Biogen Idec and Collaborative Brain Research

Dominic Paes PhD

EU Medical Sciences, Neurology

Zug, Switzerland

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AREAS OF HIGH UNMET MEDICAL NEED

NEUROLOGY

MS - Repair / Progressive Forms

Neuropathic pain

Dementias

Alzheimer's disease

Neuromuscular

SMA; ALS; DMPK

Movement Disorders

Parkinson's & Huntington's diseases; Ataxias

IMMUNOLOGY

Autoimmune

SLE; Lupus nephritis; IBD; Sjogren's; Severe asthma; Severe atopic dermatitis

Fibrosis and Tissue Injury

IPF
Liver & renal fibrosis
Scleroderma

HEMATOLOGY

Hemophilias

A & B
Hemophilia with inhibitors

Hemoglobinopathies

Sickle cell
Thalassemia

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SCIENCE DAY
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Collaborative Programs with Other Partners in Industry

Alzheimer's Disease

- Anti-amyloid and anti-tau projects with Neurimmune Therapeutics / Zurich University

- Two development projects with Eisai Co., Ltd

ALS

- Anti-TDP-43 with Neurimmune Therapeutics

Spinal Muscular Atrophy (SMA)
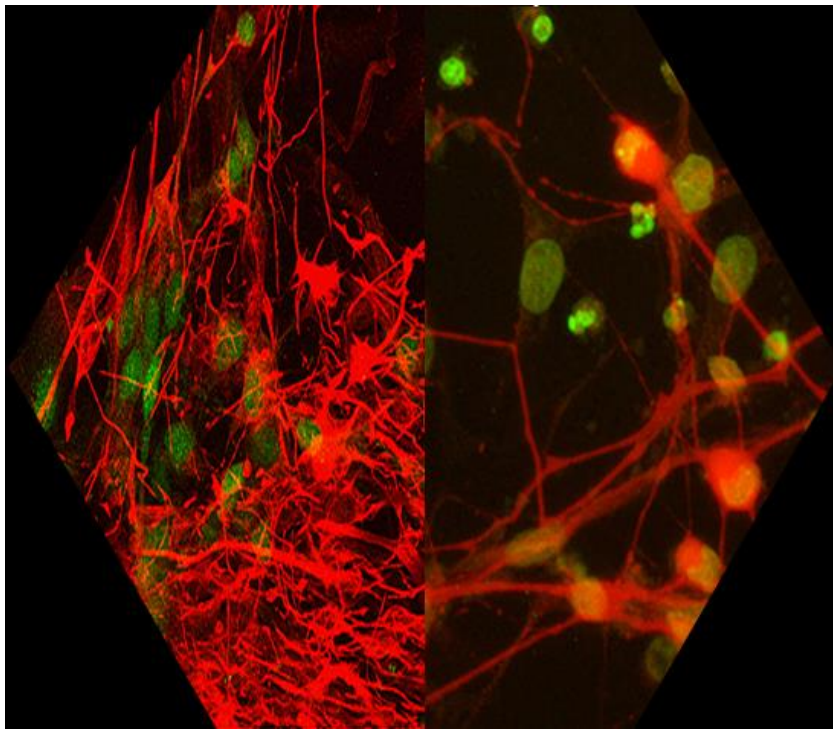
- Anti-sense therapy with Isis Pharmaceuticals

Myotonic Dystrophy

- Antisense therapy with Isis Pharmaceuticals

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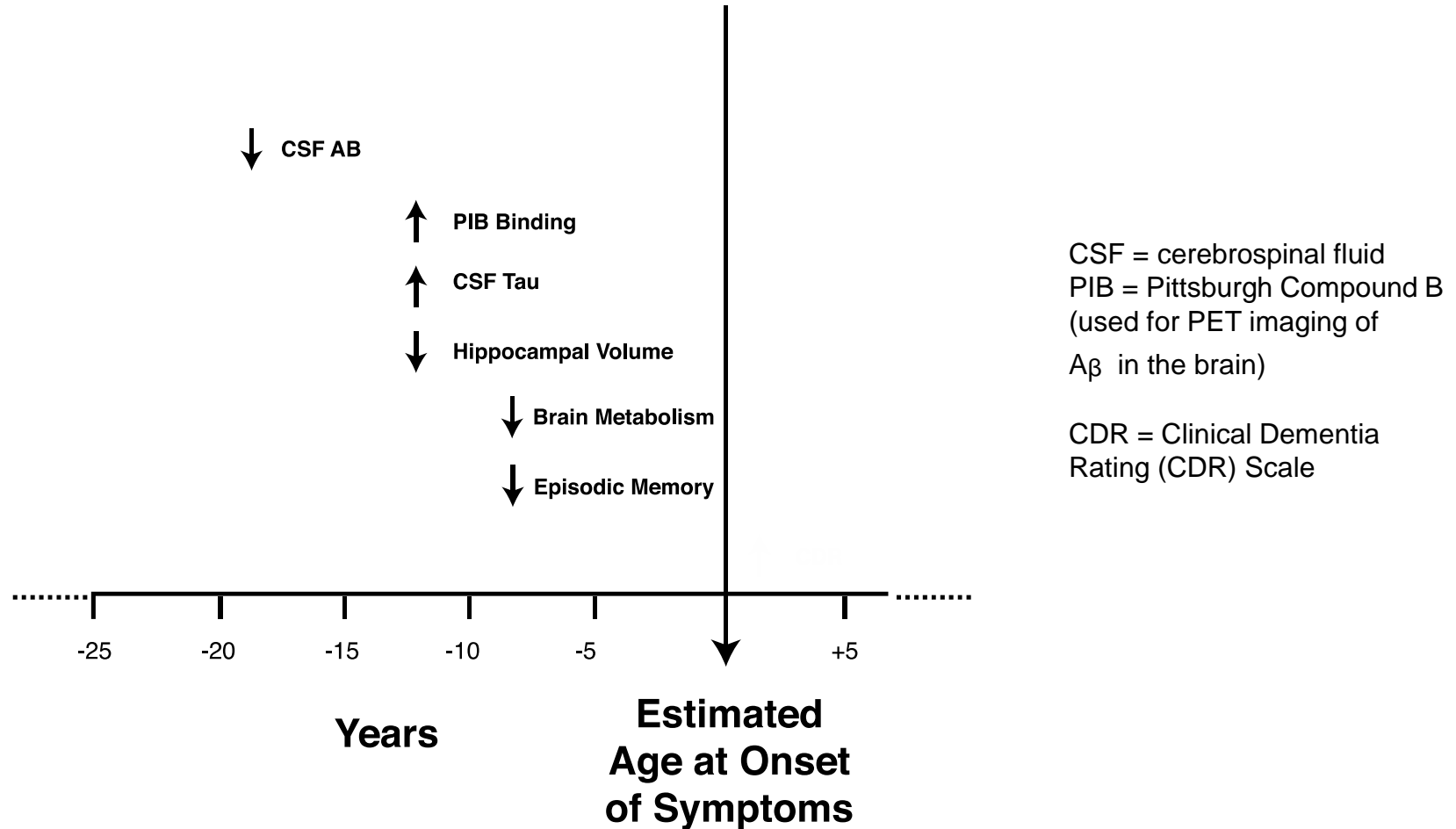# Recent Success with Academia/Industry Collaboration to Address ALS

- Collaboration between Biogen Idec, Columbia University Medical Center and HudsonAlpha Institute for Biotechnology which started 3.5 years ago. A great model of collaboration in a complex project!

- Scientists and Clinicians have identified a new gene TBK1(TANK-Binding Kinase 1) involved with disease pathogenesis

ALS motor

neurons

Normal motor

neurons

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The AD Disease Process May Begin >20 Years Before Dementia Symptoms

CSF AB

PIB Binding

CSF Tau

Hippocampal Volume

Brain Metabolism

Episodic Memory

-25   -20   -15   -10   -5   +5

Years

**Estimated
Age at Onset
of Symptoms**

CSF = cerebrospinal fluid
PIB = Pittsburgh Compound B
(used for PET imaging of

Aβ in the brain)

CDR = Clinical Dementia
Rating (CDR) Scale

Natural History of Normal Cognitive Aging and Dementia

Cognitive function
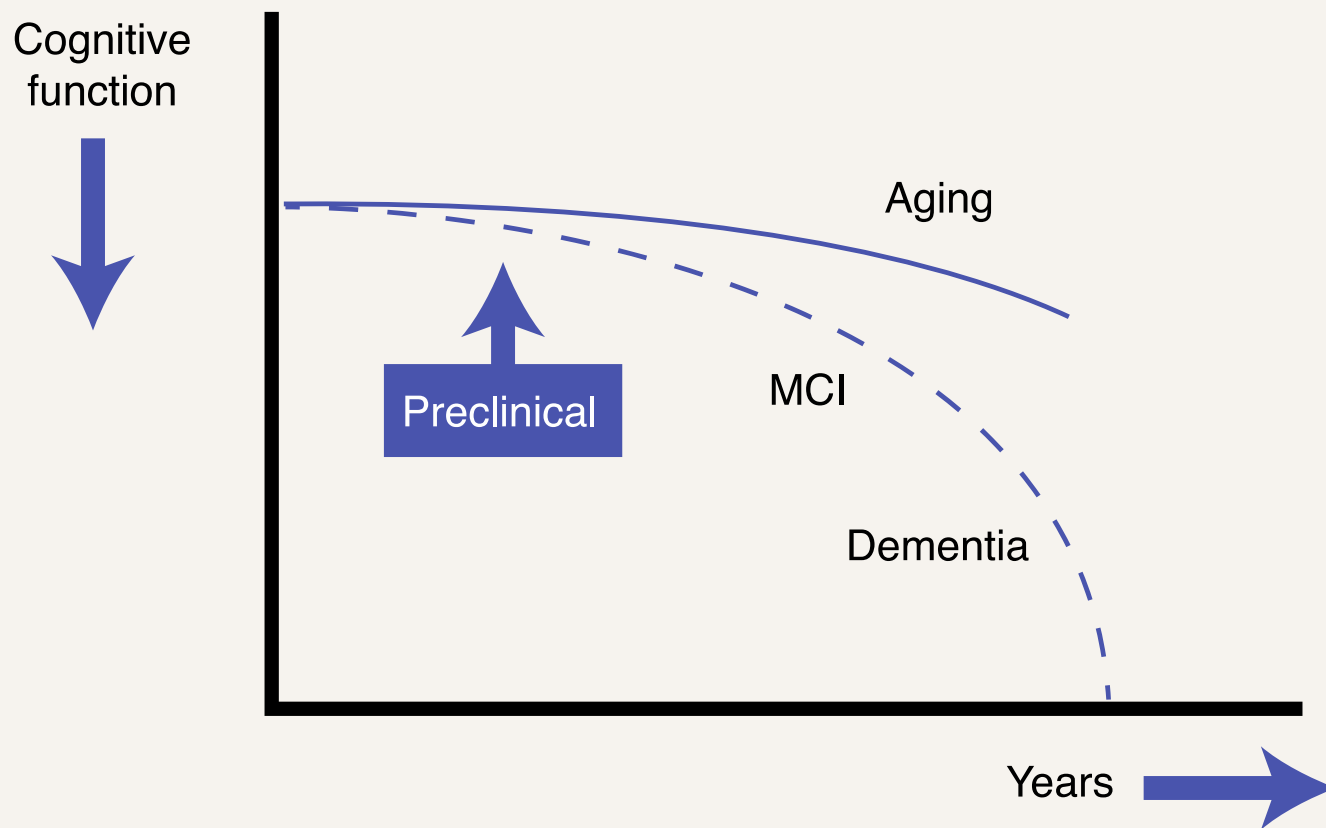
Aging

Preclinical

MCI

Dementia

Years

Image adapted from: Fuentes P. *Arch Med Res*. 2012;43(8):667-70. [p668/Figure 1]

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Scientific/Medical Challenges for AD which need to be Addressed through Collaborative Research

- Pure research to better define the pathology of AD

- Use of biomarkers and imaging for:
  - Earlier diagnosis
  - Enrichment of populations in clinical trials which may lead to better success with potential therapies
  - Prognostic markers of disease progression

- Define clinical and patient-centric outcomes that are meaningful in activities of daily living

- Collaborate to develop a disease model for AD given it is a continuum

- Registry data:
  - how best to combine data sources (clinical/imaging data) to characterise the spectrum of AD disease and
  - harmonise the collection of data across research programs and data systems

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OPTIMISE: Data capture and Management Tool for Stratified Medicine in Multiple Sclerosis (MS)

Project Scope & Strategic Alignment	• **Objectives**: The aim of this project is the development of an eTRIKS-based IT solution ("Optimise Portal") for characterization of patient populations and treatment monitoring ("Optimise Portal") facilitating the capture of prospective longitudinal, standardized clinical, imaging, biomarker and patient-centered data within a consortium including 17 of the major multiple sclerosis care centers in the UK.

Roles and Responsibilities in a 3-year collaborative agreement	• **Joint Working Agreement started October 1st 2014 between:**
	   o Imperial College London (ICL), UK
	   o Biogen Idec International GmbH, Zug
	• **Joint Project Working Group**
	   o Oversight, monitoring & evaluation of project development
	   o Paul Matthews (ICL), Yike Guo (ICL), May Yong (ICL), Joel Raffel (ICL), Sally Rennick (ICL), Robert Hyde (BIIB), Shibeshih Belachew (BIIB), Fiona Thomas (BIIB), Gavin Giovannoni (Blizard Institute), Matt Craner (Oxford University), James Overell (Glasgow).

OPTIMISE Portal Components	
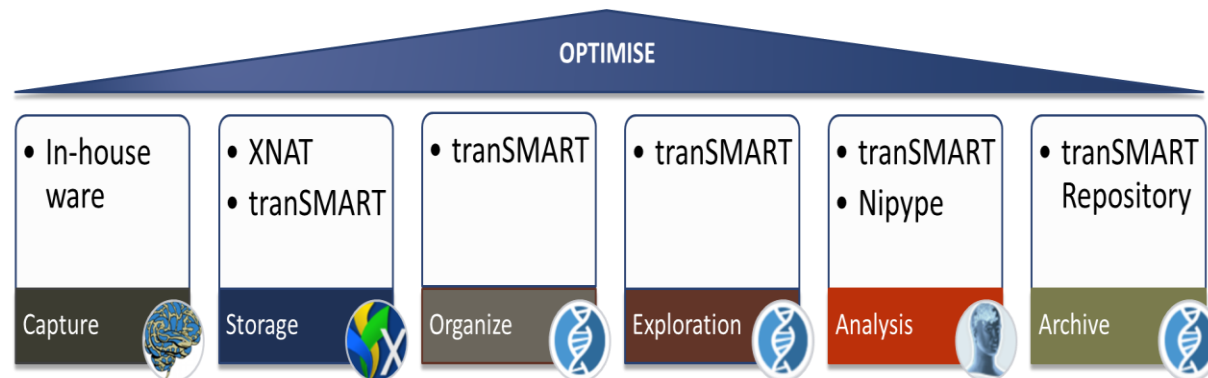
XNAT (e**X**tensible **N**euroimaging **A**rchive **T**oolkit) is an open-source software platform designed – by the Neuroinformatics Research Group of Washington University - to facilitate common management and productivity tasks for neuroimaging and associated data. In particular, XNAT enables quality control procedures and provides secure access to and storage of data.

Nipype, an open-source, community-developed initiative under the umbrella of NiPy is a Python project that provides a uniform interface to existing neuroimaging software and facilitates interaction between these packages within a single workflow.

Excellent Collaborative Initiatives in Progress

- EPAD: European Prevention of Alzheimer's Disease (IMI initiative)
    - 35 partners from industry and academia
    - 8 Workstreams addressing different aspects of AD and study design
    - Ultimate objective is to define a homogenous patient population for study in early disease to maximise successful therapeutic intervention OR early rejection

- IMI-2 Neurodegeneration Strategic Governance Group: AD Real World Evidence Platform
    - 19 EFPIA companies, EC and IMI office: 10 Work Streams
    - **ROADS**: to improve the quality and relevance of evidence available to help patients, caregivers, clinicians, employers, insurers, regulators and policy makers make informed health decisions in AD.
    - Provide recommendations on appropriate AD-related cognitive, functional, behavioural, and diagnostic endpoints that can be used across various types of research programs and data systems

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Molecular-to-Systems Approach to Myelin Plasticity and Therapeutics Applied to Co-Morbid Brain Diseases (MoSAMPT)

Horizon 2020 is the biggest EU Research and Innovation program

MoSAMPT Objectives:

(1) Investigating the functional (molecular/cellular) mechanisms of myelin maintenance and dynamics in humans with early and late stage AD, Schizophrenia or depression and animal models

(2) Assessing and characterizing the structure of myelination at the micro-level, using comparable in-vivo imaging techniques in humans and animal models

(3) Measuring the effects of brain stimulation and behavioural training on structural and functional parameters of myelination

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Challenges with Collaborative Research and What makes Partnerships Successful

- Focus on patient needs – don't get distracted with pure science alone although this is important for identifying important targets in a new therapeutic area e.g. ALS

- Trust and transparency in the working relationships

- Intellectual property and ownership i.e. who owns the data and this needs to be addressed early

- Speed: needs resource commitment. Collaborations can be time consuming and bureaucratic!!!

- Needs acceptance from Regulatory Scientists particularly with respect to clinical and patient reported outcomes

- Outcomes need to be accepted by payors especially for earlier interventions in disease