# TranSMART and beyond


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Luxembourg Centre for
Systems Biomedicine

ITTM S.A.
Luxembourg

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LCSB


ALL WE NEED

# LCSB in a nutshell

Interdisciplinary research centre of the University of Luxembourg

Aim: *Personalized medicine*

part of the Biohealth Initiative of Luxembourg

Biomedical and Systems Biology Research

Founded in Sept. 2009

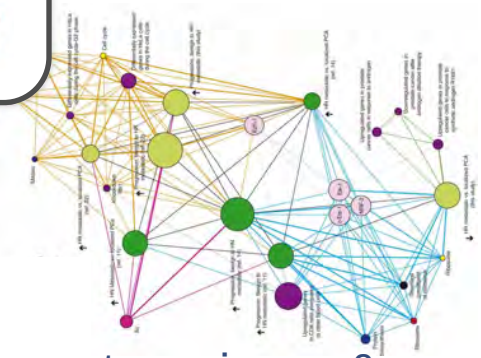
# Scientific strategy of LCSB

## Clinical translational research

## Experimental Biology

LCSB

## Technology platforms



## Computer science & Bioinformatics

# Bioinformatics Core facilities (30+ FTE's)

**Data integration and management**
Organize, store and categorize large amount of data (PetaByte scale). Providing access and management to large compute farms.

**Automatics pipelines for larges scale data-analysis**
Setup of automatic procedures to filter and extract the most relevant information out of large heterogeneous datasets

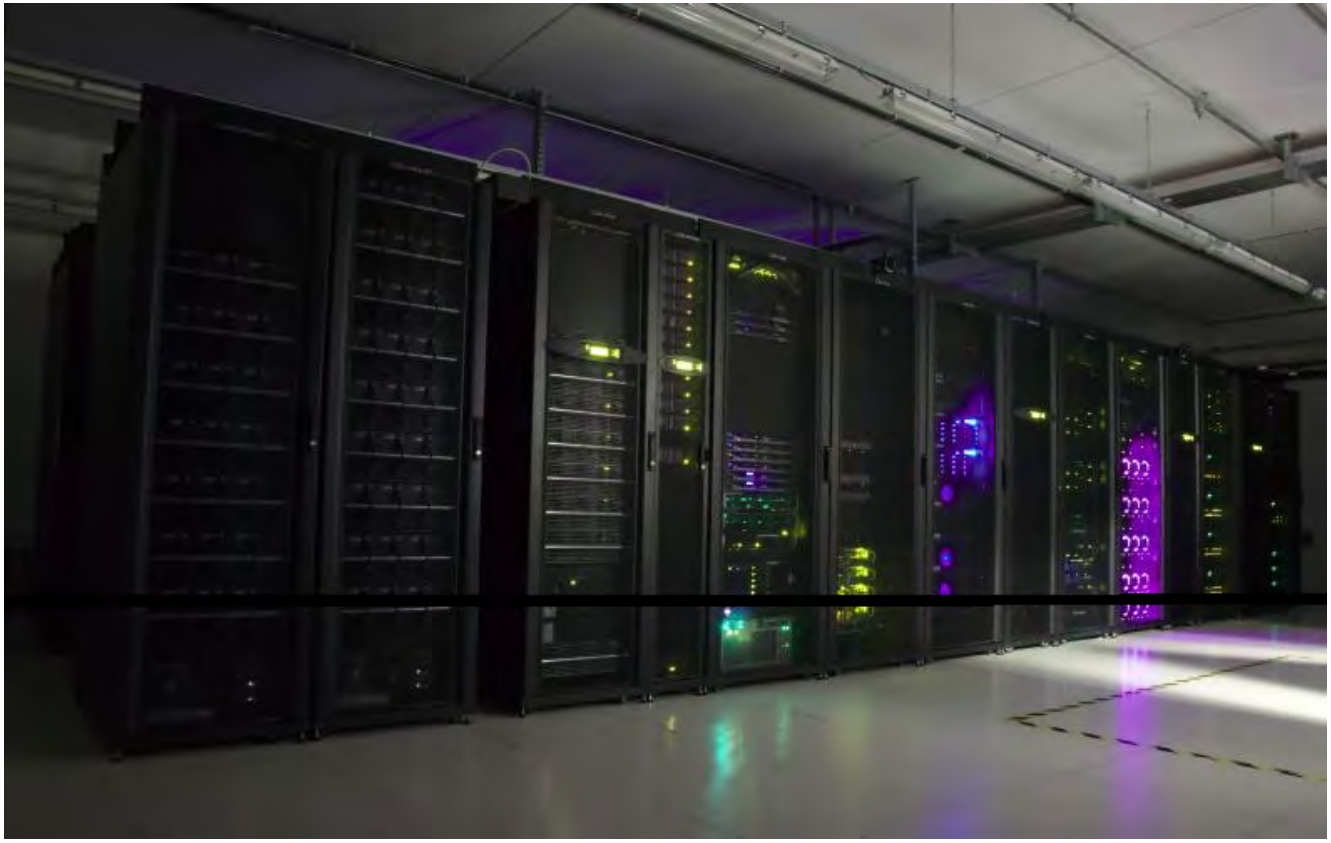
**Network (re-)construction**
Extract known and predicted networks (protein, protein-protein, protein-chemical,...) from databases and by applying text-mining technologies

**Large scale visualization tools for heterogenous data**
Development of 2D and 3D visualization tool for data exploration and hypothesis generation

**Text-mining**
Crunching large scale full-text corpora of hundreds of thousand of articles to extract knowledge map and relationships between diseases, genes, proteins etc.

**Data Analysis partner in several projects**
FP7: eTRIKS, EpiPGX; coGIE; betaJUDO

**Development of dedicated problem oriented research tools**



Cluster with >5000 cores
Several large memory machine 1-4 TB RAM
~5 PetaByte storage

# **eTRIKS:** European Translational Information & Knowledge Management Services


eTRIKS: an **umbrella project** funded by IMI to provide **data integration** and **knowledge management** solution & services **for other IMI projects**

# AETIONOMY

*To generate a mechanism-based taxonomy for neuro-degenerative and autoimmune inflammatory diseases to validate those taxonomies using prospectively collected data.*


Fraunhofer SCAI

NEURORAD CENTRU DE RADIOLOGIE

UNIVERSITÄT LUXEMBURG

Leibniz Universität Hannover

UCL

Erasmus MC

ICM Institut du Cerveau et de la Moelle épinière

PHARMACOIDEA

universitätsklinikumbonn

Alzheimer Europe

ucb

IDIBAPS Institut D'Investigacions Biomèdiques August Pi i Sunyer

NOVARTIS

Boehringer Ingelheim

SANOFI

PARKINSON

National Centre of Excellence in Research

8-year research program

NCER-PD: early-stage diagnosis of Parkinson's disease (PD) and improvement in the stratification of PD will focus on the identification and validation of clinical and molecular traits (biomarker signatures) of PD patients to improve diagnosis and characterization of their condition.

Partners:
Luxembourg Centre for Systems Biomedicine (LCSB) (coordinator)
The Luxembourg Institute of Health (LIH),
The Integrated BioBank of Luxembourg (IBBL)
Centre Hospitalier de Luxembourg (CHL).

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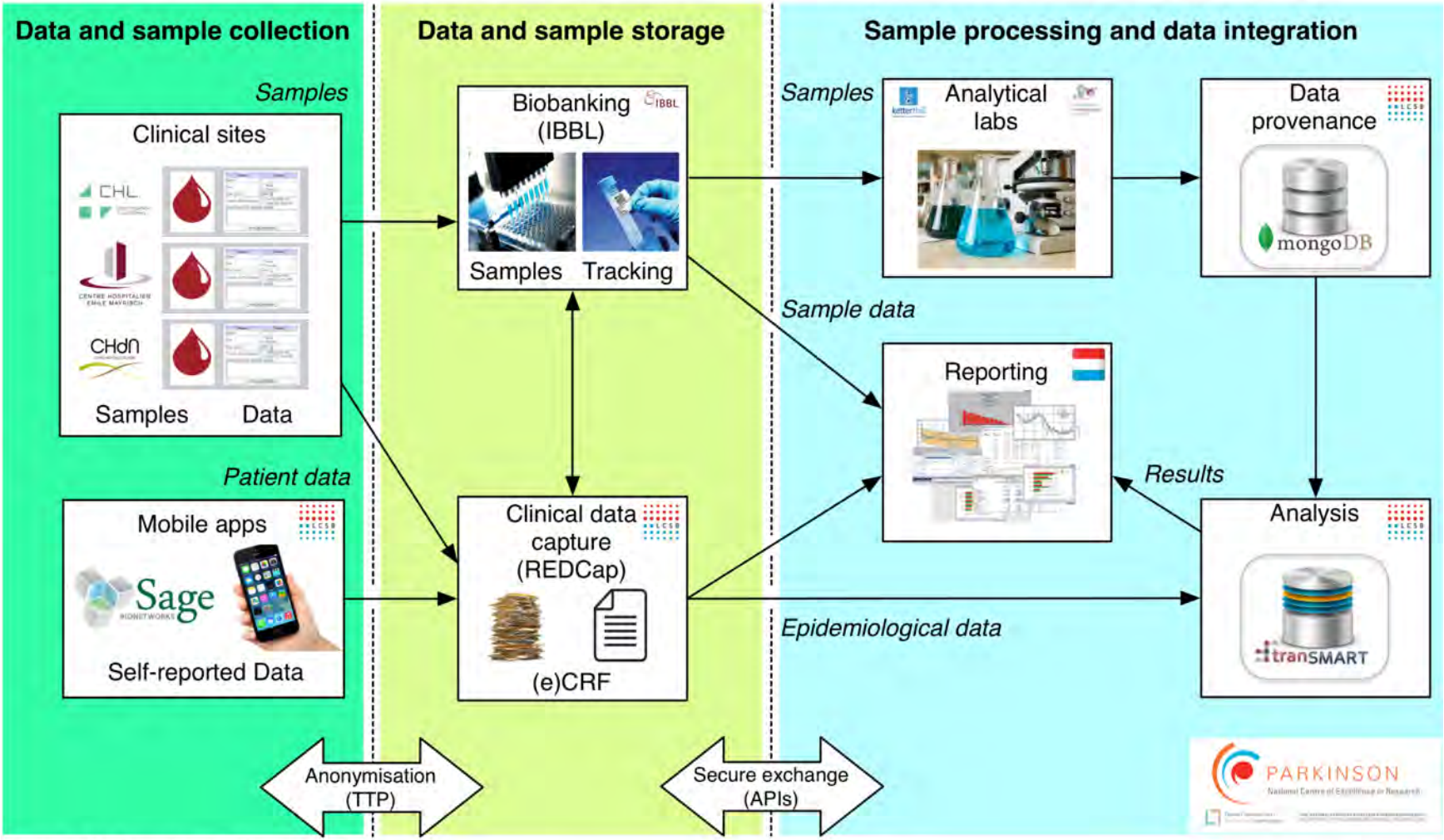
# Example: NCER-PD



# Enrollment of iPads

Unpack

Setup


Activate


Secured iPad by LCSB

MDM

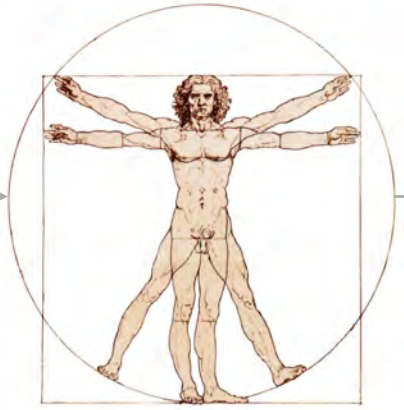
MobileIron

Apple DEP

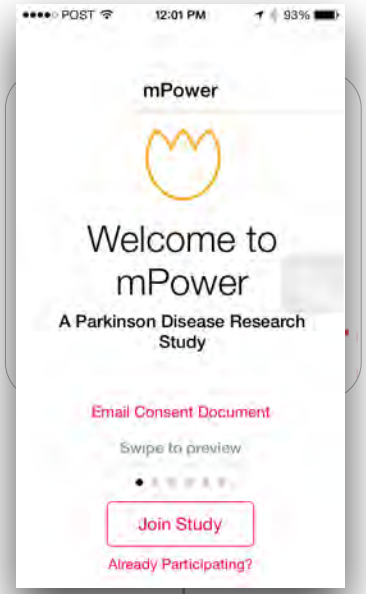
DEP

Device Enrolment Program

Clinical Team

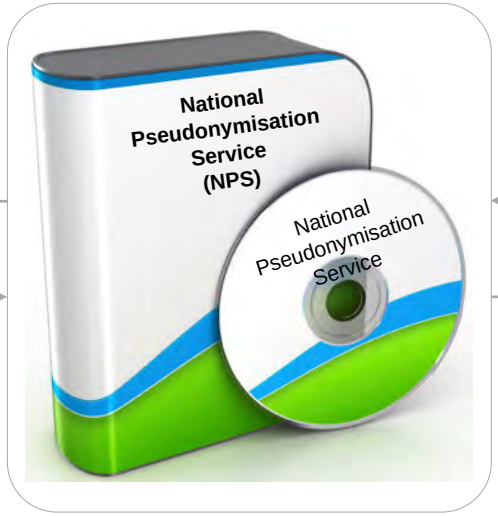


Subject




Pseudonym

Request for Pseudonym




Anonymisation Service

Request for Pseudonym


Pseudonym

Flying Team

NCER-PD Repository

**mPower mobile App Schematic:** Secure data flow of mPower mobile app in NCER-PD

## About ITTM S.A.

ITTM
Information Technology for Translational Medicine

Incorporated 2015

Spin-off of the LCSB (Luxembourg Centre of Systems Biomedicine) of the University of Luxembourg

LCSB

Université du Luxembourg

Société Anonyme (R.C.S. Luxembourg B 179.199)

Strategic Investment by

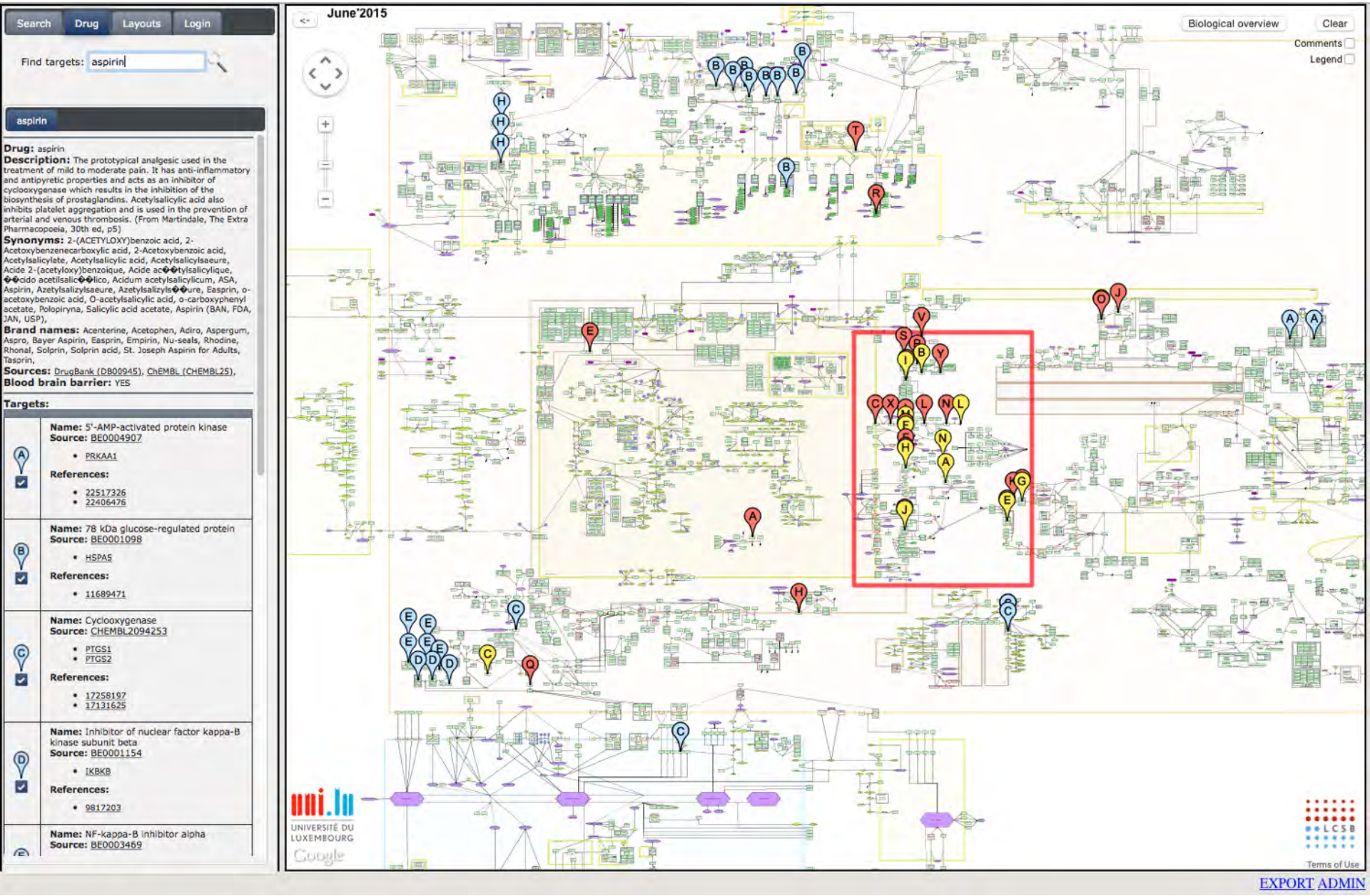
Post Luxembourg Group

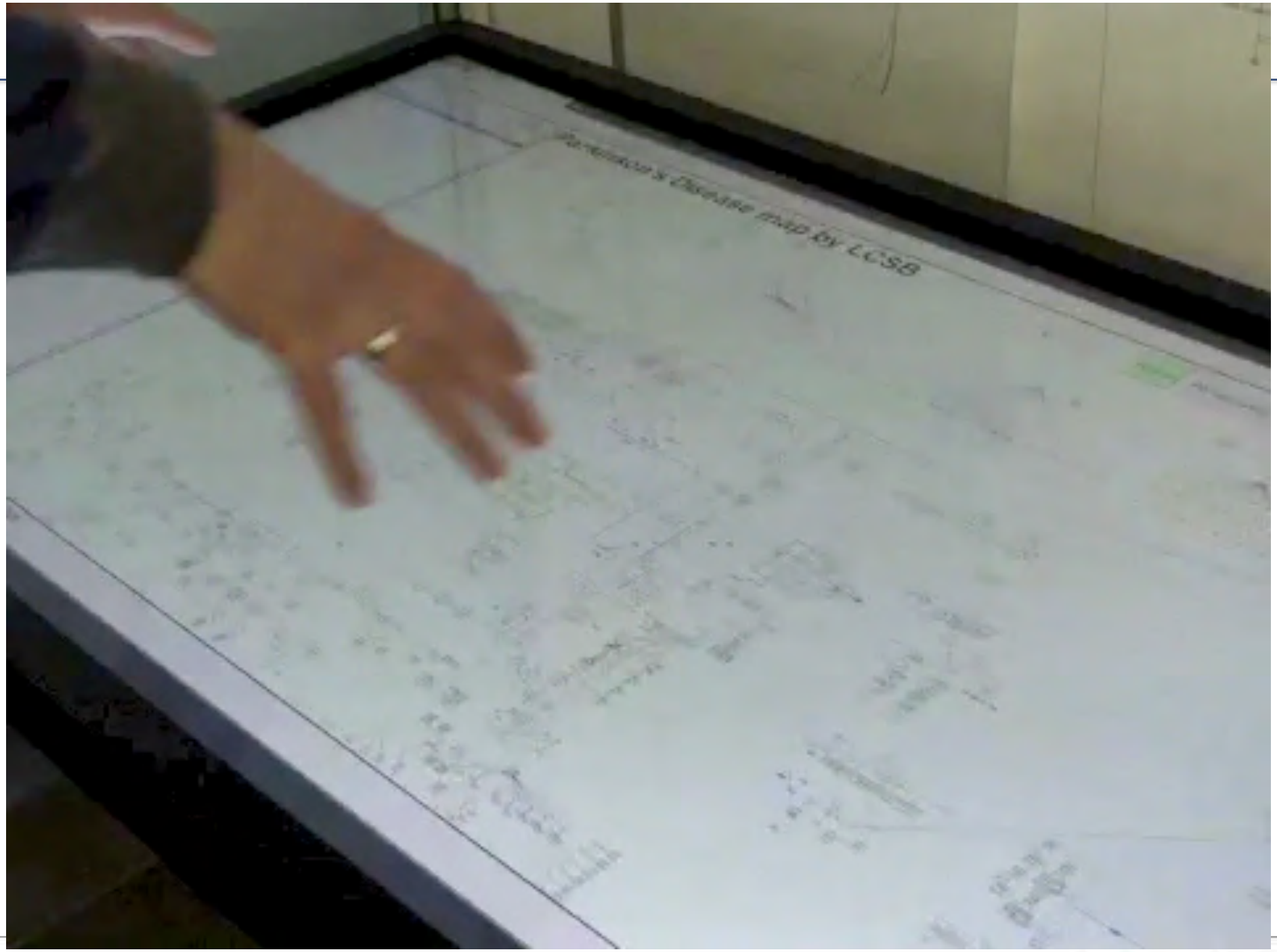
Post Luxembourg

Teralink solutions

# PD-Map

http://minerva.uni.lu




Parkinson's Disease map by LCSB

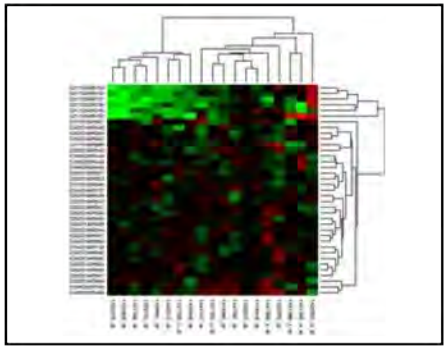
# Transmart-Galaxy-MINERVA pipeline

**tranSMART-to-Galaxy interface**
A dataset is selected from an integrated biomedical database and passed directly to the Galaxy Server

**Galaxy-to-MINERVA interface**
Analytical results from the Galaxy Server are sent to the MINERVA platform (here: PD map)

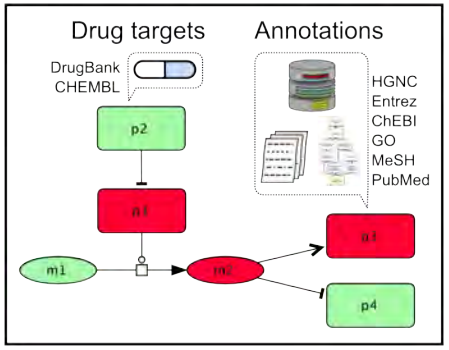
tranSMART v1.2 | Galaxy | MINERVA minerva.uni.lu

**Data integration**



**Analytical pipelines**

**Knolwedge repositories**



# Anatomical magnetic resonance (MR) imaging

- Used to study the neurobiology of various diseases;
- Tissue classification
- Classification of anatomical structures
- Cortex Parcellation

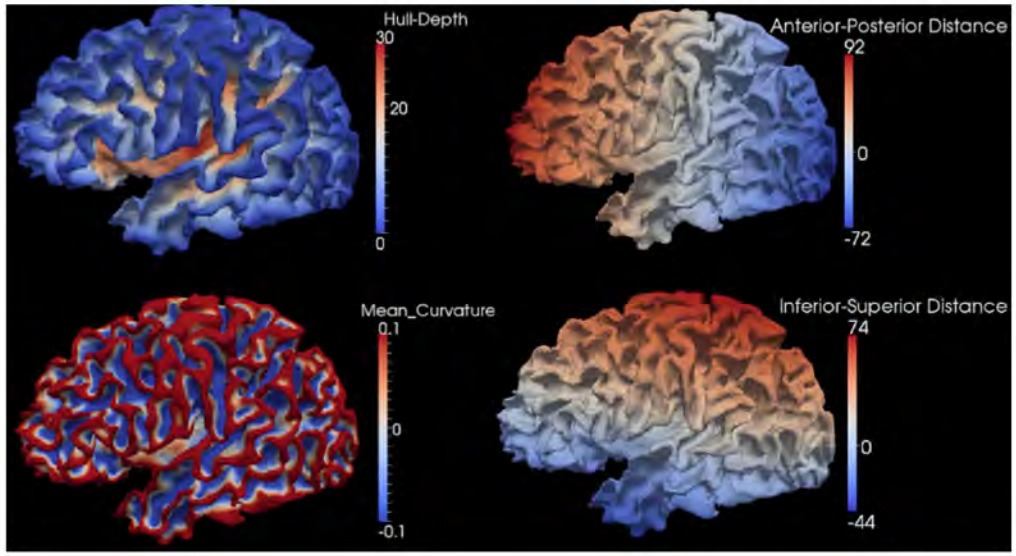



**FIGURE 1 | Four geometry features calculated for the surface of one cortical hemisphere for a single subject.** Surfaces are colored by scalar values associated with vertices. Features names and scalar ranges are shown on the right side of each surface. Units: *Inferior-Superior Distance*, *Anterior-Posterior Distance*, and *Hull-Depth* are in millimeters; *Mean-Curvature* has the units of 1/millimeter.

Li *et al.*, 2013

# FreeSurfer Method

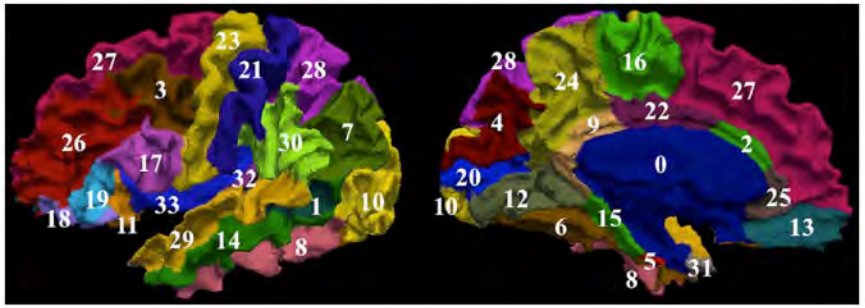



**FIGURE 4 | The surface on a single subject parcellated into 34 sub-regions using FreeSurfer.** The regions as defined by FreeSurfer are provided in **Table 5**. The surface is shown with a lateral (left) and a medial (right) view.

Li *et al.*, 2013

**Table 5 | FreeSurfer's regions.**

| Label | Region name | Label | Region name |
|---|---|---|---|
| 0 | Unlabeled subcortical region | 17 | Pars opercularis |
| 1 | Banks superior temporal sulcus | 18 | Pars orbitalis |
| 2 | Caudal anterior cingulate cortex | 19 | Pars triangularis |
| 3 | Caudal middle frontal gyrus | 20 | Pericalcarine cortex |
| 4 | Cuneus cortex | 21 | Postcentral gyrus |
| 5 | Entorhinal cortex | 22 | Posterior-cingulate cortex |
| 6 | Fusiform gyrus | 23 | Precentral gyrus |
| 7 | Inferior parietal cortex | 24 | Precuneus cortex |
| 8 | Inferior temporal gyrus | 25 | Rostral anterior cingulate cortex |
| 9 | Isthmus-cingulate cortex | 26 | Rostral middle frontal gyrus |
| 10 | Lateral occipital cortex | 27 | Superior frontal gyrus |
| 11 | Lateral orbital frontal cortex | 28 | Superior parietal cortex |
| 12 | Lingual gyrus | 29 | Superior temporal gyrus |
| 13 | Medial orbital frontal cortex | 30 | Supramarginal gyrus |
| 14 | Middle temporal gyrus | 31 | Temporal pole |
| 15 | Parahippocampal gyrus | 32 | Transverse temporal cortex |
| 16 | Paracentral lobule | 33 | Insula |

# EMC Data, 341 variables per subject

| Thick RightG temp sup-Plan tempo |
|---|
| Thick RightG and S paracentral |
| Thick RightG orbital |
| Thick RightG temporal inf |
| Thick RightG and S frontomargin |
| Thick RightG oc-temp med-Parahip |
| Thick RightG rectus |
| Thick RightG cingul-Post-dorsal |
| Thick RightG and S cingul-Ant |
| Thick RightG temp sup-Lateral |
| Thick RightG parietal sup |
| Thick RightG occipital sup |
| Thick RightG precentral |
| Thick RightG and S transv frontopol |
| Thick RightG precuneus |
| Thick RightG temp sup-G T transv |
| Thick RightG front sup |
| Thick RightG insular short |
| Thick RightG oc-temp lat-fusifor |
| Thick RightG front middle |
| Thick RightG front inf-Triangul |
| Thick RightG pariet inf-Angular |
| Thick RightG cingul-Post-ventral |
| Thick RightG and S subcentral |
| Thick RightG Ins lg and S cent ins |
| Thick RightG front inf-Opercular |
| Thick RightG cuneus |
| Thick RightG front inf-Orbital |
| Thick RightG pariet inf-Supramar |
| Thick RightG postcentral |
| Thick RightG and S cingul-Mid-Post |
| Thick RightG and S cingul-Mid-Ant |
| Thick RightG temp sup-Plan polar |
| Thick RightG oc-temp med-Lingual |
| Thick RightG occipital middle |
| Thick RightG subcallosal |
| Thick RightG temporal middle |
| Thick RightG and S occipital inf |

| Thick RightS circular insula ant |
|---|
| Thick RightS precentral-sup-part |
| Thick RightS temporal inf |
| Thick RightS temporal sup |
| Thick RightS oc-temp med and Lingual |
| Thick RightS collat transv ant |
| Thick RightS temporal transverse |
| Thick RightS central |
| Thick RightS subparietal |
| Thick RightS suborbital |
| Thick RightS circular insula inf |
| Thick RightS circular insula sup |
| Thick RightS postcentral |
| Thick RightS orbital-H Shaped |
| Thick RightS orbital med-olfact |
| Thick RightS interm prim-Jensen |
| Thick RightS front inf |
| Thick RightS cingul-Marginalis |
| Thick RightS pericallosal |
| Thick RightS oc-temp lat |
| Thick RightS collat transv post |
| Thick RightS intrapariet and P trans |
| Thick RightS oc sup and transversal |
| Thick RightS parieto occipital |
| Thick RightS front sup |
| Thick RightS occipital ant |
| Thick RightS calcarine |
| Thick RightS precentral-inf-part |
| Thick RightS orbital lateral |
| Thick RightS oc middle and Lunatus |
| Thick RightS front middle |

| Vol RightG precuneus |
|---|
| Vol RightG rectus |
| Vol RightG temporal middle |
| Vol RightG front inf-Triangul |
| Vol RightG and S cingul-Mid-Post |
| Vol RightG pariet inf-Angular |
| Vol RightG insular short |
| Vol RightG temp sup-G T transv |
| Vol RightG subcallosal |
| Vol RightG front sup |
| Vol RightG parietal sup |
| Vol RightG and S frontomargin |
| Vol RightG front inf-Opercular |
| Vol RightG cuneus |
| Vol RightG occipital sup |
| Vol RightG and S cingul-Ant |
| Vol RightG cingul-Post-dorsal |
| Vol RightG temp sup-Plan polar |
| Vol RightG and S subcentral |
| Vol RightG front inf-Orbital |
| Vol RightG temporal inf |
| Vol RightG pariet inf-Supramar |
| Vol RightG front middle |
| Vol RightG cingul-Post-ventral |
| Vol RightG postcentral |
| Vol RightG and S occipital inf |
| Vol RightG and S paracentral |
| Vol RightG and S transv frontopol |
| Vol RightG temp sup-Plan tempo |
| Vol RightG oc-temp med-Parahip |
| Vol RightG oc-temp lat-fusifor |
| Vol RightG oc-temp med-Lingual |
| Vol RightG and S cingul-Mid-Ant |
| Vol RightG precentral |
| Vol RightG Ins lg and S cent ins |
| Vol RightG temp sup-Lateral |
| Vol RightG orbital |
| Vol RightG occipital middle |

| Vol RightS temporal sup |
|---|
| Vol RightS oc sup and transversal |
| Vol RightS orbital-H Shaped |
| Vol RightS postcentral |
| Vol RightS temporal transverse |
| Vol RightS circular insula sup |
| Vol RightS precentral-inf-part |
| Vol RightS circular insula inf |
| Vol RightS collat transv post |
| Vol RightS collat transv ant |
| Vol RightS pericallosal |
| Vol RightS parieto occipital |
| Vol RightS occipital ant |
| Vol RightS intrapariet and P trans |
| Vol RightS interm prim-Jensen |
| Vol RightS orbital med-olfact |
| Vol RightS calcarine |
| Vol RightS oc-temp med and Lingual |
| Vol RightS oc middle and Lunatus |
| Vol RightS circular insula ant |
| Vol RightS front middle |
| Vol RightS temporal inf |
| Vol RightS front inf |
| Vol RightS central |
| Vol RightS front sup |
| Vol RightS orbital lateral |
| Vol RightS precentral-sup-part |
| Vol RightS subparietal |
| Vol RightS oc-temp lat |
| Vol RightS cingul-Marginalis |
| Vol RightS suborbital |

| Right-Cerebellum-White-Matter |
|---|
| Right-Thalamus-Proper |
| CC Mid Anterior |
| Left-choroid-plexus |
| Left-Hippocampus |
| 3rd-Ventricle |
| Left-Pallidum |
| Left-Accumbens-area |
| CC Anterior |
| Brain-Stem |
| CC Mid Posterior |
| Left-Cerebellum-White-Matter |
| Right-Cerebral-Cortex |
| Left-Amygdala |
| Right-vessel |
| WM-hypointensities |
| Right-Pallidum |
| Right-Amygdala |
| Right-VentralDC |
| Left-Cerebral-White-Matter |
| 4th-Ventricle |
| CC Posterior |
| Left-VentralDC |
| Left-Inf-Lat-Vent |
| Right-Caudate |
| Right-Accumbens-area |
| non-WM-hypointensities |
| Right-Hippocampus |
| Right-Putamen |
| Left-Cerebellum-Cortex |
| Left-vessel |
| CSF |
| Optic-Chiasm |
| Left-Cerebral-Cortex |
| Right-Inf-Lat-Vent |
| Left-Caudate |
| Right-choroid-plexus |
| Right-Cerebellum-Cortex |
| 5th-Ventricle |
| Left-Lateral-Ventricle |
| Left-Thalamus-Proper |
| Right-Cerebral-White-Matter |
| Right-Lateral-Ventricle |
| Left-Putamen |
| CC Central |

# Structural Brain Connectivity

- Brain connectome

- Diffusion (dMRI) and functional (fMRI) magnetic resonance imaging are two well-established modalities providing powerful and complementary ways to investigate how different areas of the brain are interconnected and interact.

- In particular, dMRI exploits the thermal random motion of water molecules in biological tissues for mapping the local axonal structure at each imaging voxel

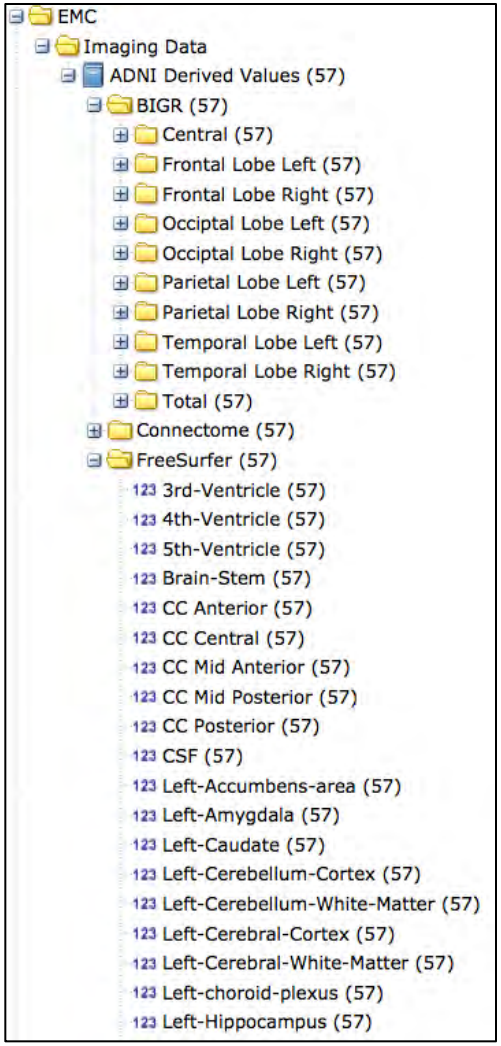
- At the macroscopic scale, the connectome can be seen as a *network*, where each *vertex* represents a well-defined cortical or sub-cortical structures and the *edges* quantify the structural white matter connectivity as measured with tractography.

Daducci *et al.*, 2012

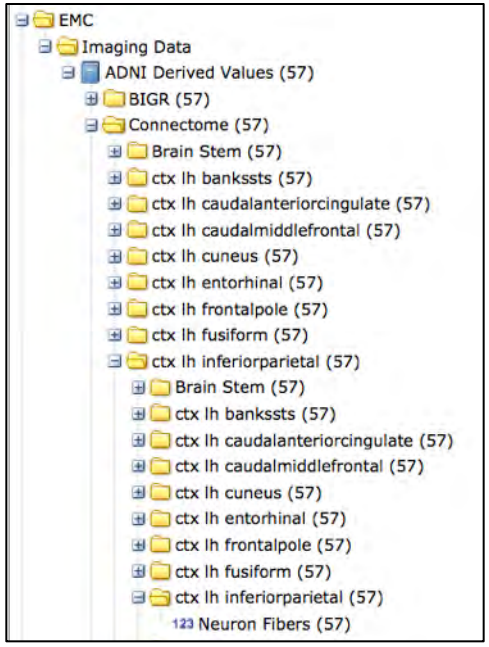
# All this data loaded to tranSMART

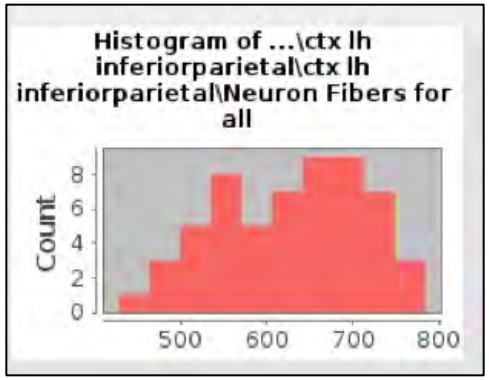
tranSMART v1.2

## Volumetric Data




## Connectome Data

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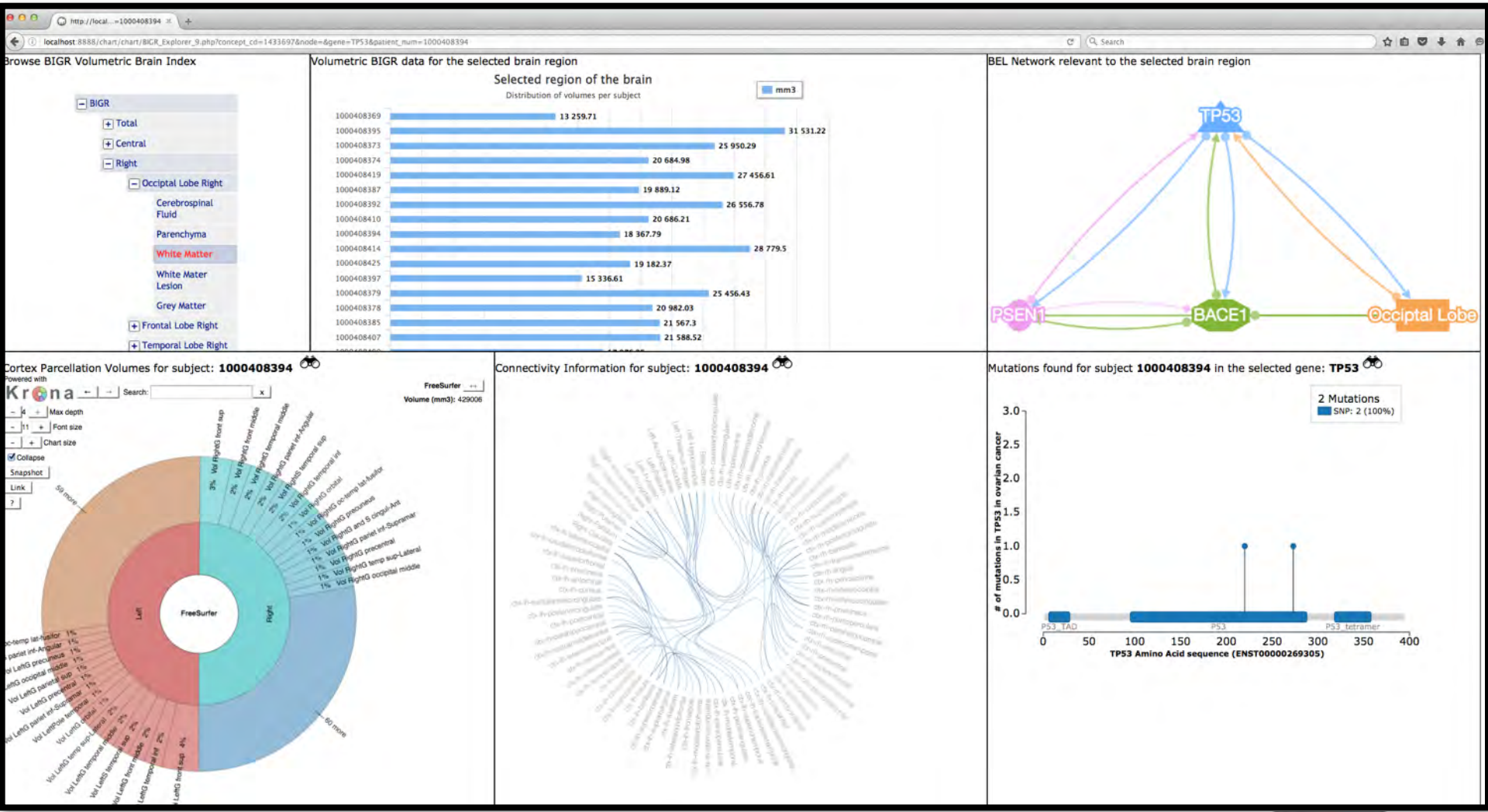
# GUI


Browse BIGR Volumetric Brain Index
BIGR
Total
Central
Right
Occipital Lobe Right
Cerebrospinal Fluid
Parenchyma
White Matter
White Mater Lesion
Grey Matter
Frontal Lobe Right
Temporal Lobe Right
Volumetric BIGR data for the selected brain region
Selected region of the brain
Distribution of volumes per subject
mm3
1000408369 13 259.71
1000408395 31 531.22
1000408373 25 950.29
1000408374 20 684.98
1000408419 27 456.61
1000408387 19 889.12
1000408392 26 556.78
1000408410 20 686.21
1000408394 18 367.79
1000408414 28 779.5
1000408425 19 182.37
1000408397 15 336.61
1000408379 25 456.43
1000408378 20 982.03
1000408385 21 567.3
1000408407 21 588.52
BEL Network relevant to the selected brain region
TP53
PSEN1
BACE1
Occiptal Lobe
Cortex Parcellation Volumes for subject: 1000408394
Powered with Krona
Search:
Max depth
Font size
Chart size
Collapse
Snapshot
Link
FreeSurfer
Volume (mm3): 429006
Left
Right
50 more
Connectivity Information for subject: 1000408394
Mutations found for subject 1000408394 in the selected gene: TP53
2 Mutations
SNP: 2 (100%)
# of mutations in TP53 in ovarian cancer
3.0
2.5
2.0
1.5
1.0
0.5
0.0
P53_TAD
P53
P53_tetramer
0
50
100
150
200
250
300
350
400
TP53 Amino Acid sequence (ENST00000269305)

# Acknowledgements


**PARTNERSHIP**

Erasmus MC
University Medical Center Rotterdam

Luxembourg Centre for Systems Biomedicine

**SCOPE**

eTRIKS

AETIONOMY

**FUNDING**

imi innovative medicines initiative

European Union

efpia
European Federation of Pharmaceutical Industries and Associations

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