Phelan McDermid Syndrome: from mechanisms to treatments

Sindrome di Phelan McDermid: dai meccanismi patogenetici al trattamento

MAIN OBJECTIVES

OBBIETTIVI PRINCIPALI,

progetto proposto da Thomas Bougeron Istituto Pasteur, Parigi

1. Collecting and pooling existing clinical datasets on patients with PMS across Europe

Collezionare e assemblare tutti i dati clinici dei pazienti PMS europei

2. Producing novel high resolution genetic and clinical profiles of patients with PMS

Produrre un nuovo profilo genetico ad alta risoluzione e clinico dei pazienti PMS europei

3. Providing a resource for researchers to address informative questions on a larger scale

Creare una banca dati estesa che possa fornire informazioni su una larga scala di pazienti

4. Developing a European 'Trial-ready' network for PMS

Sviluppare un network subito disponibile per possibili trial clinici

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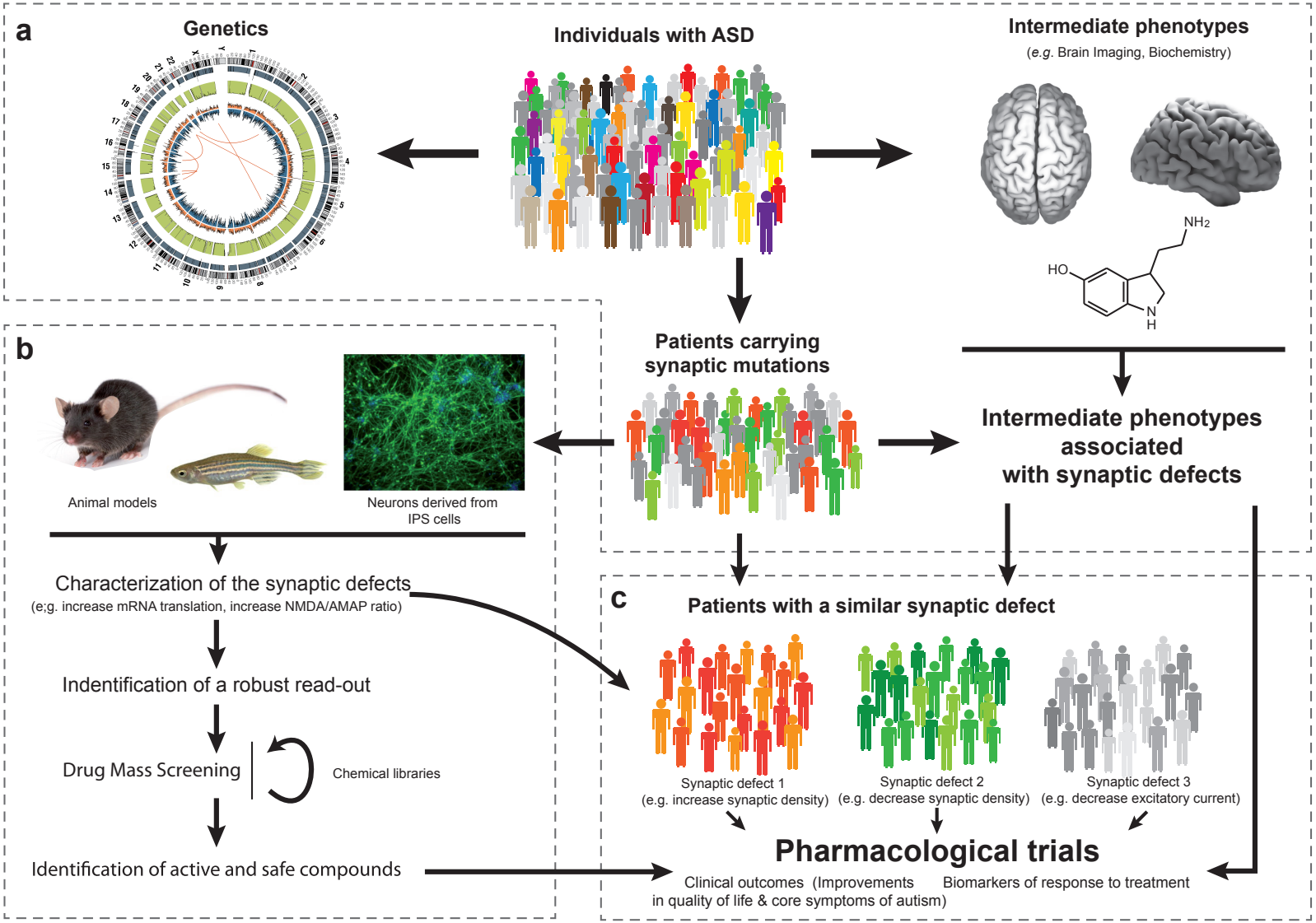
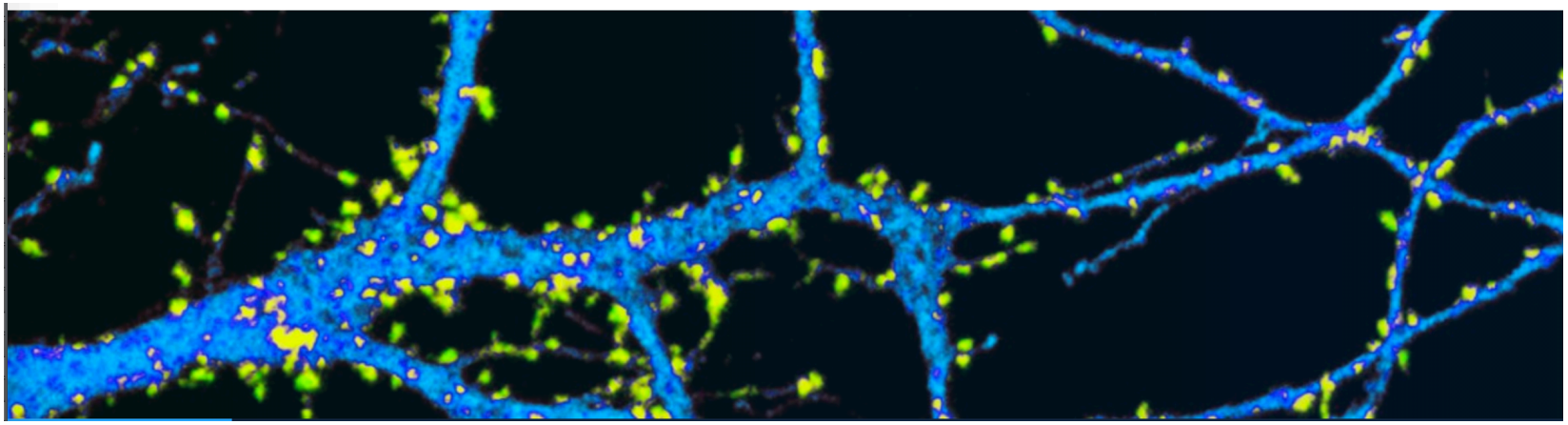
La strategia del progetto





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La diversità genetica e fenotipica dei pazienti con PMS in Europa

Al fine di identificare i fattori che possono modulare la gravità della sindrome, ci proponiamo di analizzare la relazione genotipo-fenotipo in tutti i pazienti con la sindrome PMS in Europa. Invece di concentrarsi sulla dimensione del 22q13 delezione, vogliamo analizzare l'intero genoma di tutti i pazienti con PMS.

Modelli cellulari e murini di PMS

Al fine di identificare i meccanismi causali coinvolti nella PMS, stiamo attualmente studiando i neuroni derivati da cellule staminali pluripotenti indotte (iPSC) dei pazienti con sindrome o con mutazioni de novo nel gene SHANK3 e modelli murini privi del gene SHANK3.

Foundations and collaborative groups

The Phelan-McDermid syndrome foundation in USA : http://www.pmsf.org

The Phelan-McDermid syndrome foundation in France: http://22q13.fr

The Phelan-McDermid syndrome foundation in Denmark : pmsf-danmark@youseeme.dk

The Phelan-McDermid syndrome foundation in UK: http://www.pmsf.org.uk

The Phelan-McDermid syndrome foundations in Italy: http://www.aisphem.it/; http://www.labbracciodiuma.it

The EU-AIMS: http://www.eu-aims.eu/

Clinicians/Geneticists

USA: Prof. Katy Phelan: https://tulane.edu/som/hayward-genetics/faculty/katy-phelan.cfm

France (Paris): Prof. Richard Delorme: https://research.pasteur.fr/en/member/richard-delorme/;
http://robertdebre.aphp.fr/equipes-cliniques/pole-pediatrie/psychopathologie-enfant-adolescent/

France (Paris): Dr. Anne Claude Tabet: http://robertdebre.aphp.fr/consultation/247/
France (Nimes): Prof. Serge Lumbroso: http://www.chu-nimes.fr/pole-biologies/laboratoire-de-biochimie.html
France (Angers): Prof. Dominique Bonneau :
https://www.chu-angers.fr/offre-de-soins/pr-dominique-bonneau-52344.kjsp

Belgique (Leuven): Prof. Hilde Van Esch: http://www.kuleuven.be/wieiswie/nl/person/00010621

Denmark (Odense) : Dr. Christina Fagerberg: http://www.ouh.dk

Netherland (Groningen): Prof. Conny van Ravenswaaij-Arts: 22q13@umcg.nl;
http://www.rug.nl/research/genetics/research/phelan-mcdermid-syndrome/

Germany (Ulm): : sarah.jesse@uni-ulm.de; michael.schoen@uni-ulm.de

United Kingdom (London): Eva Loth: eva.loth@kcl.ac.uk

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filippo.santorelli@fsm.unipi.it
Italy (Roma):Università Cattolica Sacro Cuore, Zollino Marcella: marcella.zollino@unicatt.it
Italy (Sicilia): Ospedale Oasi di Troina, Maurizio Elia: melia@oasi.en.it


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Università Cattolica Sacro Cuore
Bari
?
Troina
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Bolzano
Trento
Belluno
Aosta
Milano
Brescia
Verona
Padova
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Torino
Alessandria
Ferrara
Parma
Modena
Cuneo
Genova
Ravenna
Viareggio
Lucca
Firenze
Sanremo
Livorno
Ancona
Perugia
Foligno
Grosseto
Elba
Terni
Giglio
Pescara
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Mar Ionio
Cosenza
Cagliari
San Pietro
Sant'Antioco
Lamezia Terme
Catanzaro
Lipari
Trapani
Calabria
Marsala
Troina
Mar Mediterraneo
Agrigento
Catania
Sicilia
Ragusa
Siracusa
Pantelleria
MALTA
Lampedusa
0 50 100 150 km
0 20 40 60 mi

A framework to identify modifier genes in patients with Phelan-McDermid syndrome

Short running title: Mapping modifier genes in Phelan-McDermid Syndrome

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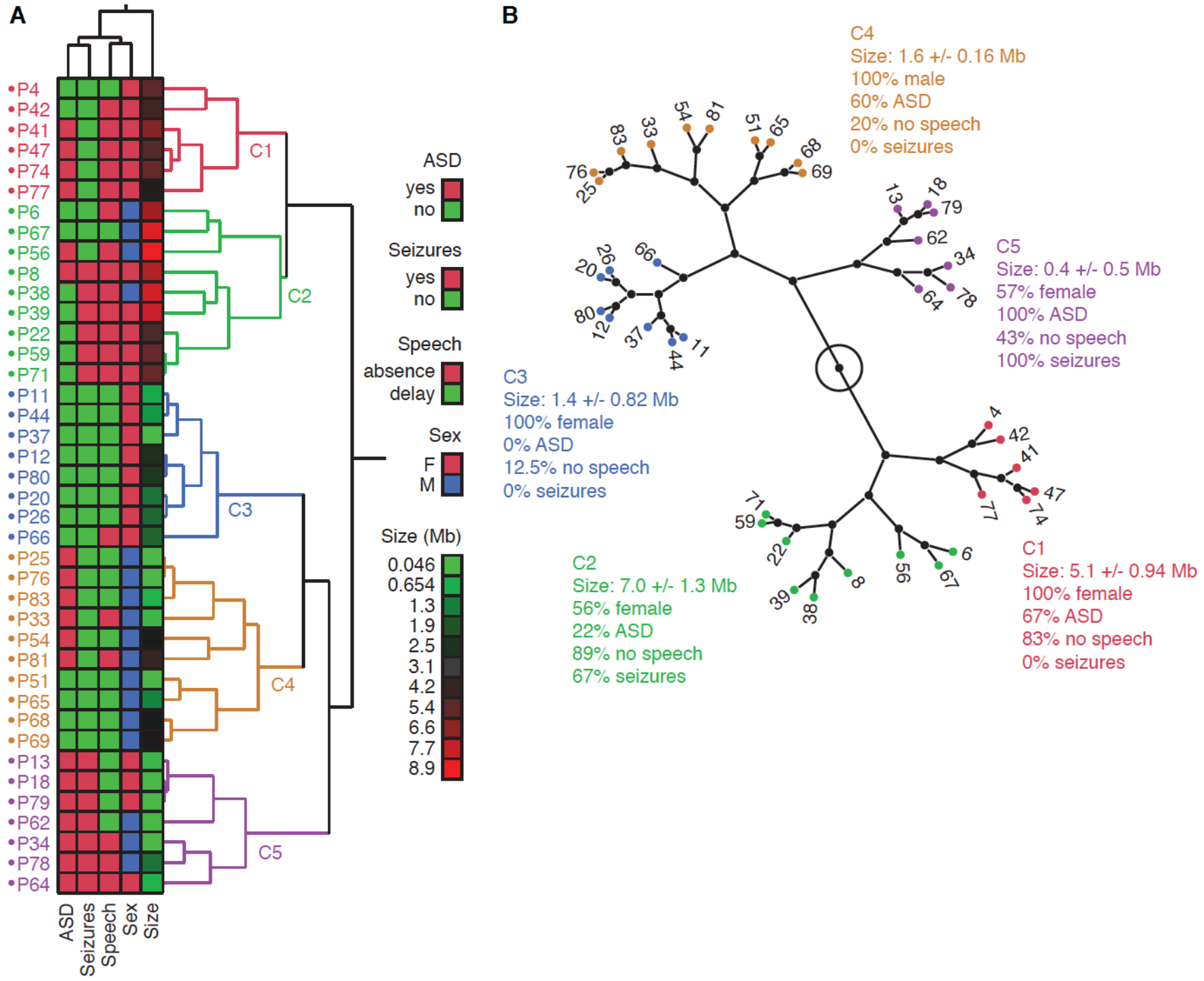
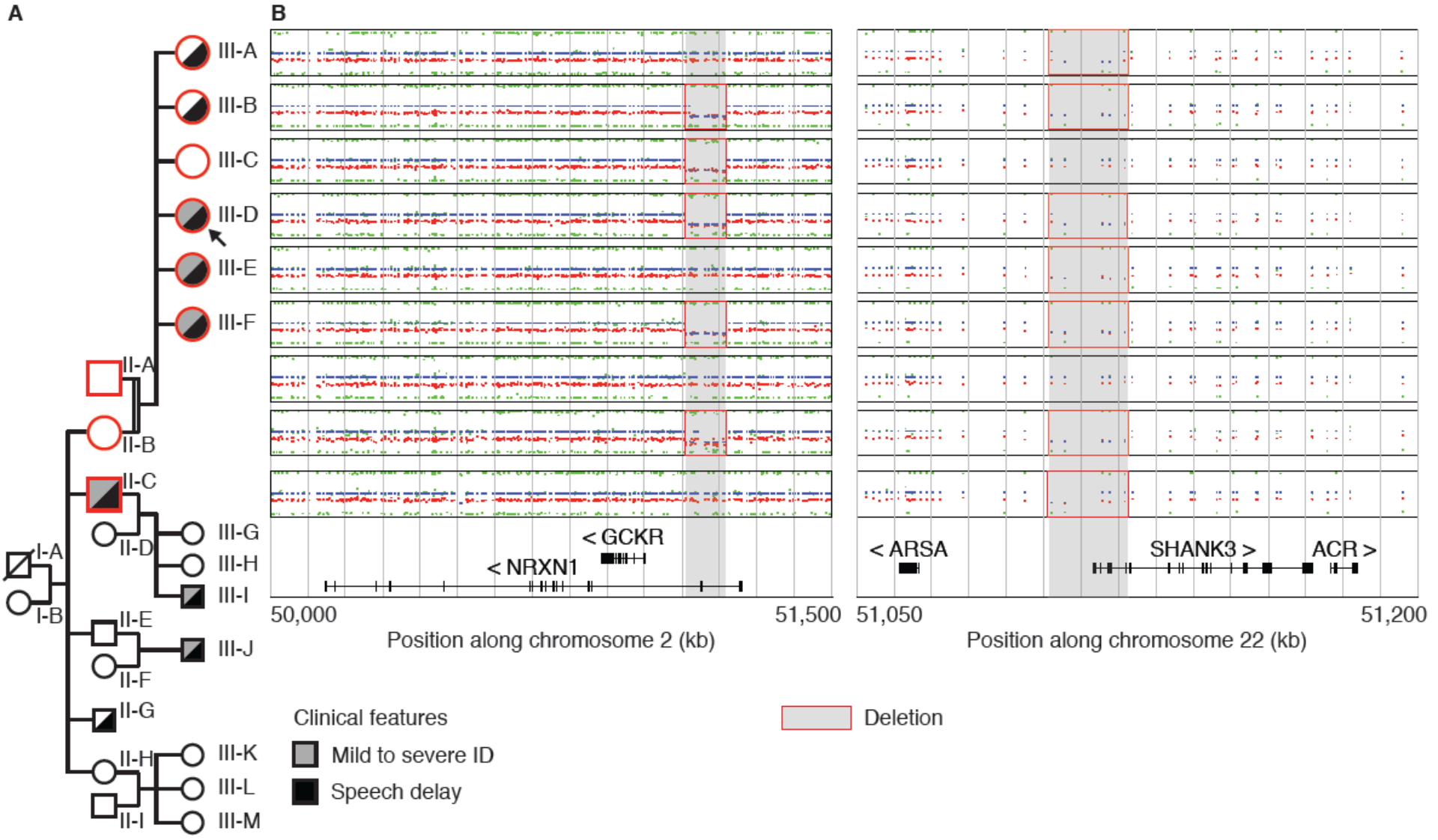
Population

Eighty-five patients (39 males, 44 females and two fetuses) carrying a genomic rearrangement at the 22q13 locus encompassing *SHANK3* were recruited through a French national network of cytogeneticists from 15 centers (ACHROPUCE network).


A
P4
P42
P41
P47
P74
P77
P6
P67
P56
P8
P38
P39
P22
P59
P71
P11
P44
P37
P12
P80
P20
P26
P66
P25
P76
P83
P33
P54
P81
P51
P65
P68
P69
P13
P18
P79
P62
P34
P78
P64
C1
C2
C3
C4
C5
ASD
Seizures
Speech
Sex
Size
ASD
yes
no
Seizures
yes
no
Speech
absence
delay
Sex
F
M
Size (Mb)
0.046
0.654
1.3
1.9
2.5
3.1
4.2
5.4
6.6
7.7
8.9
B
C4
Size: 1.6 +/- 0.16 Mb
100% male
60% ASD
20% no speech
0% seizures
C5
Size: 0.4 +/- 0.5 Mb
57% female
100% ASD
43% no speech
100% seizures
C3
Size: 1.4 +/- 0.82 Mb
100% female
0% ASD
12.5% no speech
0% seizures
C2
Size: 7.0 +/- 1.3 Mb
56% female
22% ASD
89% no speech
67% seizures
C1
Size: 5.1 +/- 0.94 Mb
100% female
67% ASD
83% no speech
0% seizures


A
B
III-A
III-B
III-C
III-D
III-E
III-F
II-A
II-B
II-C
II-D
III-G
III-H
III-I
I-A
I-B
II-E
III-J
II-F
II-G
II-H
III-K
III-L
II-I
III-M
< GCKR
< NRXN1
50,000
51,500
Position along chromosome 2 (kb)
< ARSA
SHANK3 >
ACR >
51,050
51,200
Position along chromosome 22 (kb)
Clinical features
Mild to severe ID
Speech delay
Deletion

Cosa fatto e cosa potremmo fare

Identificati quattro centri clinici italiani in grado di:

- raccogliere campioni di sangue dei pazienti, genitori e fratelli/sorelle sani

- separare il DNA dai campioni di sangue

- raccogliere i dati clinici

- sottoporre il protocollo ai comitati etici