

FP7-HEALTH AgedBrainSYSBIO: 2013-2017

Initiative CH Sainte-Anne-INSERM-Paris Descartes

Neurones humains dérivés des fibroblastes des patients



Michel Simonneau MD PhD



Institut national
de la santé et de la recherche médicale



1. FP7-HEALTH AgedBrainSYSBIO: 2013-2017

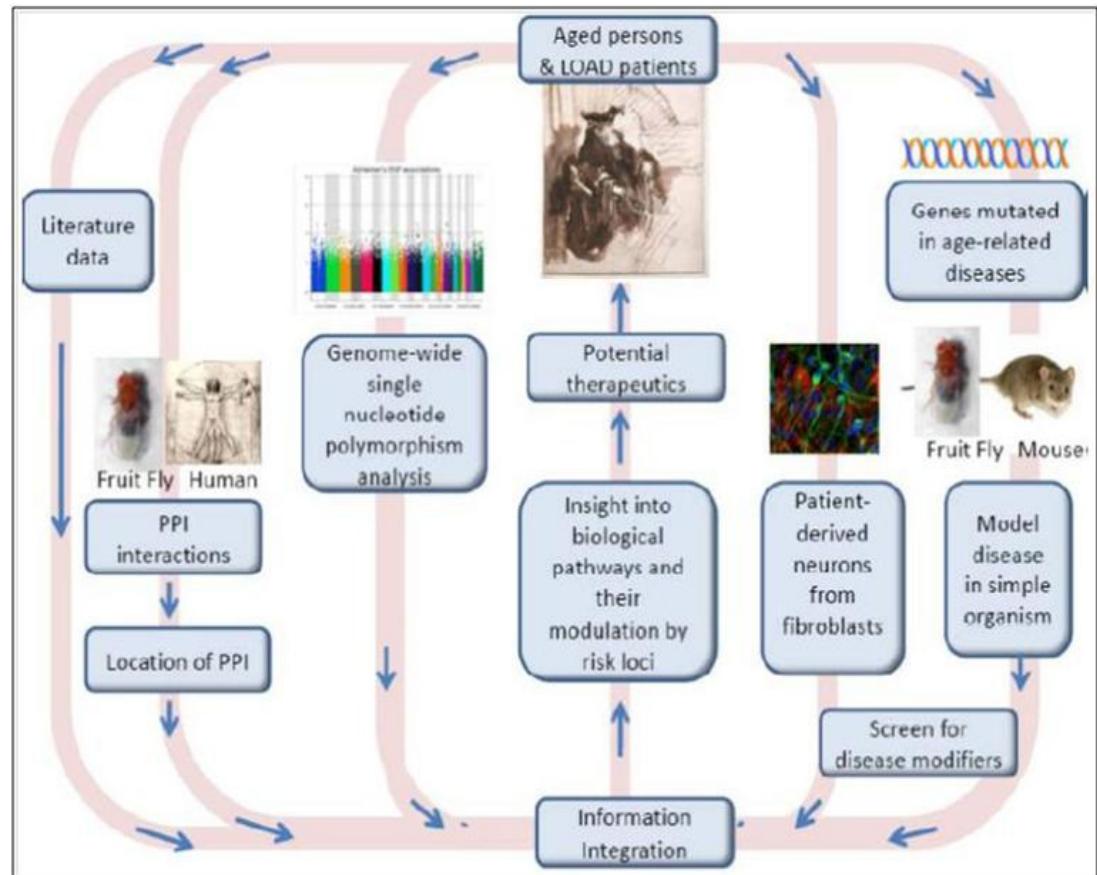


SYSTEMS BIOLOGY OF PATHWAYS INVOLVING BRAIN AGEING

AGEDBRAINSYSBIO

Type of funding scheme
SME-targeted Collaborative Project (Medium-scale focused research project)

HEALTH.2012.2.2.2-1 Integrative systems biology & comparative genomics for studying human ageing and/or most common age-related diseases.



List of participants

Participant number	Participant organisation legal name	Organisation short name	Country
1 (CO)	Institut National de la santé et de la recherche clinique	INSERM	France
2	VIB	VIB	Belgium
3	Institut Pasteur de Lille	IPL	France
4	Centre Européen de Recherche en Biologie et Médecine	CERBM-GIE	France
5	Max Planck Gesellschaft zur Foerderung der Wissenschaften E.V.	MPG	Germany
6	Tel-Aviv University	TAU	Israel
7	HYBRIGENICS SA	HYBRIGENICS	France
8	OU QURETEC	QURETEC	Estonia
9	Gene Bridges GmbH	GENEBRIDGES	Germany
10	reMYND NV	reMYND	Belgium
11	European Molecular Biology Laboratory	EMBL-EBI	Germany
12	Swiss Institute of Bioinformatics	SIB	Switzerland
13	The Babraham Institute	BI	UK
14	Inserm Transfert SA	IT	France

Getting new sets of data

Spatial resolution

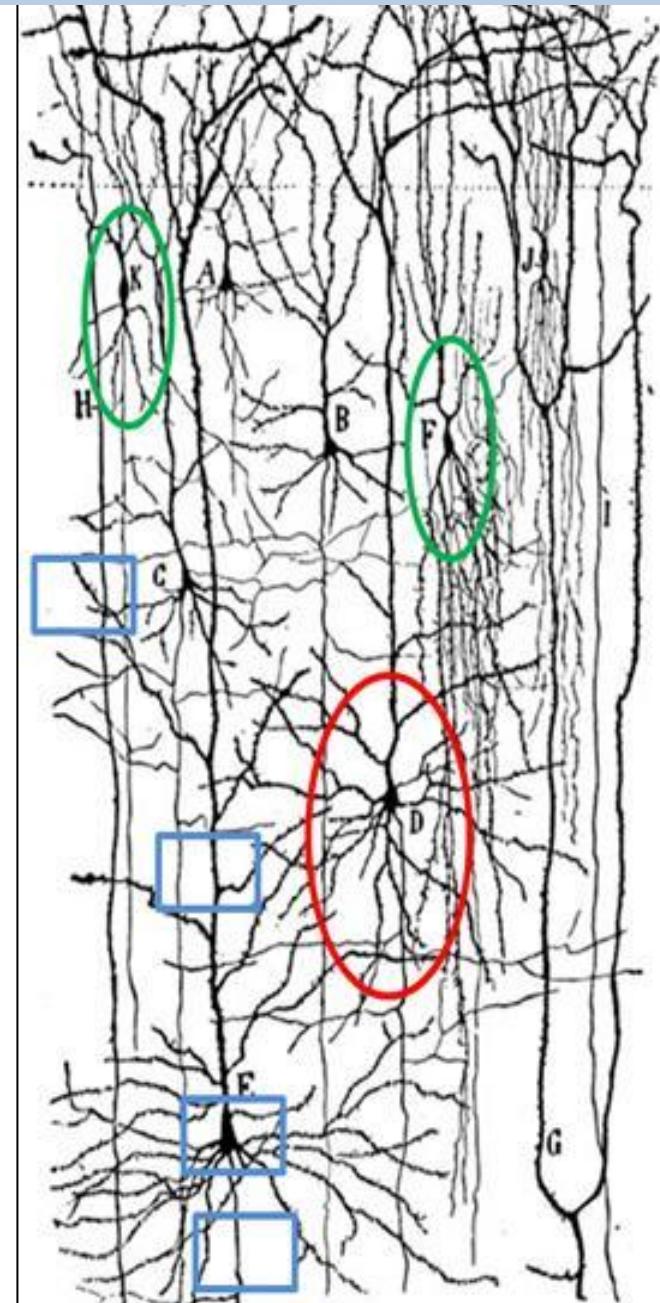
-> subsets of neurons

-> subregions of neurons

-> evolutionary data

-> humanized mouse lines

-> human neurons from iPSCs



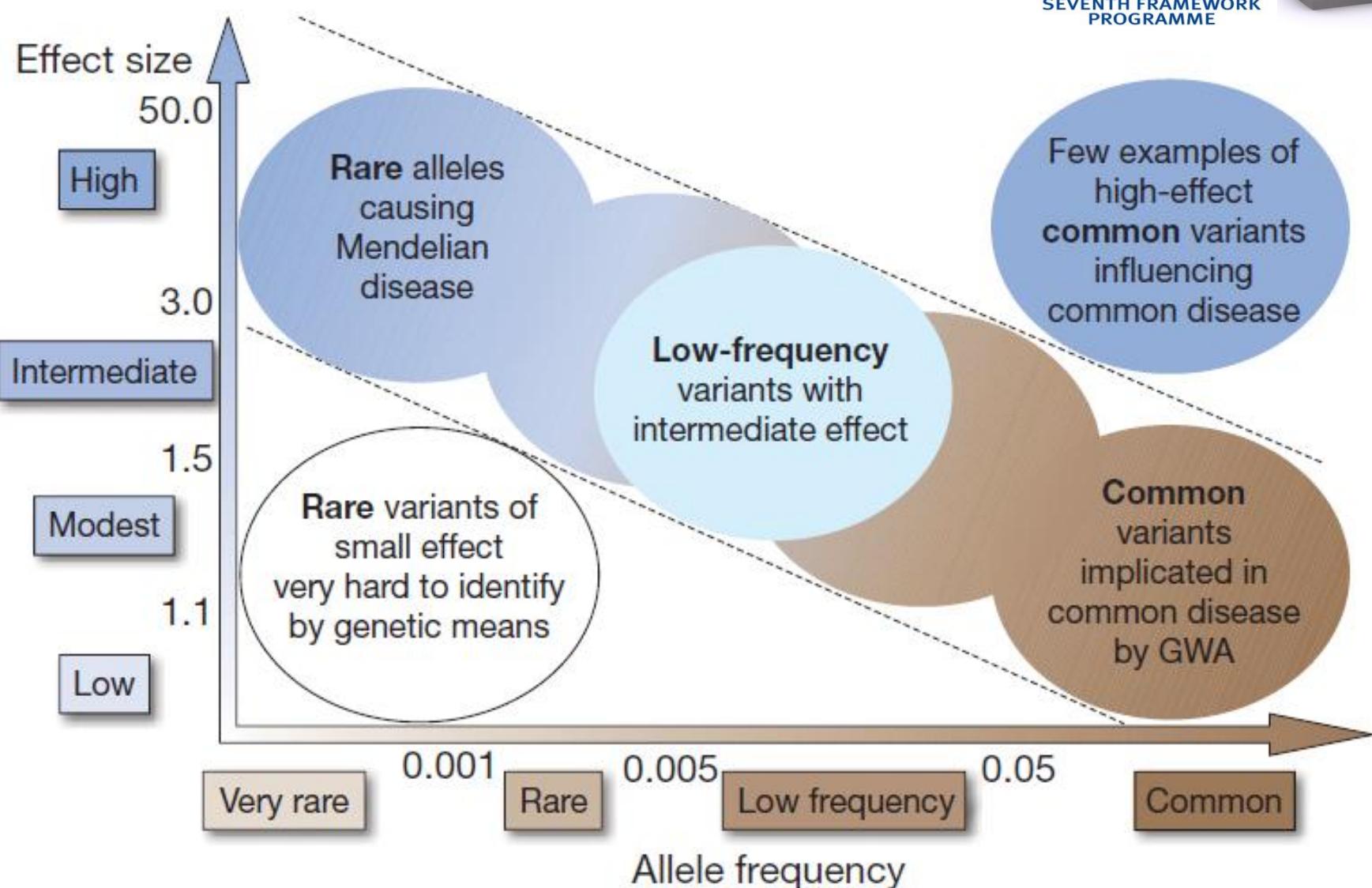
2. Approches génétiques

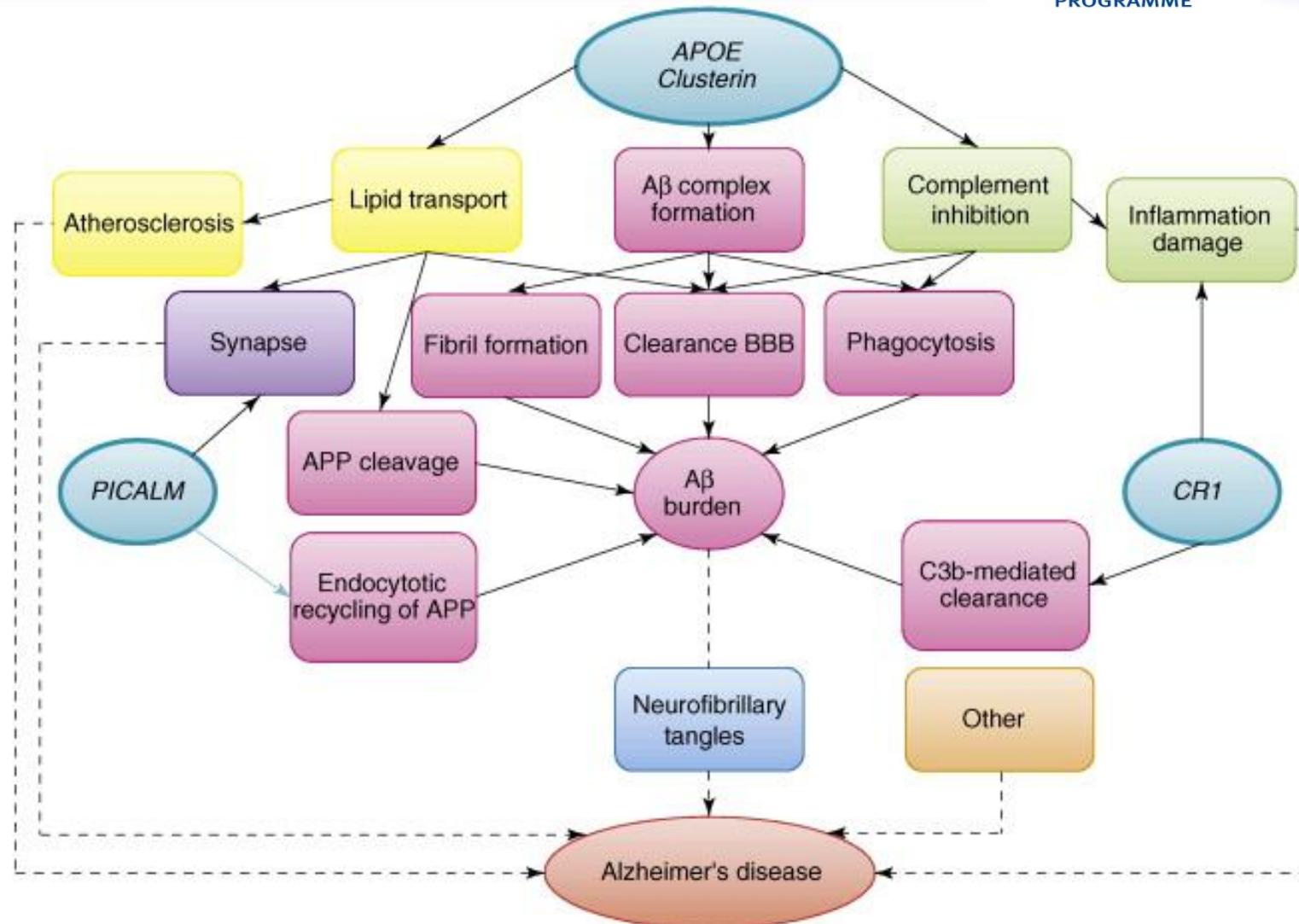


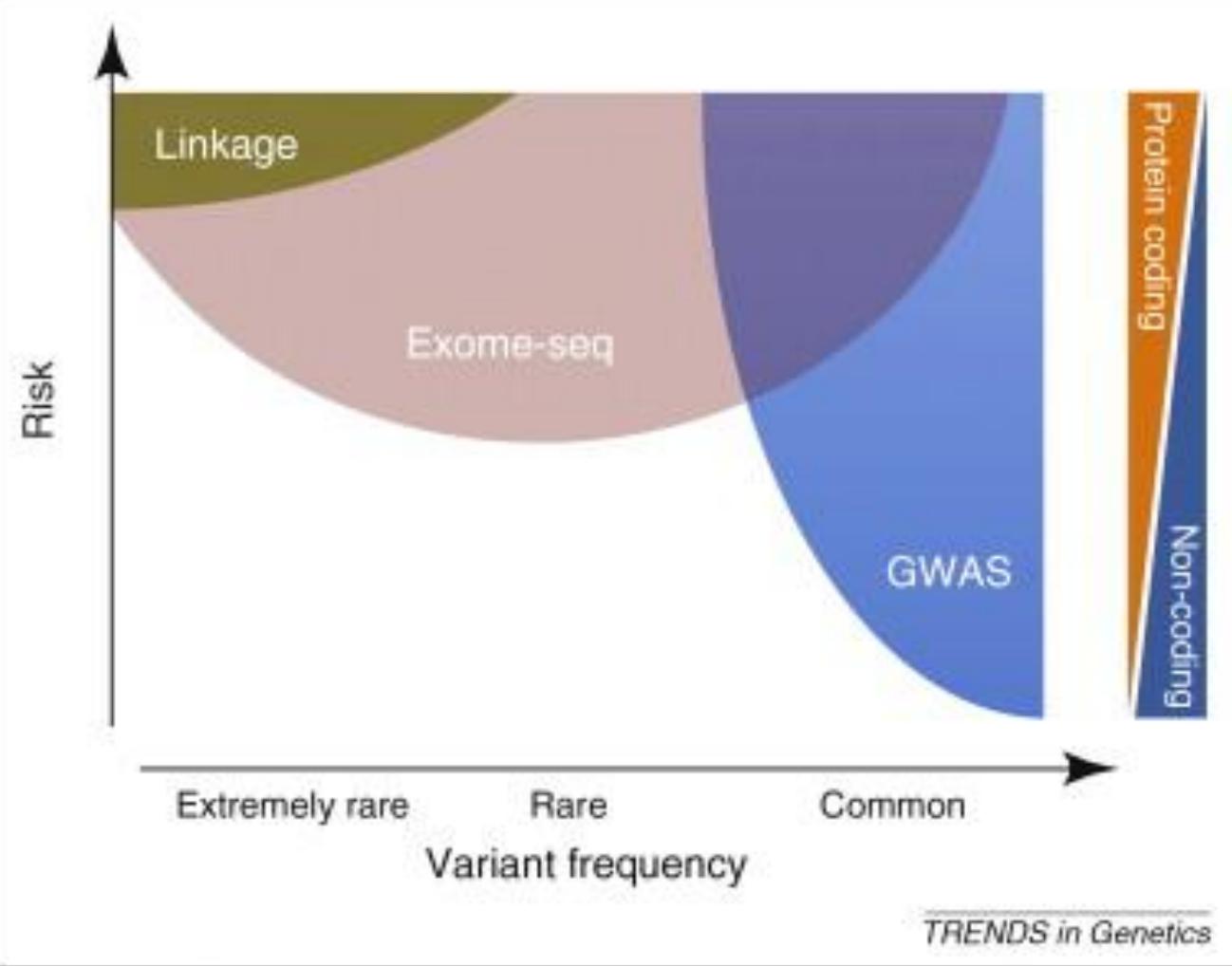
Christine VAN BROECKHOVEN, Antwerpen

Jean Charles LAMBERT, Institut Pasteur, Lille

Jacques EPELBAUM, INSERM U894







- High-risk–rare alleles (Mendelian disease)
- Low-risk–common alleles (GWAS)
- Moderate-risk–low-frequency alleles
‘dark matter of disease risk’

Singleton, Hardy et al., 2010

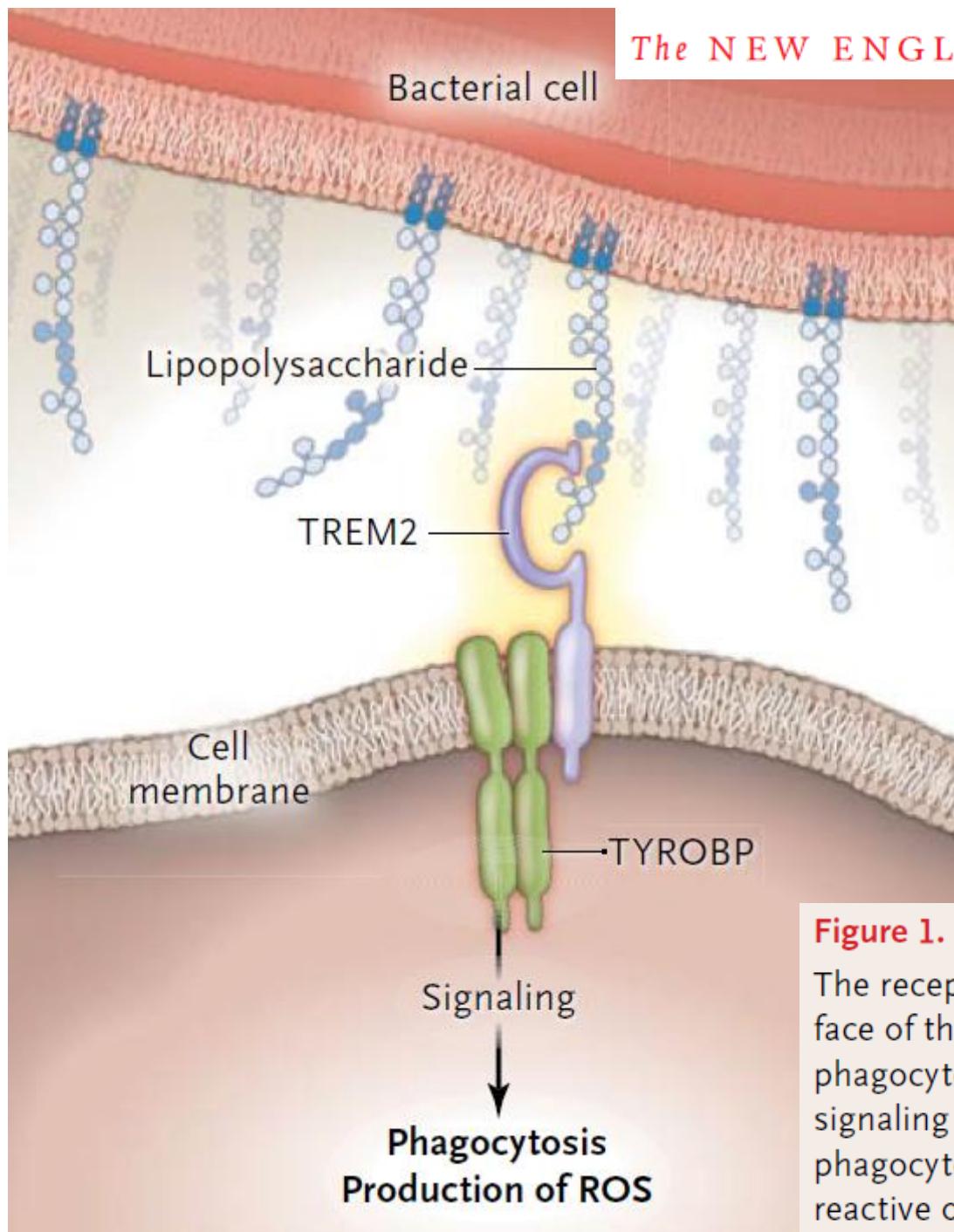
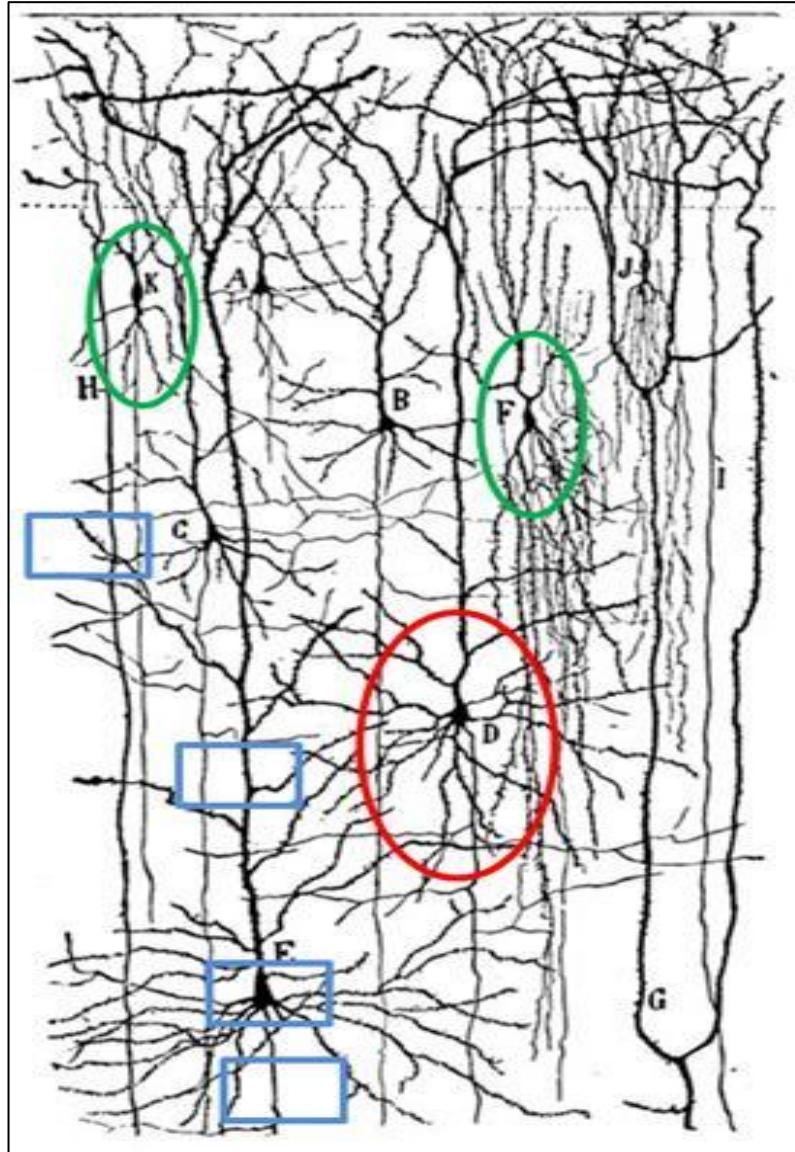


Figure 1. Phagocytosis and TREM2.

The receptor molecule TREM2 is expressed on the surface of the microglial cell and is known to mediate phagocytosis of bacteria. Binding of TREM2 promotes signaling through the molecule TYROBP, resulting in phagocytosis and elevated short-term production of reactive oxygen species (ROS).

3. Analyse des interneurones: Approches génétiques



Analysis of pathways using novel ontology elements

Subsets of identified neuronal types as indicated (coloured circles) on an original cortex drawing from Santiago Ramon y Cajal (1904).

Superficial layers of the human frontal cortex were drawn by Cajal on the basis of Golgi impregnation. The main cell types of the cerebral cortex i.e. small and large pyramidal neurons (A, B, C, D, E) (red oval) and non pyramidal (F, K) cells (interneurons in the modern nomenclature) (green ovals) are remarkably outlined.

Localisations in a neuronal compartment: dendrite, dendritic spines, cell body and axon are indicated (blue boxes).

List of interneuronal genes

Gene Name	Access to human version (Ensembl release 65 - Dec 2011)
ARX	ENSG00000004848
CALB2	ENSG00000172137
CCK	ENSG00000187094
COL19A1	ENSG00000082293
DLX1	ENSG00000144355
DLX2	ENSG00000115844
DLX5	ENSG00000105880
DLX6	ENSG00000006377
GAD1	ENSG00000128683
GAD2	ENSG00000136750
IGF1	ENSG00000017427
LHX6	ENSG00000106852
NLGN2	ENSG00000169992
PNOC	ENSG00000168081
SLC32A1	ENSG00000101438
SST	NSG00000157005
TAC1	ENSG00000006128
VIP	ENSG00000146469



18 genes analyzed

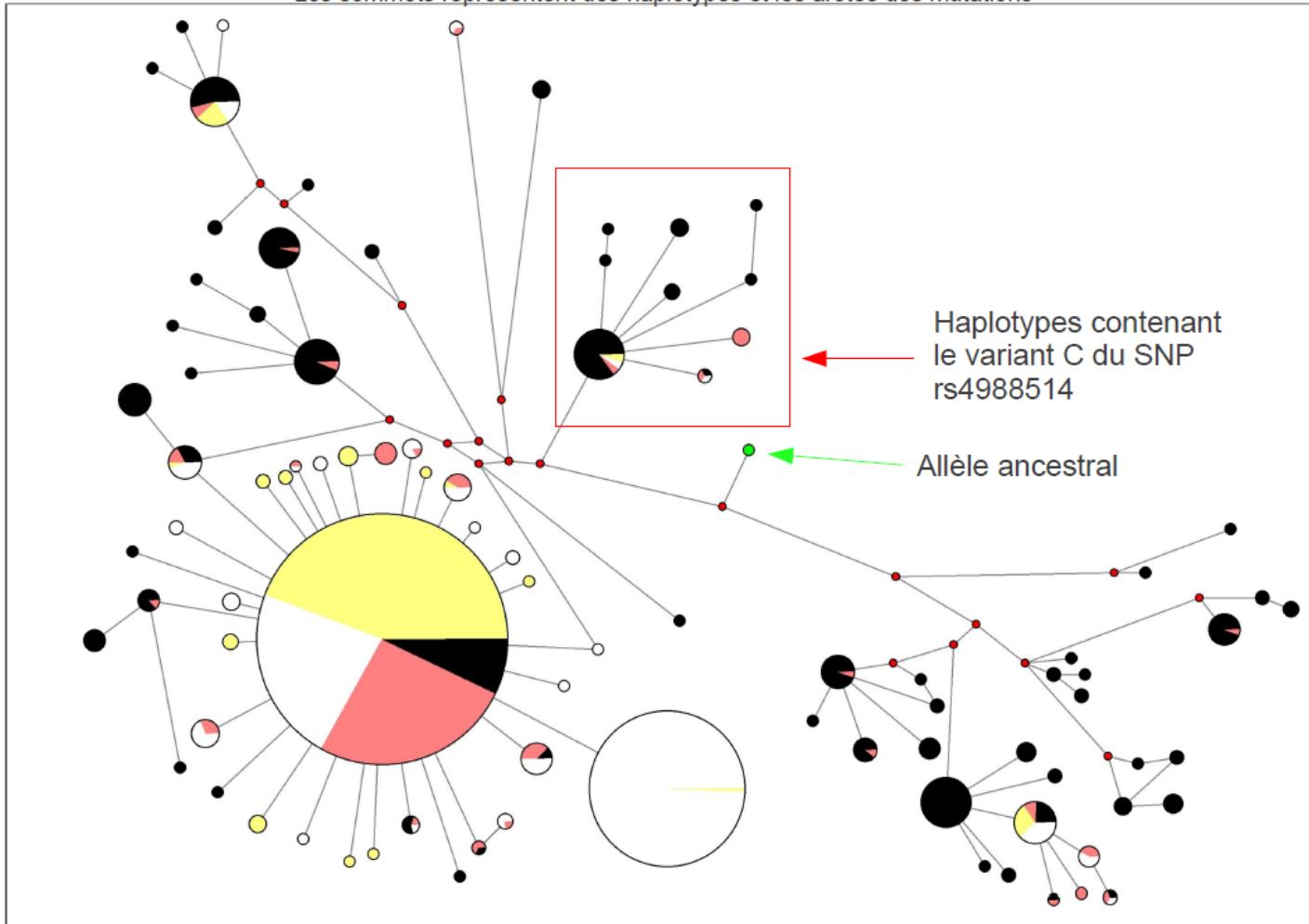
Alice THOMAS,
Yann LOE-MIE,
INSERM U894

Tal PUPKO
TEL AVIV UNIVERSITY



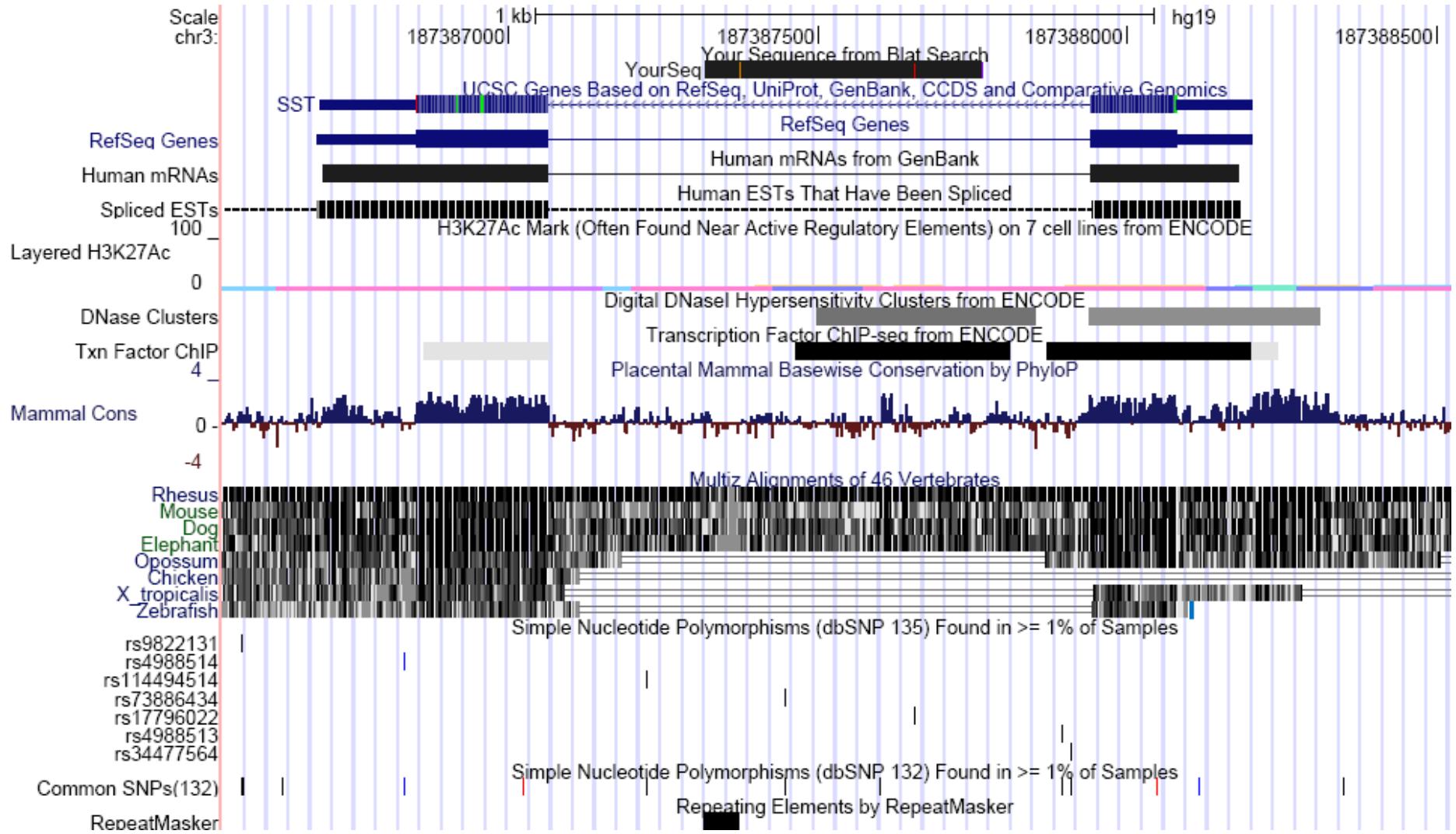
Représentation en réseau des allèles du bloc haplotypique du gène SST

Les sommets représentent des haplotypes et les arêtes des mutations



Données issues des 1000 génomes. L'allèle ancestral est calculé à partir d'un alignement homme, chimpanzé, macaque et gorille.

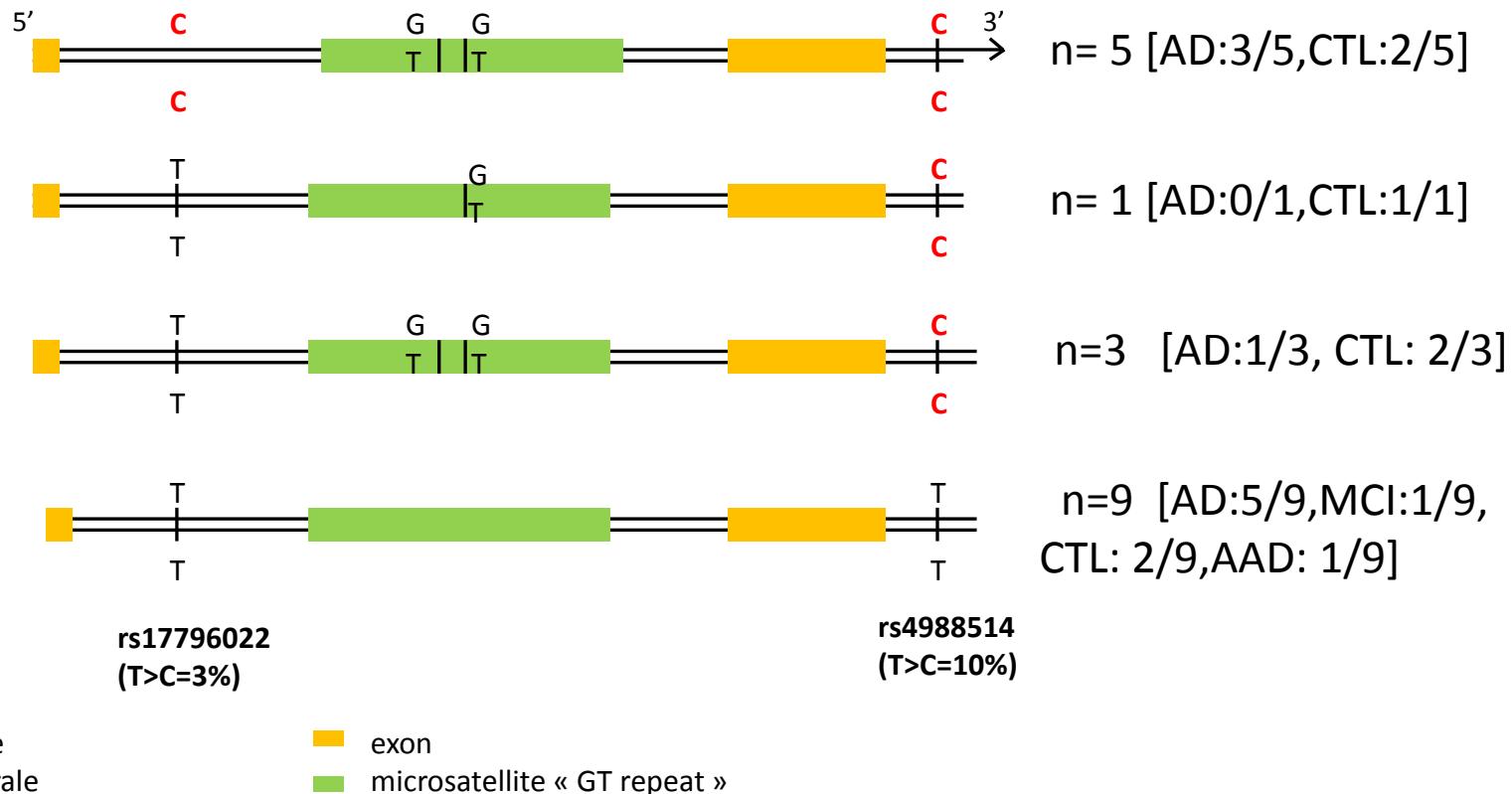
SST gene



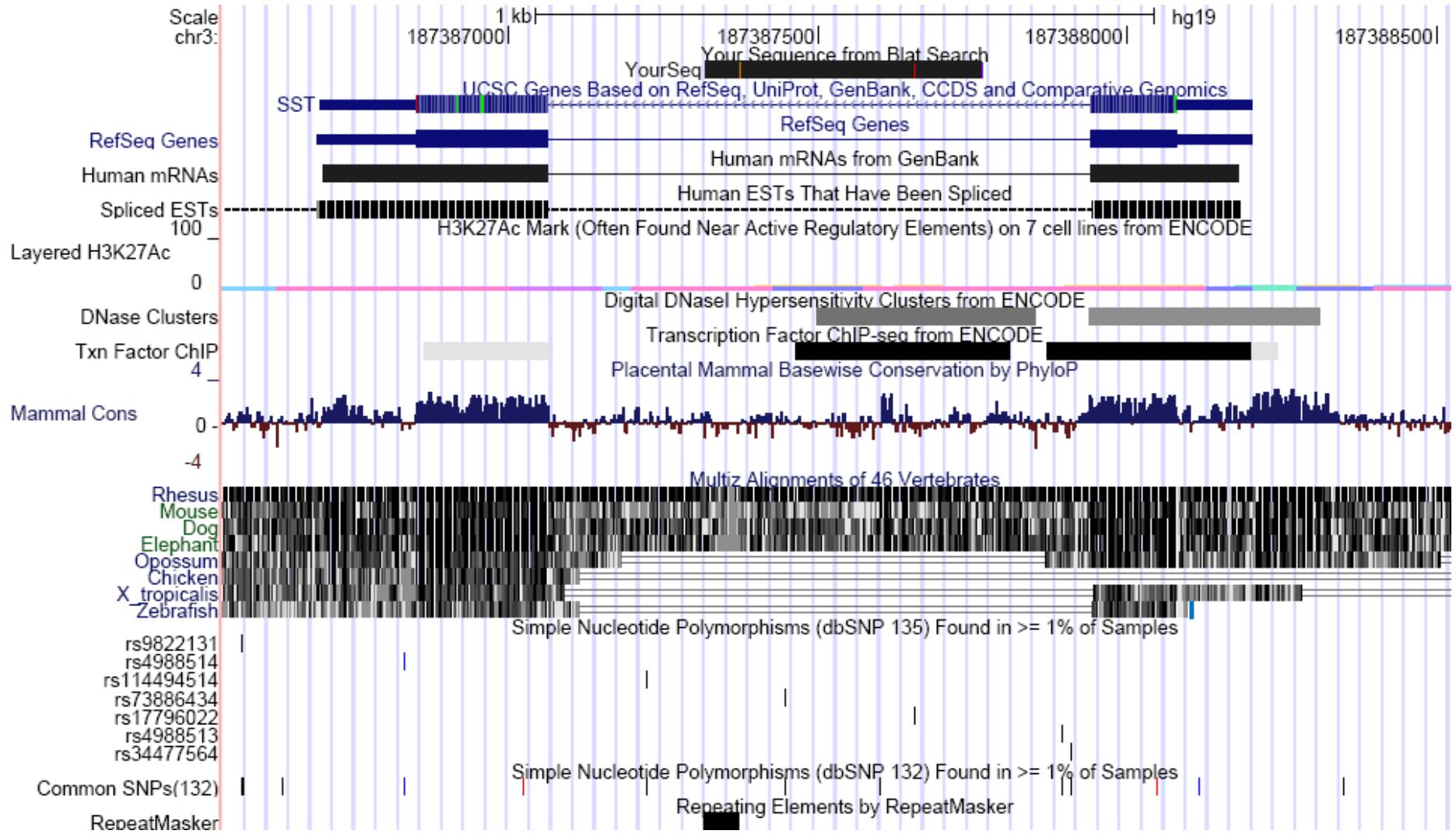


sequencing data

Schéma bilan séquençage Anvers 05.01.2012



SST gene



A Resource of Cre Driver Lines for Genetic Targeting of GABAergic Neurons in Cerebral Cortex

Hiroki Taniguchi,¹ Miao He,¹ Priscilla Wu,¹ Sangyong Kim,¹ Raehum Paik,¹ Ken Sugino,² Duda Kvitsani,¹ Yu Fu,¹ Jiangteng Lu,¹ Ying Lin,¹ Goichi Miyoshi,³ Yasuyuki Shima,² Gord Fishell,³ Sacha B. Nelson,² and Z. Josh Huang^{1,*}

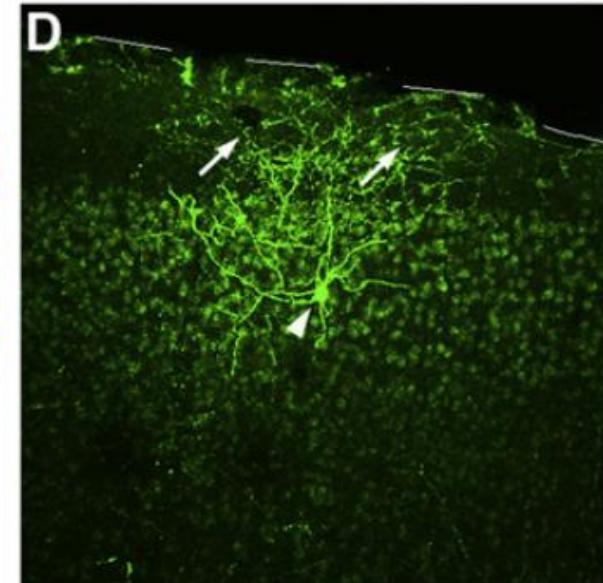
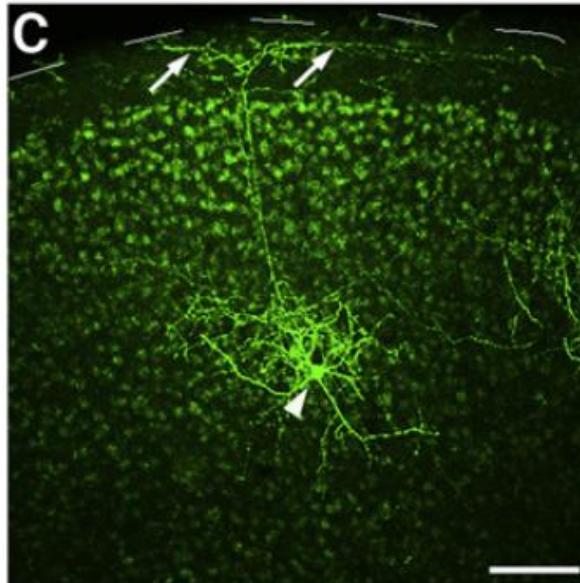
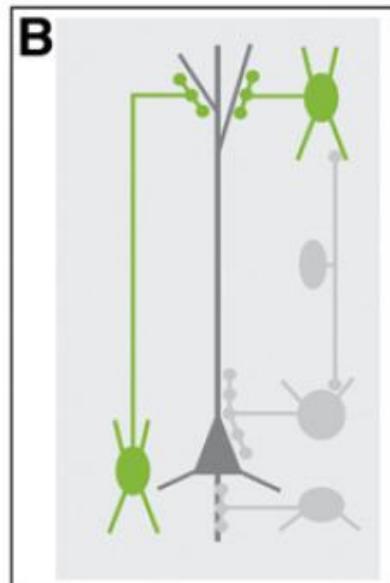
¹Cold Spring Harbor Laboratory, Cold Spring Harbor, NY 11724, USA

²Department of Biology and Center for Behavioral Genomics, Brandeis University, Waltham, MA 02154, USA

³Smilow Neuroscience Program, Department of Cell Biology, New York University Medical Center, New York, NY 10016, USA

*Correspondence: huangj@cshl.edu

DOI [10.1016/j.neuron.2011.07.026](https://doi.org/10.1016/j.neuron.2011.07.026)

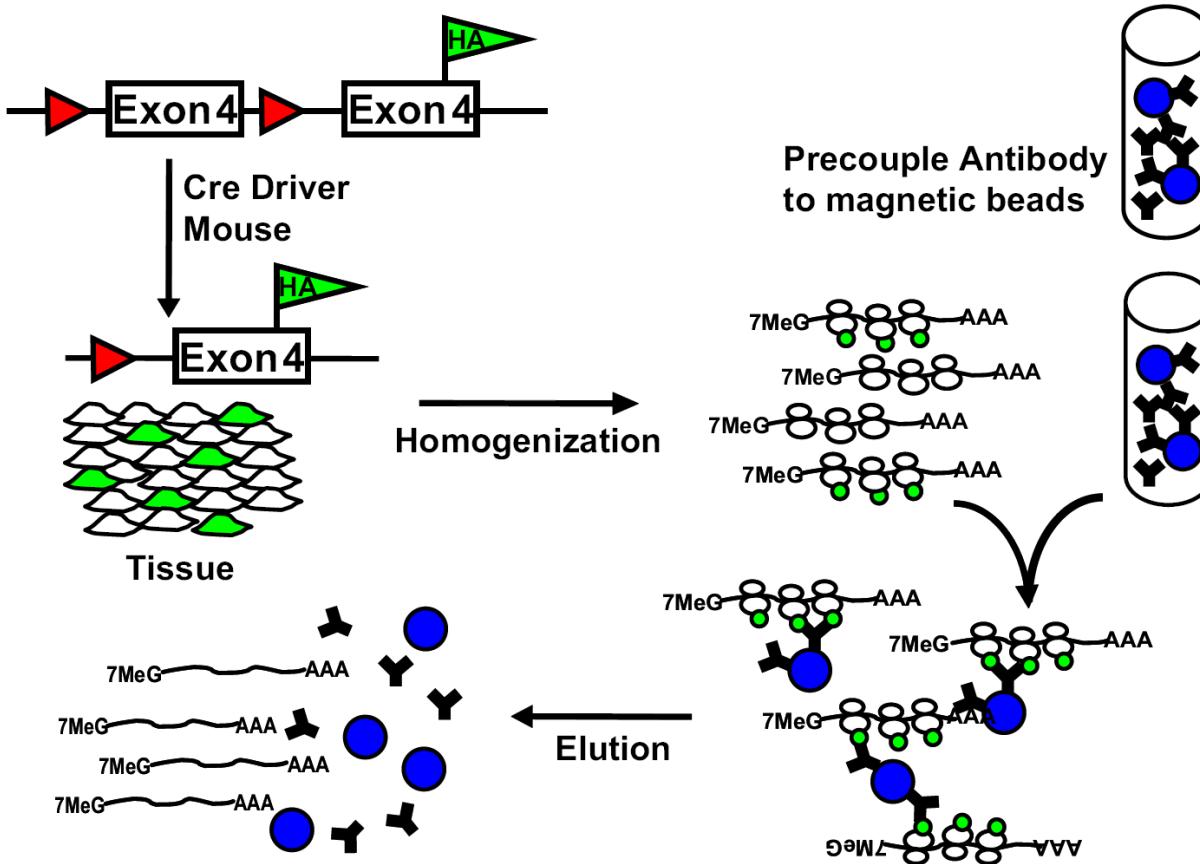


Cell-type-specific isolation of ribosome-associated mRNA from complex tissues

Elisenda Sanz^a, Linghai Yang^a, Thomas Su^a, David R. Morris^b, G. Stanley McKnight^a, and Paul S. Amieux^{a,1}

Departments of ^bBiochemistry and ^aPharmacology, University of Washington, Seattle, WA 98195

Communicated by Richard D. Palmiter, University of Washington School of Medicine, Seattle, WA, June 26, 2009 (received for review May 1, 2009)



4. Data mining



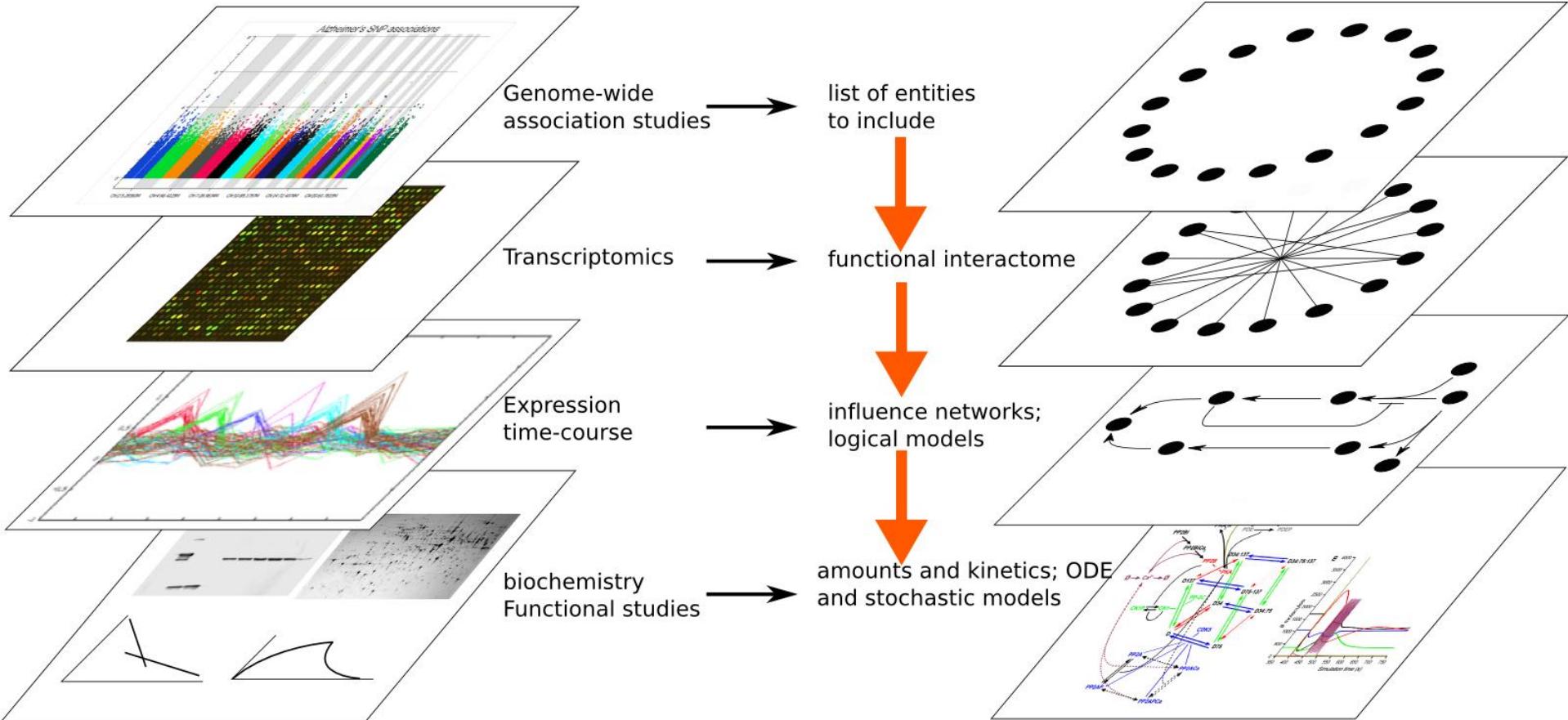
Quretech, Estonia Jaak VILO

EBI , Nicolas le NOVERE

SWISS PROT , Ioannis XENARIOS

Babraham Institute, Cambridge

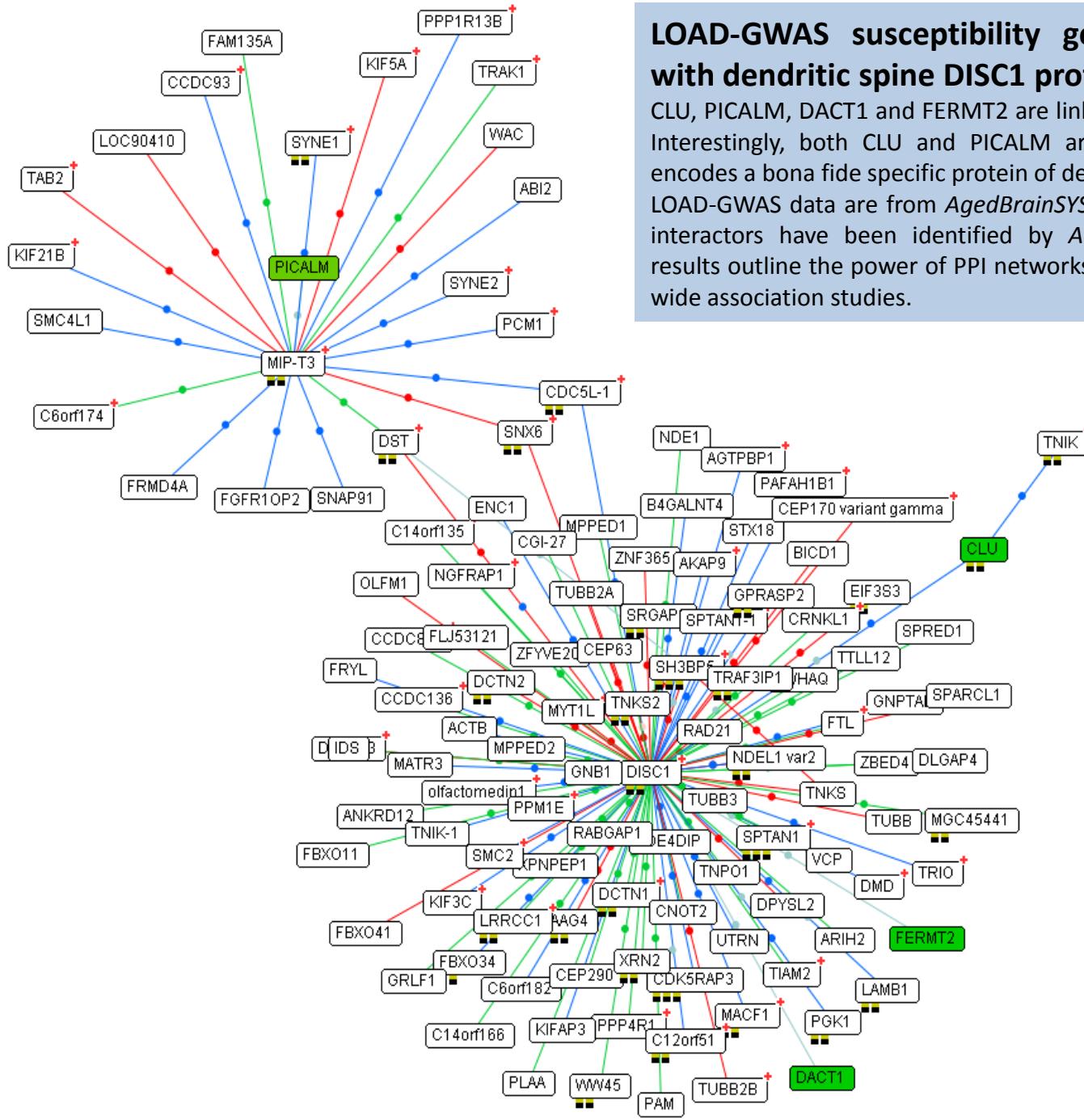
Tel-Aviv University, Tal PUPKO



LOAD-GWAS susceptibility gene products interacting with dendritic spine DISC1 protein interactors.

CLU, PICALM, DACT1 and FERMT2 are linked to this dendritic spine network. Interestingly, both CLU and PICALM are top list candidates and DACT1 encodes a bona fide specific protein of dendritic spine.

LOAD-GWAS data are from *AgedBrainSYSBIO* Partner 1, 2 and 3 and DISC1 interactors have been identified by *AgedBrainSYSBIO* Partner 7. These results outline the power of PPI networks to prioritize results from genome-wide association studies.

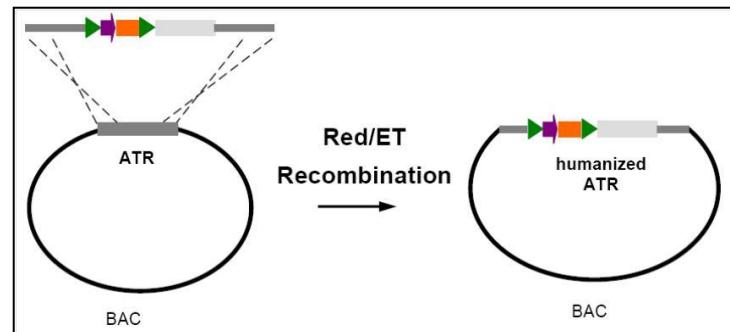
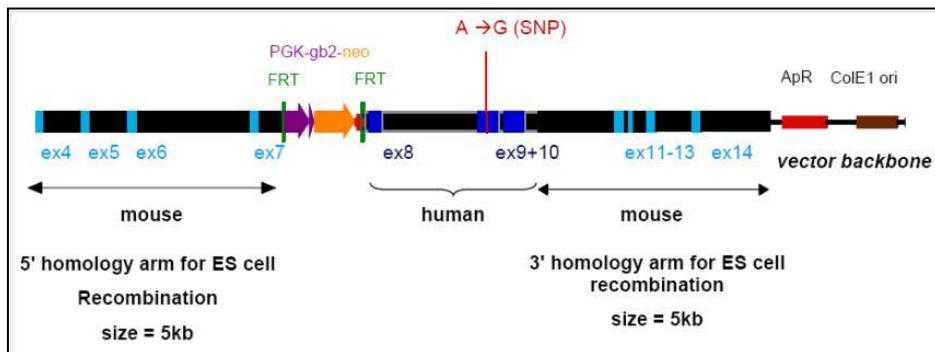


5. Modèles murins humanisés

Clinique de la souris, Illkirch



6. Drug discovery : ReMynd company, Belgium

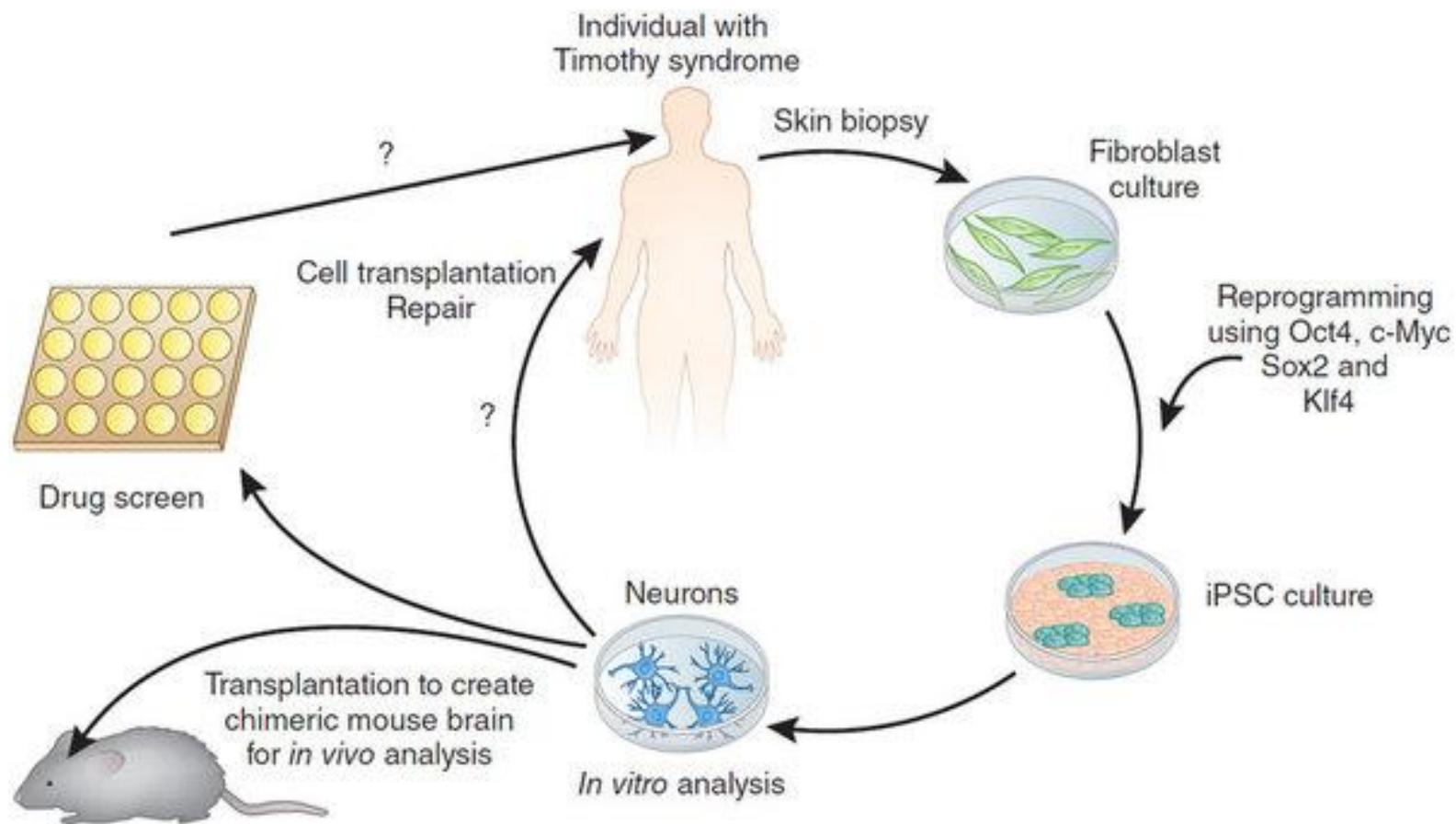


reMYND



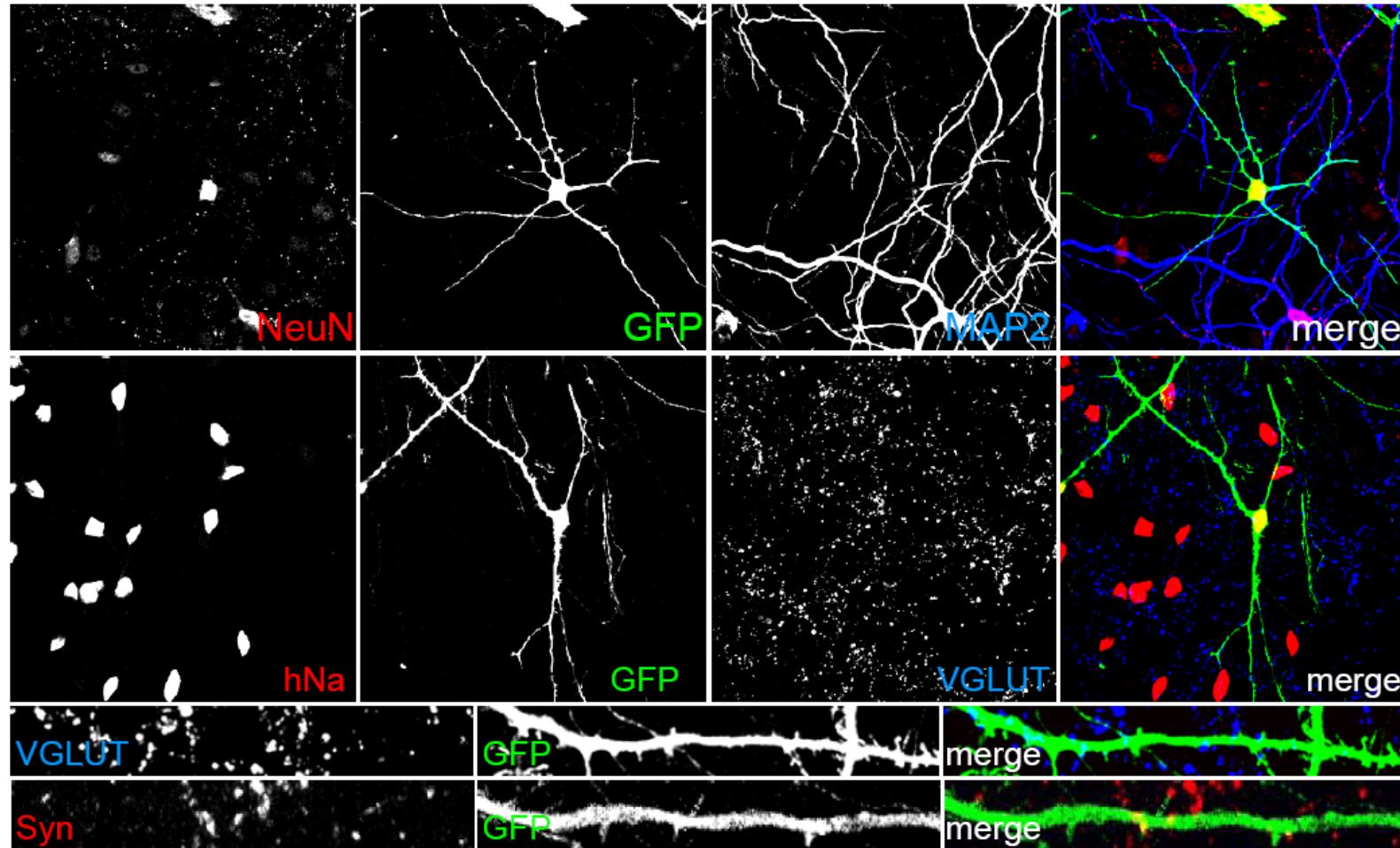
7. Initiative CH Sainte-Anne/INSERM/ Paris Descartes

Neurones humains dérivés de fibroblastes Des patients



Functional genomics & psychiatric diseases

Analysis of mutations in iPSCs-derived human neurons: Pr Carlo SALA, CNR, Milano



Human neurons derived from patients iPSCs (James Adjaye, MPI; Michel Simonneau INSERM U894)

