Oxford Rare Disease Initiative

UNIVERSITY OF OXFORD

What's unique about the Oxford ecosystem

- >250 basic and clinical scientists working on >350 rare diseases
- Commitment to open access/ science crowdsourcing, innovation, reproducibility and rapid translation into patients
- Track record in generating early reagents and novel tools for drug discovery
- Access to World-leading functional genomics and thousands of on-demand mouse knock-outs
- Close partnerships with industry enabling access to clinical molecules
- International network of clinicians
- Transformative approach to working with patient and disease foundations

Oxford Rare Disease Initiative

- Founded in 2012 in response to increased industry interest in rare diseases
- Main objective is to connect Oxford's researchers and provide networking opportunities
- Led by a scientific working group and supported by Business Development


Dame Kay Davies


Matthew Woods


Frances Platt


Jenny Taylor


Chas Bountra

Oxford Rare Disease Initiative

Three Pronged Approach

Internal Communications
- Email list comprising of all rare disease researchers in Oxford

External Communications
- Website

Networking and Showcases
- Oxford Rare Disease Conference
- Exhibiting at international conferences and trade shows
- Hosting networking events at Oxford

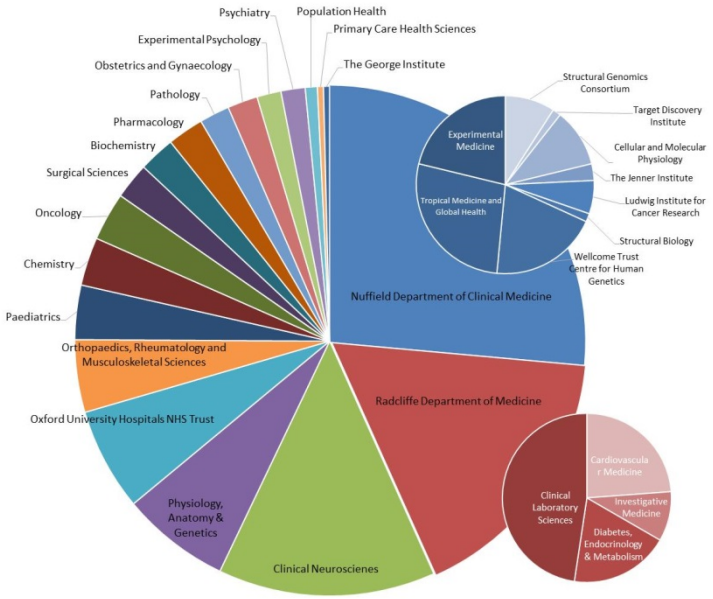
Oxford Research Database

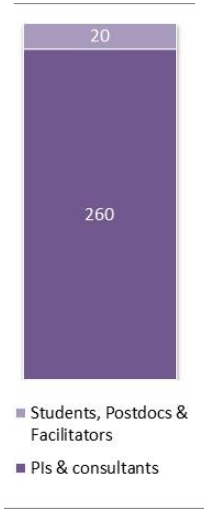
Industry Research Database

Industry Contacts Database

Internal Communications and Oxford Research Database

Network of more than 250 researchers across the University and the Oxford University Hospitals Trust





Research Database

Data source

- GMEC Questionnaire 2012
- ORDI Questionnaire 2014

134 Researchers – 308 rare diseases

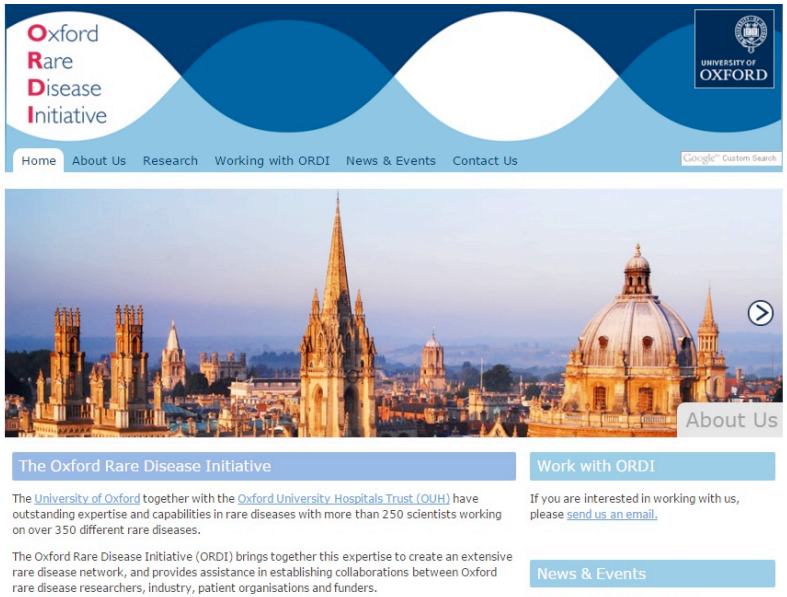
Challenges

- Incomplete
- Regular Updates

External Communications

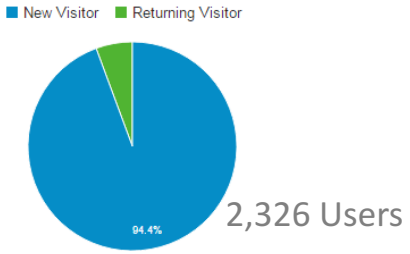
www.rarediseases.ox.ac.uk

- Provides information on Oxford's rare disease community and how to work with us
- Has over 2,000 users



Challenges

- Small percentage of returning users



Industry Engagement

Funding Calls

Company	EoI	1-2-1	Project Plan	Contracting	Signed
2 x Pfizer	35	22	7	1	4
1x Genzyme	16		2	1	
1x GW Pharmaceuticals	11	6			

Muscular Dystrophies


Matthew Wood, Kay Davies

FA Consortium

Michele Lufino

Haematological Disorders


Hal Drakesmith, Simon Draper

Friedreich Ataxia

Wyatt Yue

£ 3m

Gene Therapy


Deb Gill, Steve Hyde

£ 0.8 m

Industry Engagement

Early Discussions

Company	Interaction
Pfizer	3rd Funding Call
Alexion	Umbrella Agreement
Roche	Early Partnering
Novartis	Project Specific

Company	Interaction
Silence Therapeutics	Project Specific
Kyowa Hakko Kirin	Funding Call
Takeda	Repositioning
AstraZeneca	Repositioning

NETWORKING AND SHOWCASES

Oxford Rare Disease Conference 2015

150 attendees
15 companies
7 universities
11 patient and funding organisations

~ 30 talks, one-to-one meetings, poster presentations, networking sessions

World Orphan Drug Congress Europe 2014 and 2015

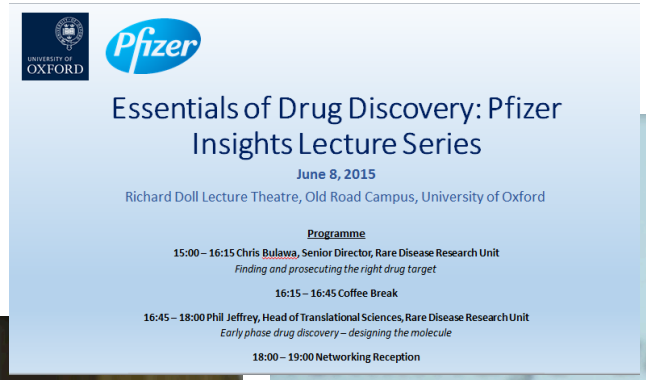
~ 500 representatives from industry, patient organisations and funders

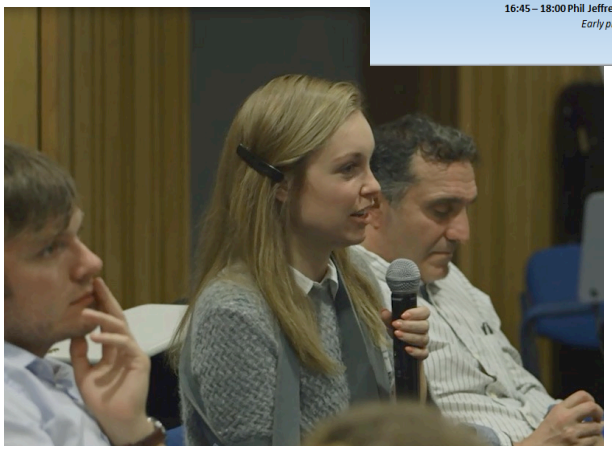
15th Annual Biotech in Europe Forum

NETWORKING AND SHOWCASES

Essential Drug Discovery Pfizer Insights Lecture Series

160 attendees
140 students, postdocs
20 PIs, Business Development, OUI, research facilitators





Access to on-demand creation of mouse knock-out/ CRISPR models

Member of the International Mouse Phenotyping Consortium (IMPC)

- IMPC has been set-up to undertake broad-based phenotyping of 20,000 mutants by 2021; IMPC coordinates several mouse centres worldwide
- In addition to on-demand knock-out mouse models (IMPC), the MRC Harwell Centre also conducts mouse-based, large-scale functional genomics efforts such as the Ageing Screen and CRISPR/Cas9 platform to generate mutant mice.

Dept. of Health-funded biomedical research centres bring significant added value

BRCs fund NHS-University partnerships to translate discovery science into clinical innovations

Oxford University Hospitals NHS
NHS Foundation Trust

Existing BRC

Neurology
Lead:Husain
Imaging
co-lead: Jezzard

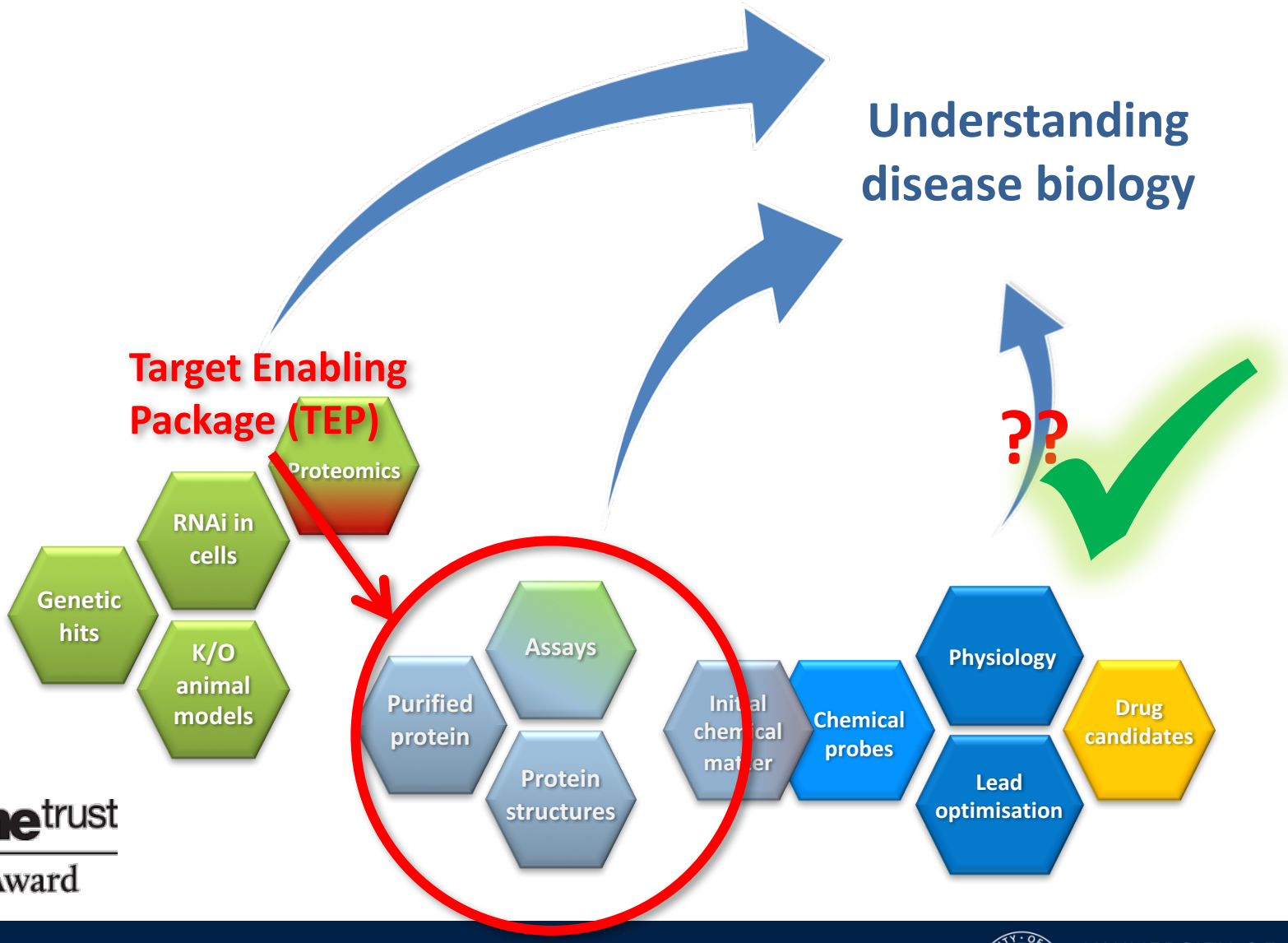
Oxford Health NHS
NHS Foundation Trust

New Mental Health BRC

Adult mental health
Lead: Harrison
Dementia
Lead:Mackay
Imaging and cognition
Lead:Nobre

~£25million for patient-facing translational neuroscience research

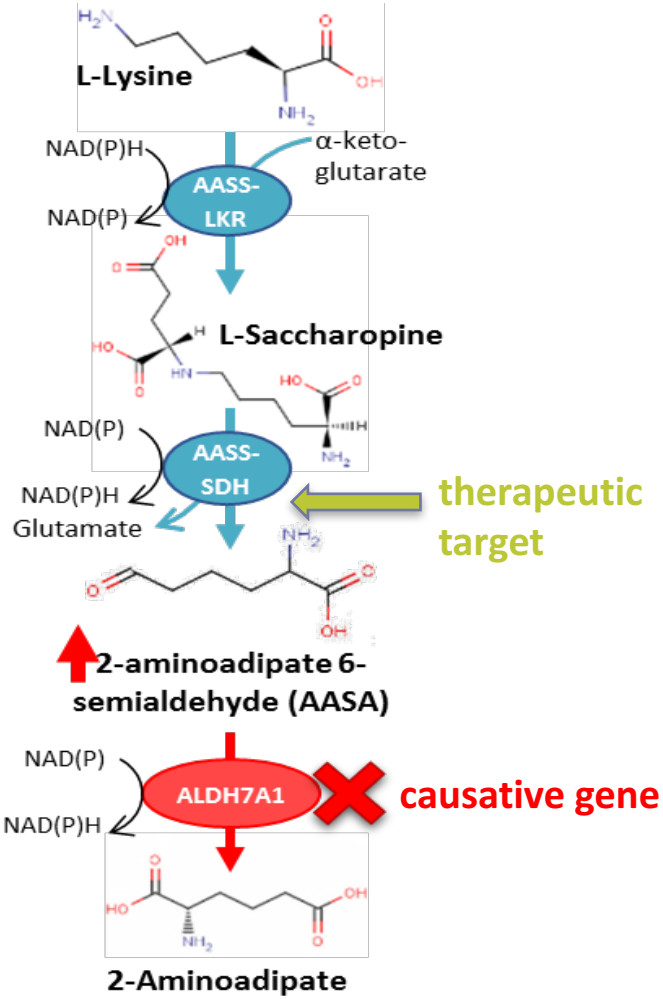
Open Access Tools to accelerate novel therapeutics

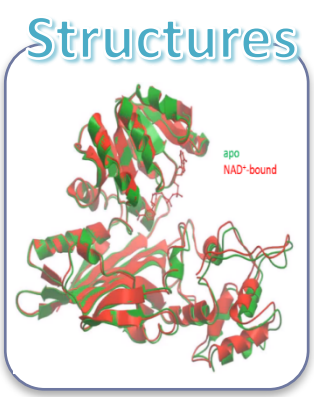


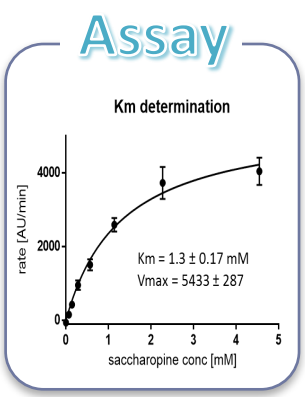
wellcome trust
Strategic Award

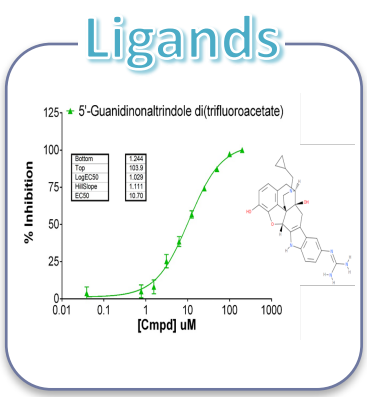
...FOR A RARE METABOLIC DISEASE

- Mutations of ALDH7A1 cause the rare disease ***Pyridoxine dependent epilepsy***
- knock-down of upstream *AASS* reduced ALDH7A1 substrate level and rescued survival of patient fibroblast cells
- Hence inhibiting AASS enzyme may be an avenue for substrate reduction therapy
- Data package for AASS to catalyse drug discovery









UNICAMP

Paulo Arruda
Izabella Pena

Wyatt Yue

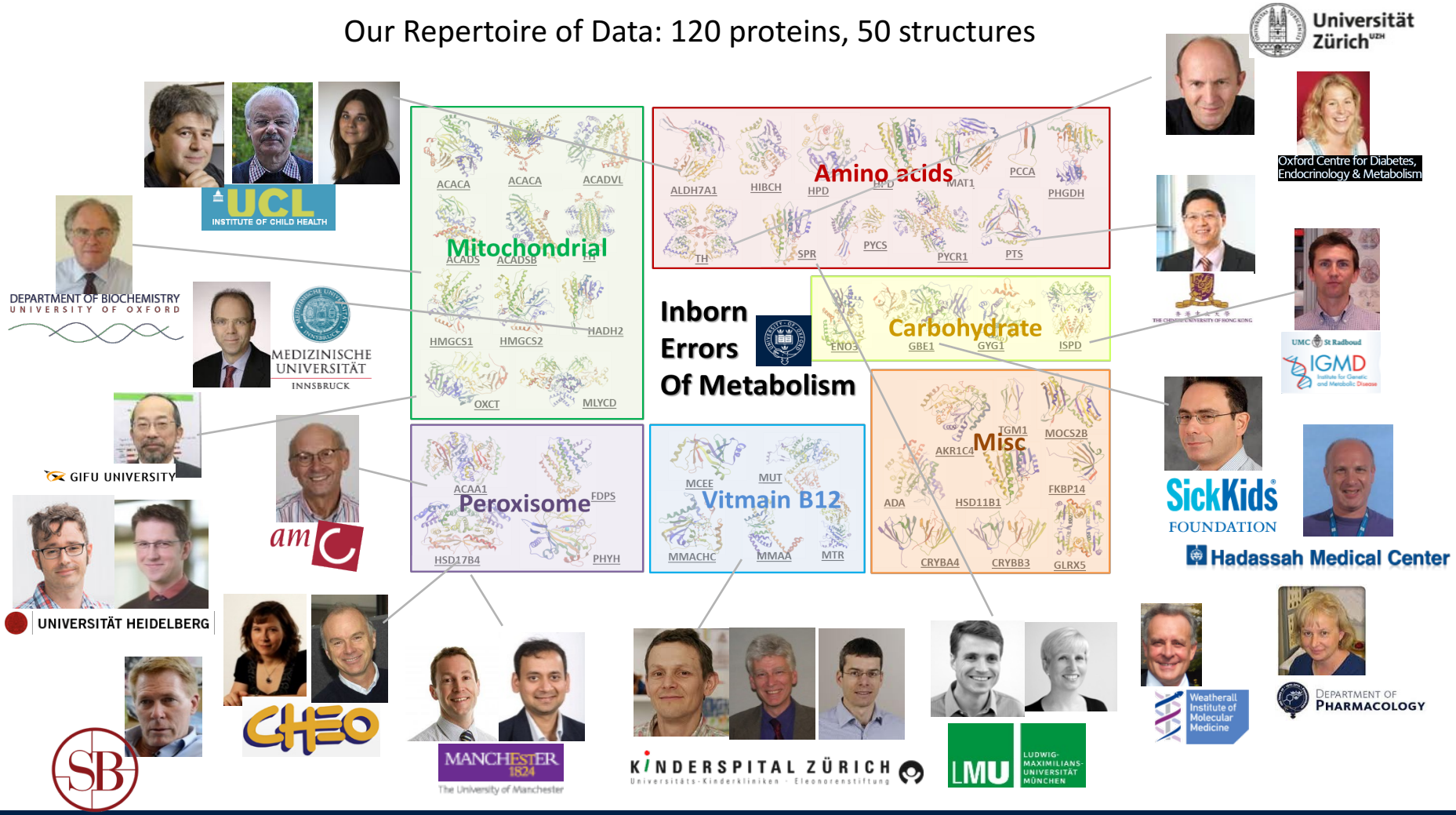
UNIVERSITY OF OXFORD

EFFECTIVE CLINICIAN PARTNERSHIP FOR RARE METABOLIC DISEASES

BIMDG British Inherited Metabolic Disease Group

SSIEM SOCIETY FOR THE STUDY OF INBORN ERRORS OF METABOLISM

Our Repertoire of Data: 120 proteins, 50 structures



EXAMPLE OF IMPACT

Disorders in Vitamin B_{12} Cofactor Processing

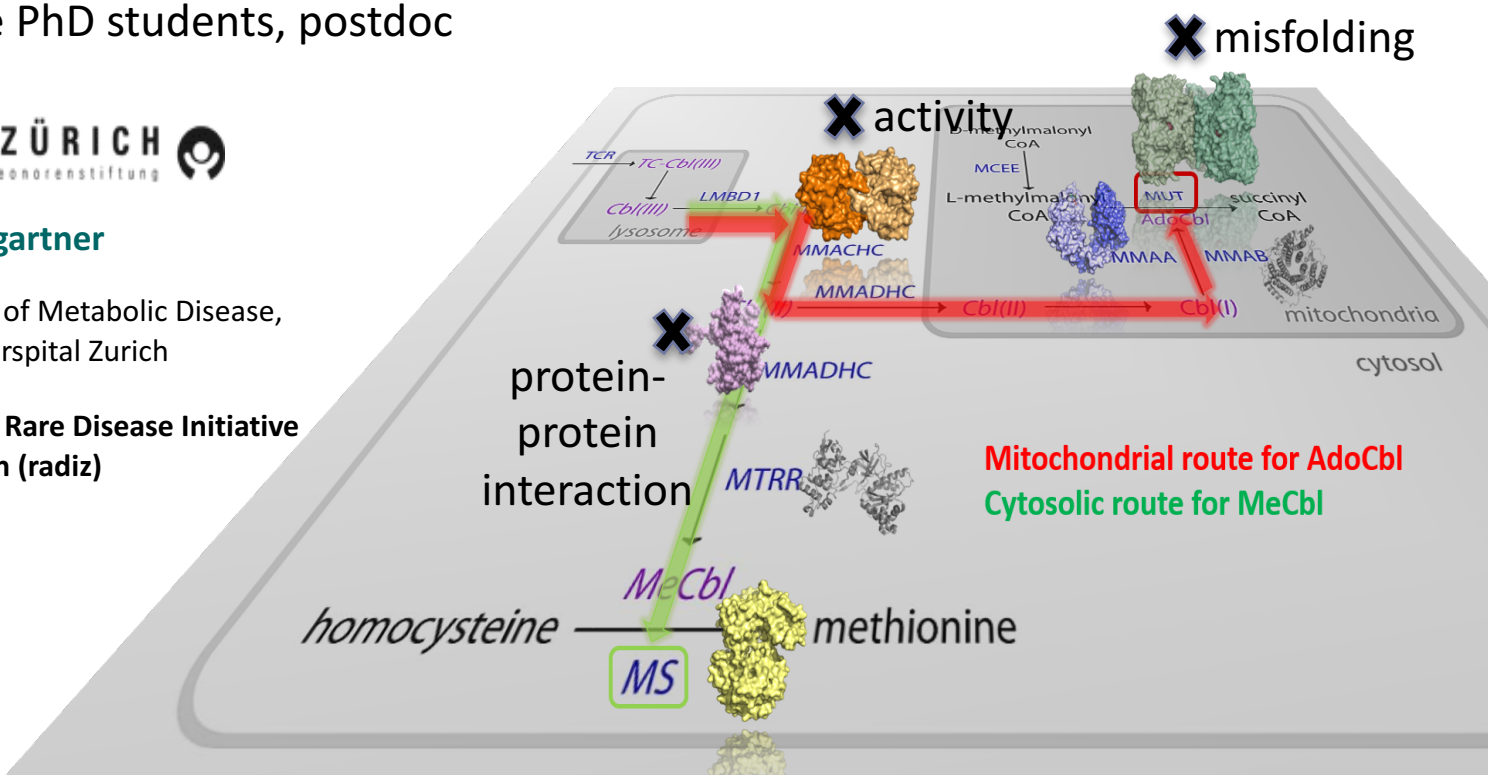
- From biochemical/structural studies to mouse model
- Catagorized mutations via recombinant proteins & patient cells
- 6 crystal structures, 4 publications
- 2 collaborative PhD students, postdoc

KINDERSPITAL ZÜRICH
Universitäts-Kinderkliniken · Eleonorenstiftung

Matthias Baumgartner

Head of Metabolic Disease, Kinderspital Zurich

Lead, **Rare Disease Initiative Zurich (radiz)**



Fibrodysplasia Ossificans Progressiva (FOP):

Fast translation from gene to clinical candidate **in the Open**

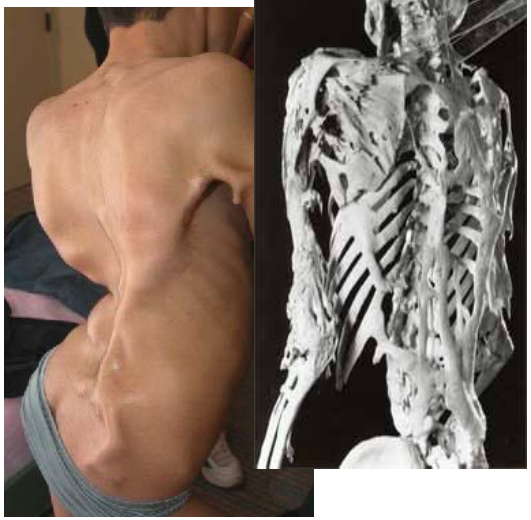
Gene → Mechanism → Pre-clinical → Clinical candidate

Apr 2006

Gene causing FOP was discovered

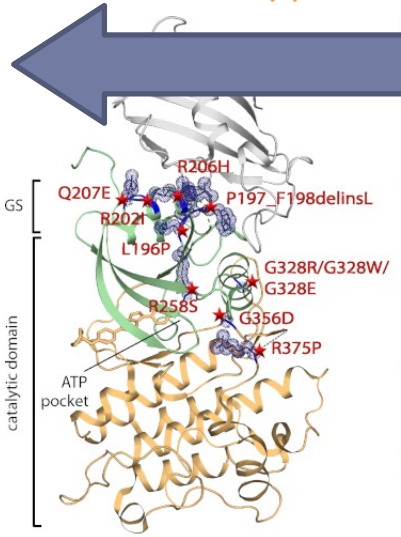
A recurrent mutation in the BMP type I receptor ACVR1 causes inherited and sporadic fibrodysplasia ossificans progressiva

nature genetics



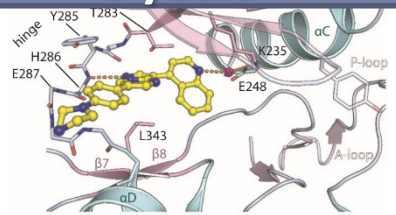
Apr 2009

Structure solved; mutations mapped

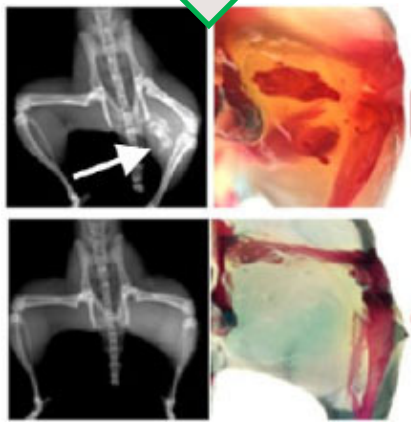


2012-2013

New tool compounds & animal models

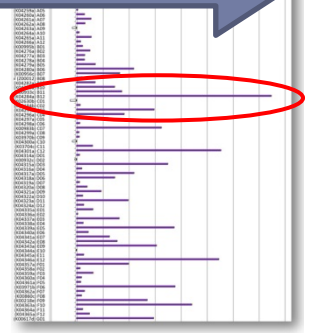


Tool compounds



2015

Clinical study being designed



Potent and selective

6 years

I'MPATIENT

Open access enabling early-stage drug discovery by patient & disease foundations

Wen Hwa Lee

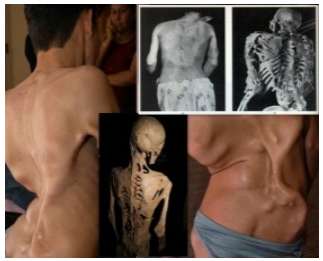
UNIVERSITY OF OXFORD

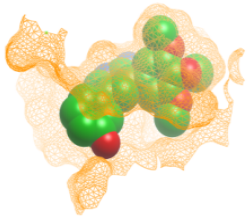
I'MPATIENT PROGRAMME PARTNERSHIPS

Heterotopic ossification FOP

fopaction
Fibrodysplasia Ossificans Progressiva

Friends of Oliver

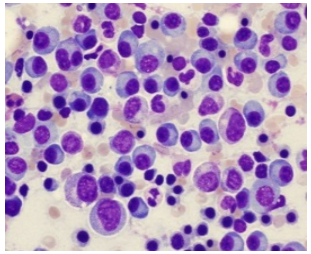




Ultra-rare disease
No treatment
SGC co-dev. compounds.
assays & models

Multiple Myeloma

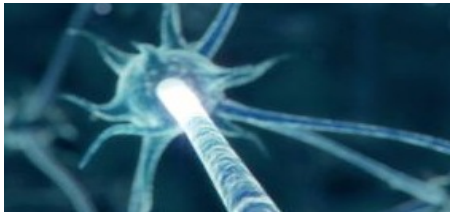
MyelomaUK



Identify novel targets for new treatments
Myeloma UK already established Translational Research Programme & Clinical Trials Network

Brain Tumour Charity

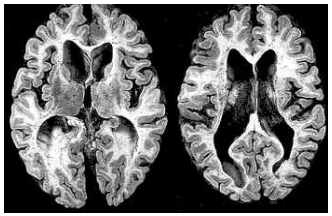
The BRAIN TUMOUR CHARITY



Novel tissue platform and follow-up med chem to generate open clinical compounds for DIPG

Huntington's Disease

CHDI FOUNDATION
Accelerating therapeutic development for Huntington's disease



Role of epigenetic regulation in HD
Novel proteins and strategies identified by CHDI network (eg. clearance, DNA repair, autophagy, energetics)

How can RE(ACT)x Switzerland and Oxford deliver for patients, **QUICKLY** ?

- **2017: Oxford Rare Disease Conference**
- **5 year: 5 completed patient studies**
- **10 year: 20 completed patient studies**

SUGGESTED NEXT STEPS

- Build a taskforce to exploit clinical and patient networks, academic and industrial resources
- Select 10 candidate targets to work up
- Leverage appropriate resources (e.g. target, asset, patient, clinician)