Mining Gene-Disease Associations with Open Targets

Part of “Bioinformatics for Discovery”

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Wellcome Genome Campus, United Kingdom
Open Targets Consortium
Core Bioinformatics team

Open Targets

Outline

- Drug Discovery and its the challenges
- The Open Targets Consortium
- The Open Targets Platform

Open Targets

Objectives for the next 30 minutes

What is the **Open Targets Consortium**?

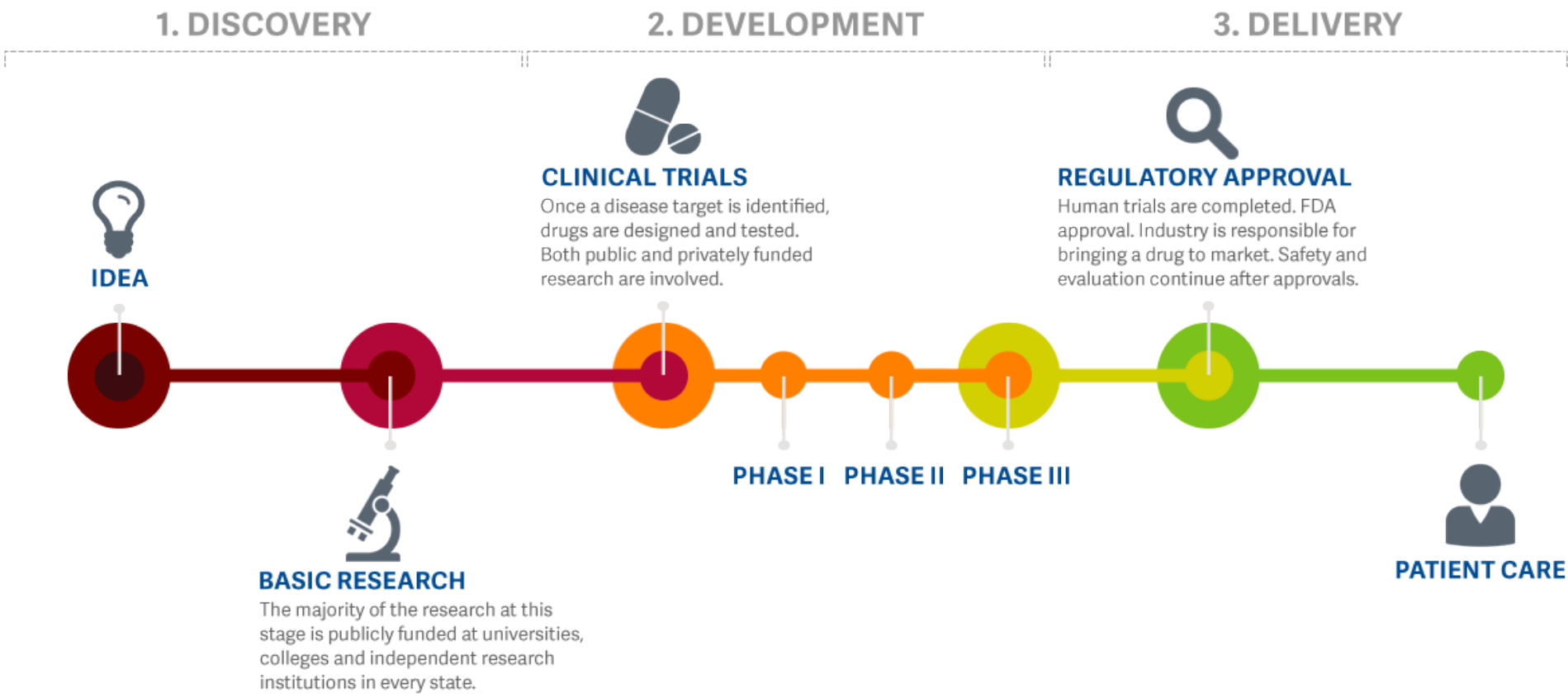
What is the **Open Targets Platform**?

How to **navigate** the Platform?

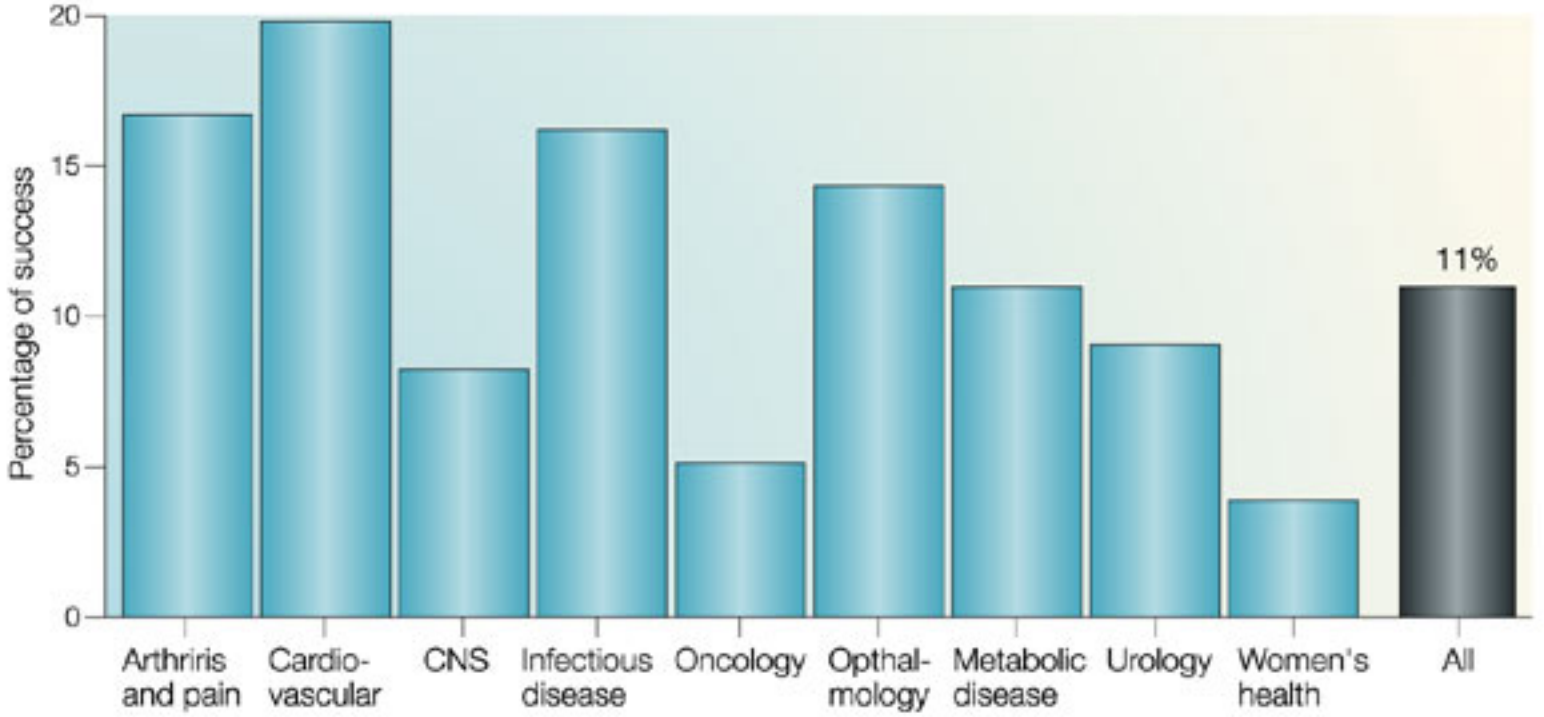
How to **connect** with us

Open Targets

Drug discovery path: timeline



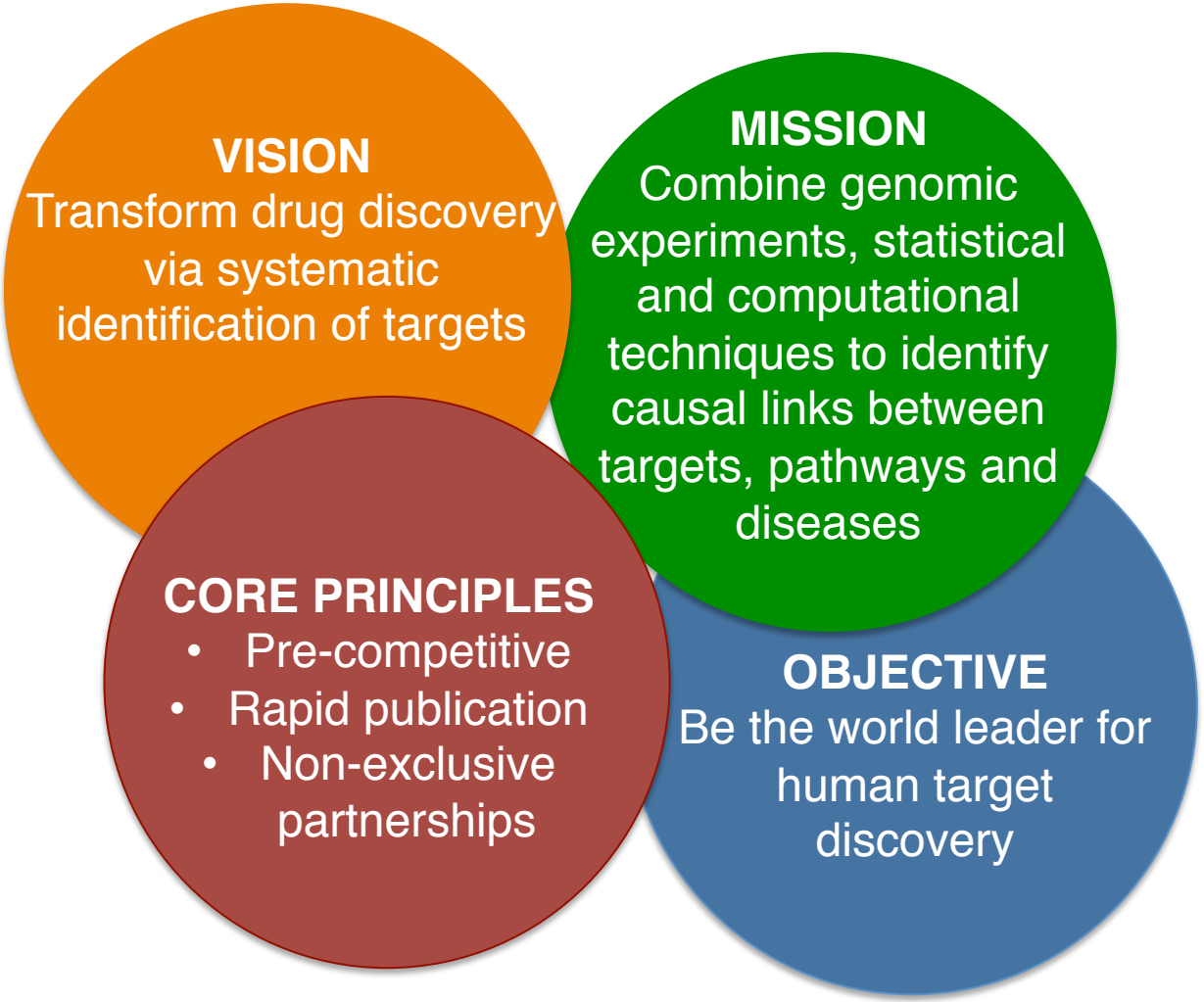
Drug discovery: the challenges



Lengthy, costly, low success rate, **HIGH ATTRITION RATES**

Source: doi:10.1038/nrd1470

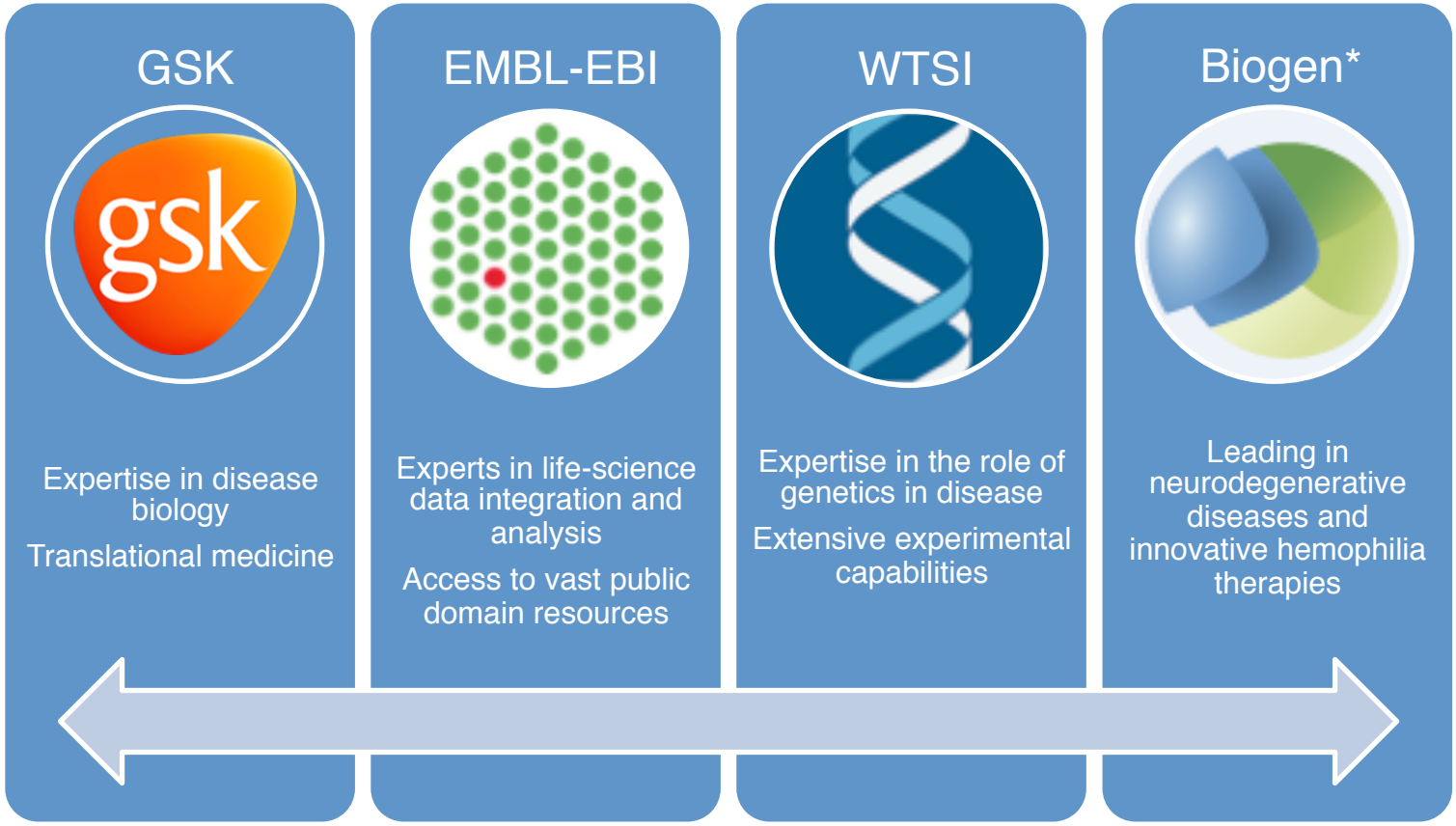
Open Targets Consortium*



* Launched in March 2014
Three founding partners

gsk wellcome trust sanger institute EMBL-EBI

Who is Open Targets?



***Biogen joined the consortium in February 2016**

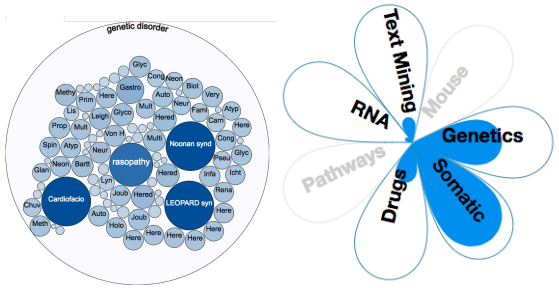
Open Targets

The two major areas of work* within Open Targets

Experimental projects

Generate new evidence
CRISPR/Cas9 and Organoids
(cellular disease models)

Core bioinformatics pipelines



Database for data integration
Web portal
REST API and data dumps

* Concurrent
www.opentargets.org/projects

Open Targets

The two major areas of work* within Open Targets

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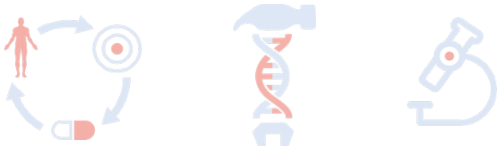

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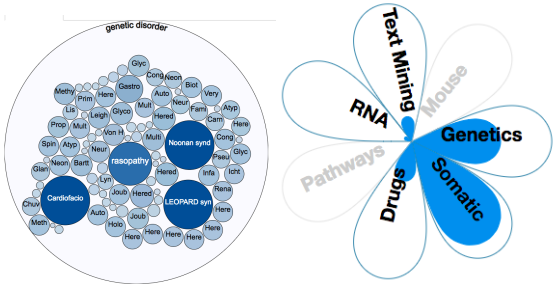

Database for data integration
Web portal
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* Concurrent

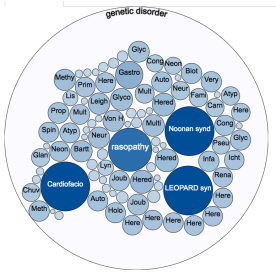
www.opentargets.org/projects

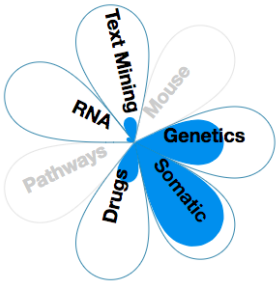
Open Targets

Open Targets Platform*

- Developed by the Core Bioinformatics team at EMBL-EBI
- Allow users to identify target–disease associations
- Improvements driven by you

https://www.targetvalidation.org/





* First release: December 2015

Open Targets

Currently: Integration of existing data

Public Databases and Pipelines

ChEMBL
UniProt
Europe PMC
REACTOME
IntAct
intOgen Integrative Onco Genomics
G2P

E
T
D

Open Targets Platform

Open Targets experimental data: NEW
Physiologically relevant and at scale

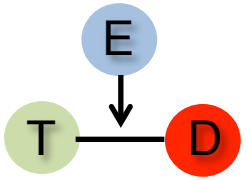
Oncology
Immunity
Neuro
Cross-Disease

Being generated as we speak

Open Targets

Evidence from publicly available data

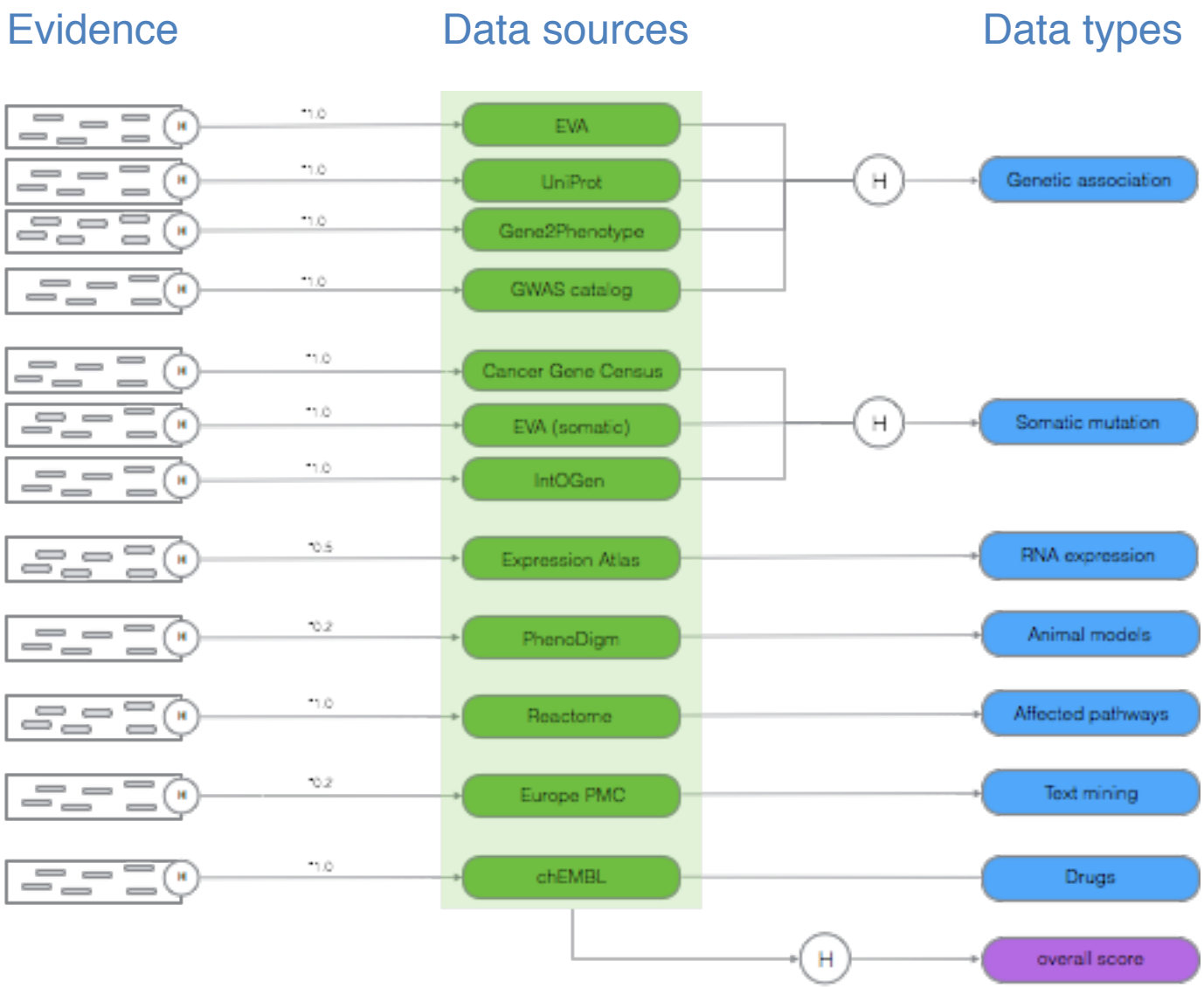
- Similar data sources are grouped into data types



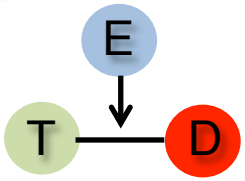
Data sources	Data types
GWAS catalog, UniProt, EVA, G2P	Genetic associations
Cancer Gene Census, EVA, IntOgen	Somatic mutations
Expression Atlas	RNA expression
ChEMBL	Drugs
Reactome	Affected pathways
Europe PMC	Text mining
PhenoDigm	Animal models
Your favourite data?	**Let us know!**

Open Targets

Confidence score



Its allow for replication and deflates the effect of large amounts of data



We support decision-making

B) What evidence supports this target-disease association?

C) Are there FDA drugs for this association?

A) Which targets are associated with a disease?

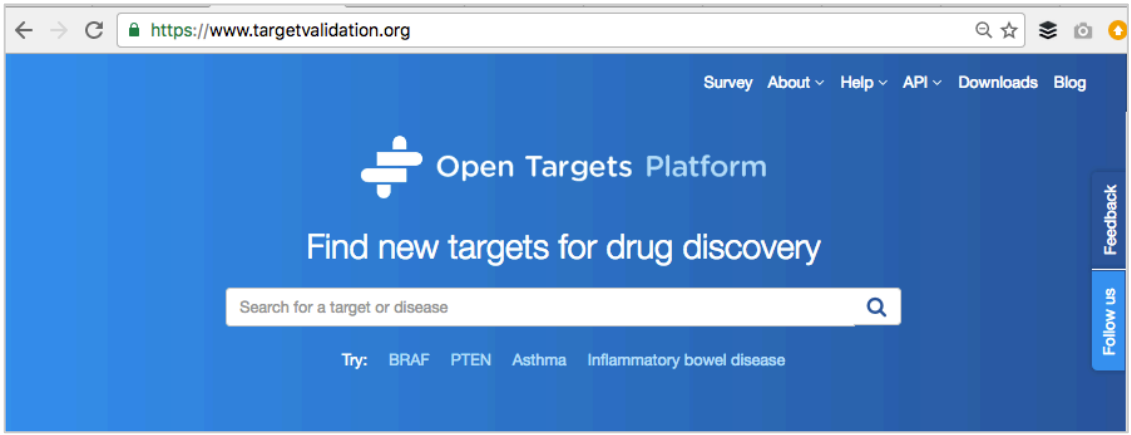
D) For a target, are there other diseases associated with it?

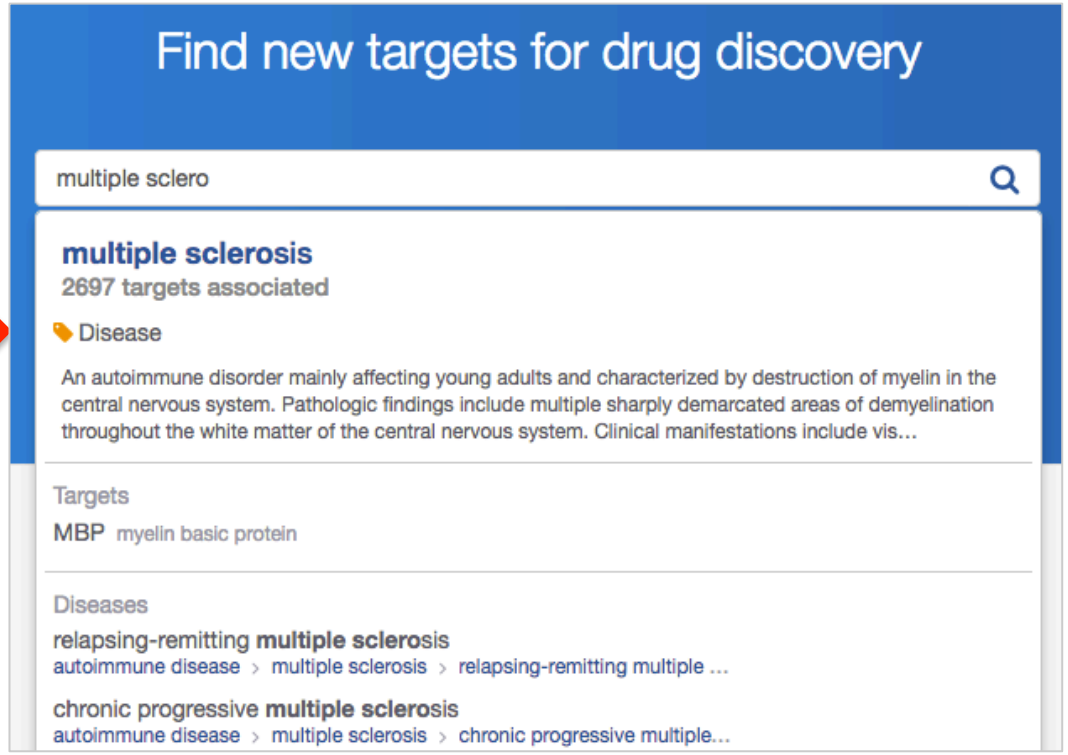
G) Can I find out about the mechanisms of the disease?

E) If so, can I get associations for diseases from different therapeutic areas?

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

Which targets are associated with a disease?

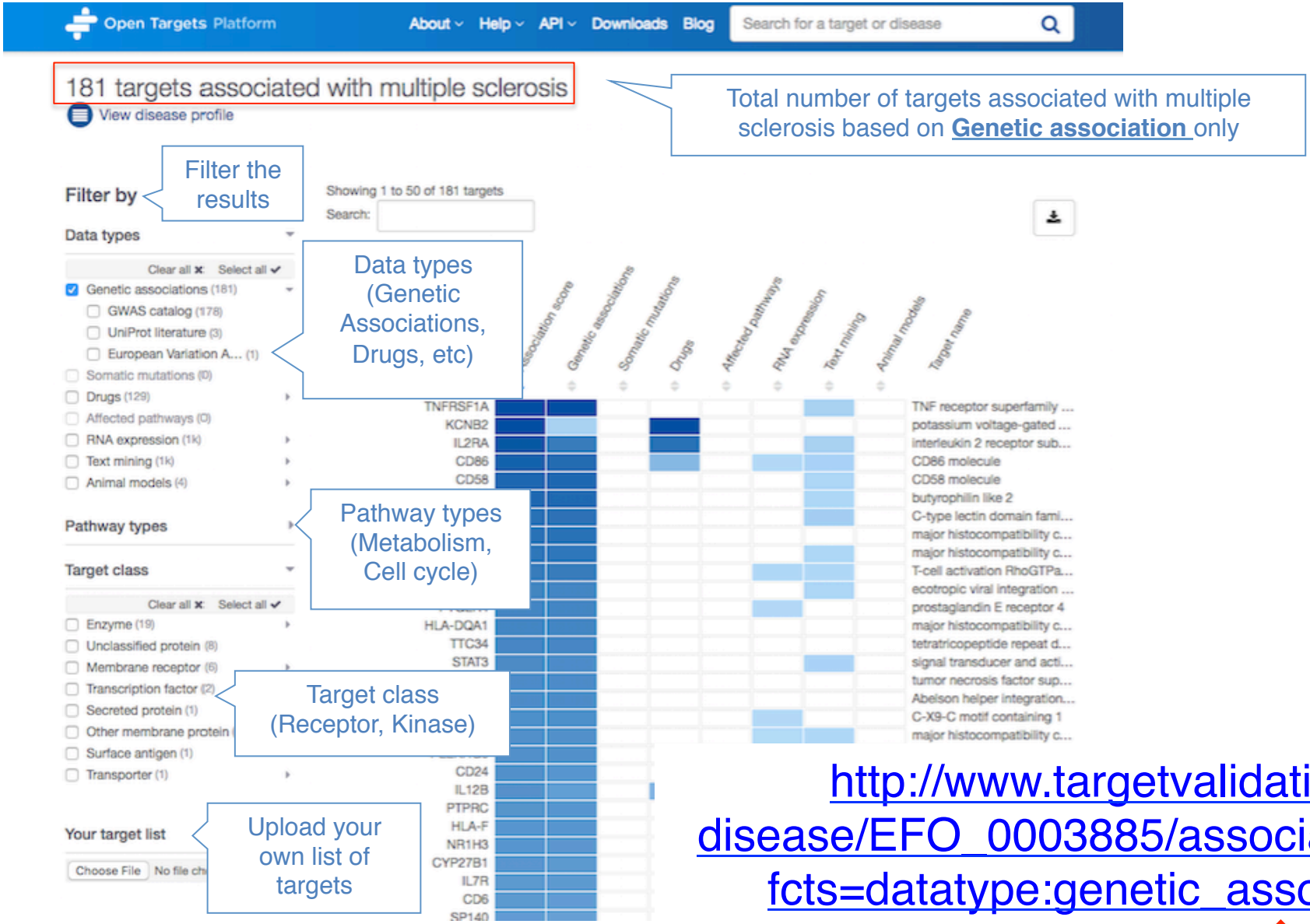




Demo 1:

screenshots: next slides
coursebook: pages 9 - 15

https://www.targetvalidation.org/



http://www.targetvalidation.org/disease/EFO_0003885/associations?fcts=datatype:genetic_association

http://www.targetvalidation.org/disease/EFO_0003885

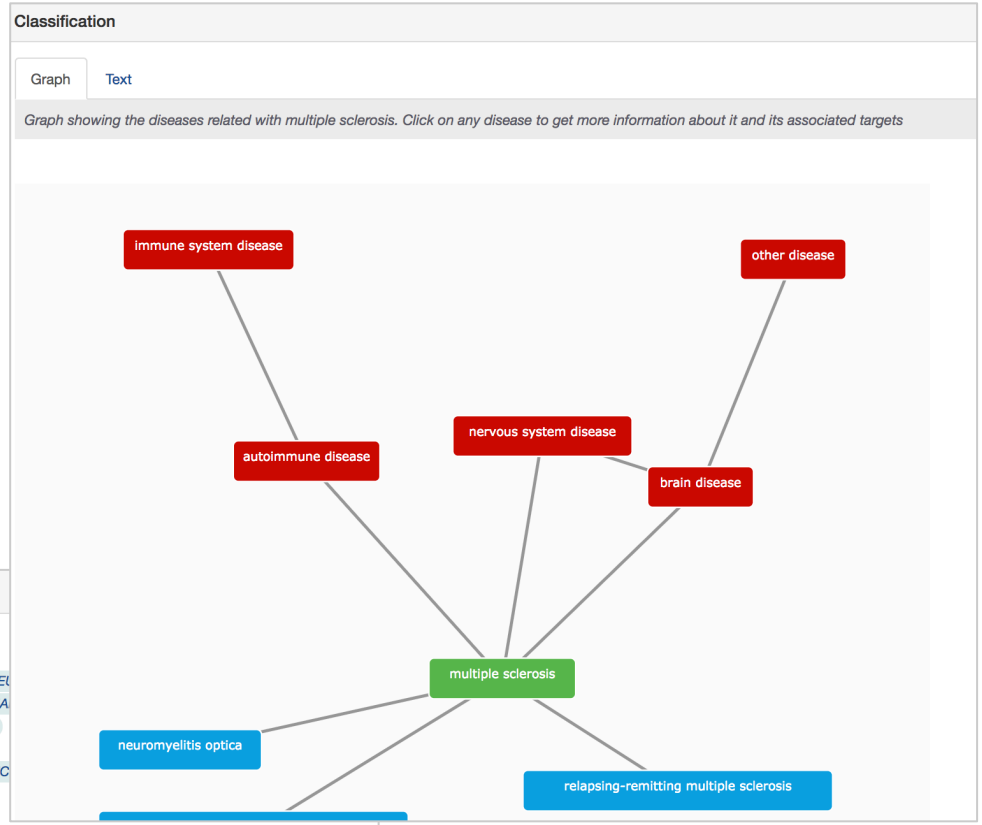
2697 targets associated with multiple sclerosis

View disease profile

Phenotypes

Drugs

Disease Classification



Drugs

Source: CHEMBL

Found 40 unique drugs: ABATACEPT ALEMTUZUMAB BACLOFEN BOTULINUM TOXIN TYPE A PURIFIED NEU CORTICOTROPIN DACLIZUMAB DALFAMPRIDINE DEXTROAMPHETAMINE DICLOFENAC DIMETHYL FUMA FINGOLIMOD GSK239512 HYDROXYUREA INTERFERON BETA-1A INTERFERON BETA-1B LAMOTRIGINE METHYLPHENIDATE METHYLPREDNISOLONE MIRABEGRON MITOXANTRONE MYCOPHENOLATE MOFETIL OCRELIZUMAB OXCARBAZEPINE PEGINTERFERON BETA-1A PREDNISOLONE PREDNISOLONE PHOSPHORIC RITUXIMAB SIMVASTATIN Siponimod TERIFLUNOMIDE

Showing 1 to 10 of 1,000 entries

Search:

	Drug Information						Gene-Drug Evidence	
Disease	Drug	Phase	Status	Type	Mechanism of action	Activity	Target class	Evidence source
relapsing-remitting multiple sclerosis	INTERFERON BETA-1A	Phase IV	Completed	Protein	Interferon alpha/beta receptor agonist 1 publication DailyMed	agonist	Membrane receptor	Curated from Clinical Trials Information

Coming up: 13:30-14:30 tomorrow

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What is the **Open Targets Platform**?

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