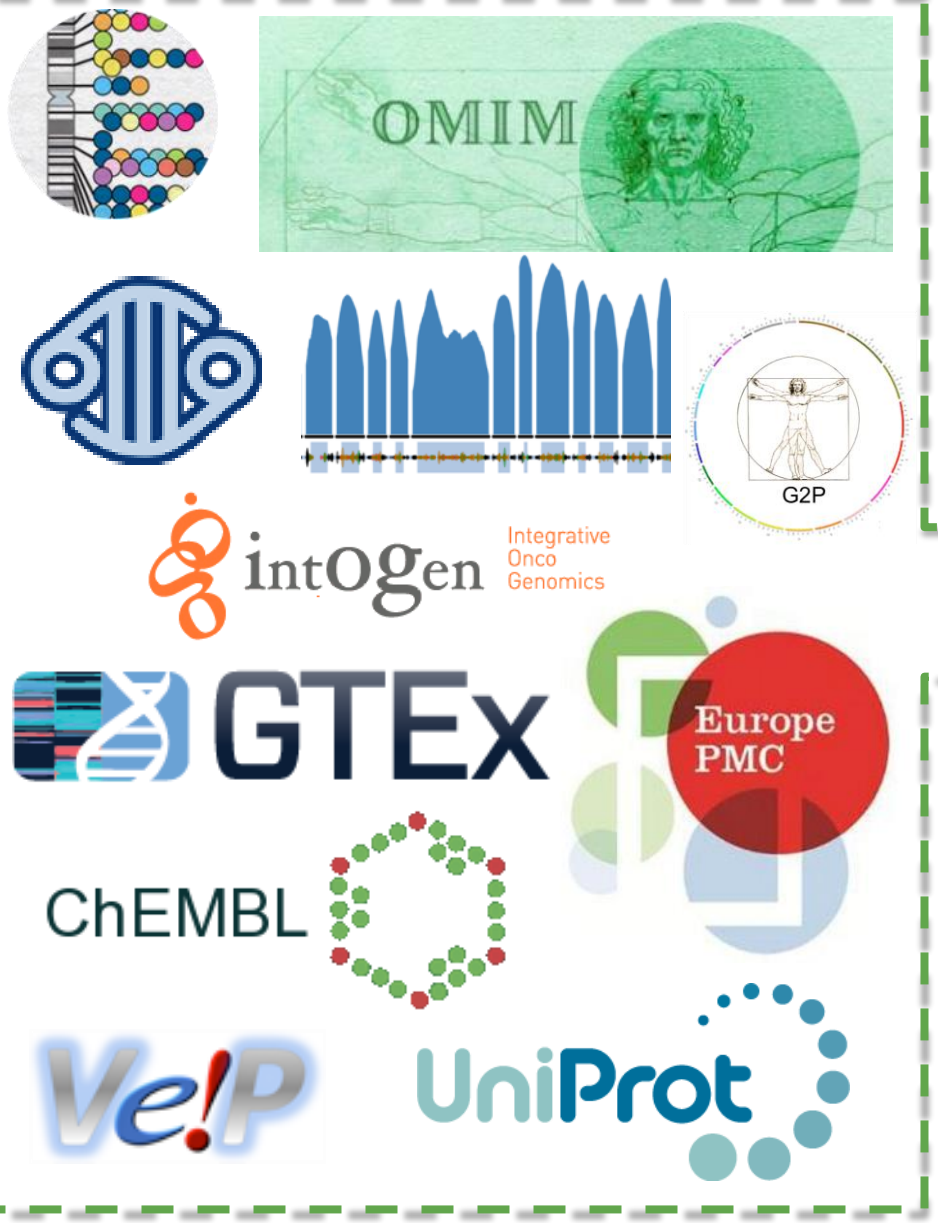
Open Targets

Comprehensive, robust data integration



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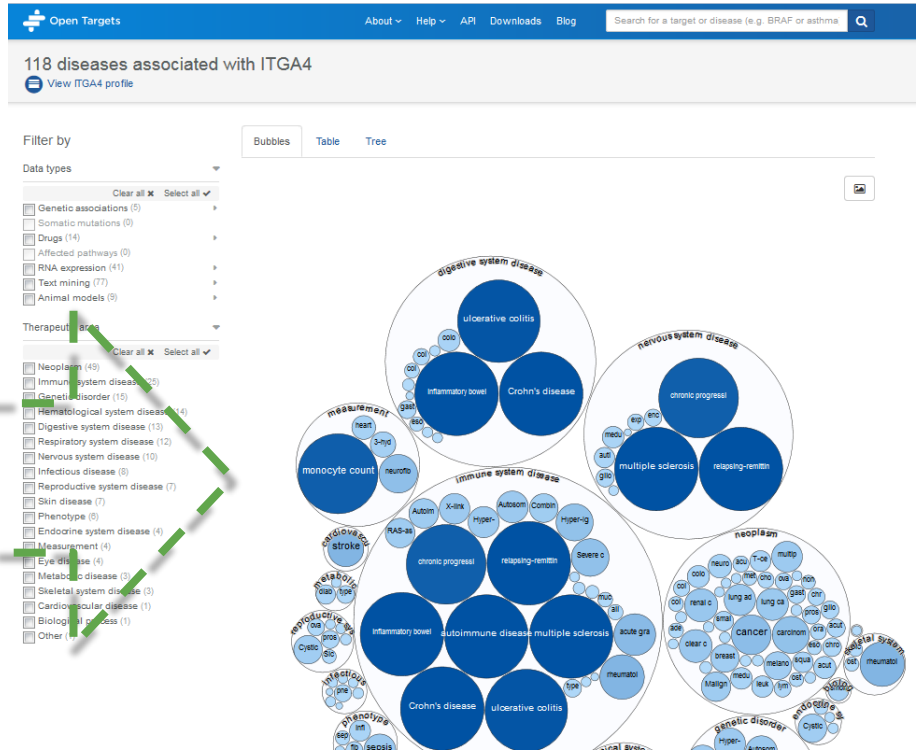

United data model, pathways, statistical integration

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