



National Alliance
for Life and Health Sciences

ITMO Genetics, Genomics
and Bioinformatics

**NATIONAL AND STRATIFIED DEVELOPMENT
OF GENOMIC MEDICINE
IN FRANCE**



HUMAN GENETICS IN THE POST-NGS ERA : THE CHALLENGE OF GENETIC VARIATION INTERPRETATION

Per exome
34 Mb : **1.2%** of the total genome



- ✓ **20000 Single Nucleotide Variations (SNV)**
- ✓ **500 rare (<0.1%) SNVs not present in the data bases**
- ✓ **1 *de novo* SNV with potential impact *per* generation**

Main medical challenge :
Interpretation of rare genetic variations

Statistical analyses

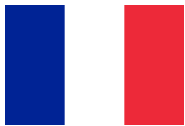


Phenotypic evaluation

**Development of
national clinical and molecular genetics
networks**

Animal models





I. THE FRENCH PLAN FOR RARE DISEASES



25 million European Citizen
3.5 million French Citizen

2011 - 2014

Plan national maladies rares

Qualité de la prise en charge, Recherche, Europe : une ambition renouvelée

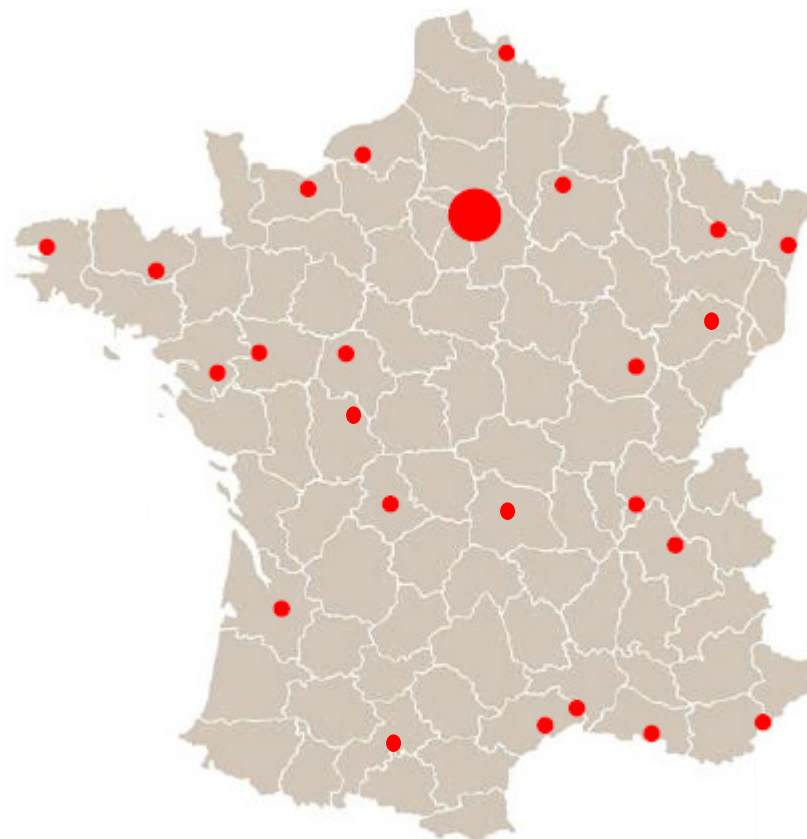
Axes, Mesures, Actions

MINISTÈRE DE L'ÉCONOMIE, DES FINANCES ET DE L'INDUSTRIE

MINISTÈRE DE L'ÉDUCATION SUPÉRIEURE ET DE LA RECHERCHE

MINISTÈRE DES SOLIDARITÉS ET DE LA COHÉSION SOCIALE

MINISTÈRE DU TRAVAIL, DE L'EMPLOI ET DE LA SANTÉ

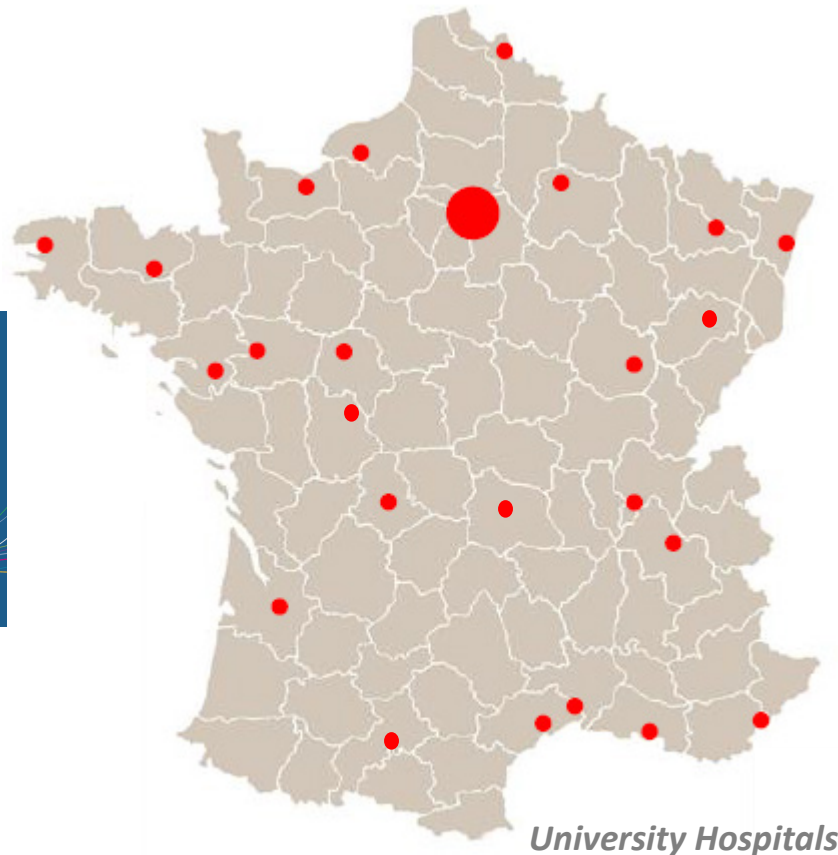


French population : 65.026.885



The National Organization

IA. CREATION OF A NATIONAL NETWORK OF REFERENCE AND COMPETENCE CLINICAL CENTERS FOR RARE DISEASES



1. **Systemic and auto-immune disorders**
2. **Cardio-vascular diseases**
3. **Abnormal development and related syndromes**
4. **Rare skin diseases**
5. **Endocrine diseases**
6. **Gastrointestinal and liver diseases**
7. **Metabolic diseases**
8. **Rare neurological diseases**
9. **Neuro-muscular diseases**
10. **Rare Lung diseases**
11. **Sensorial diseases**
12. **Haematologic non malignant rare diseases**
13. **Rare kidney diseases**
14. **Rare bone diseases**
15. **Rare immune diseases**
16. **Conjunctive rare diseases**
17. **Head and neck malformations**
18. **Others**

131 Reference Centers
500 Competence Centers

IB. CREATION OF A NATIONAL NETWORK OF MOLECULAR GENETICS LABORATORIES



Ministry of
Health and Solidarity



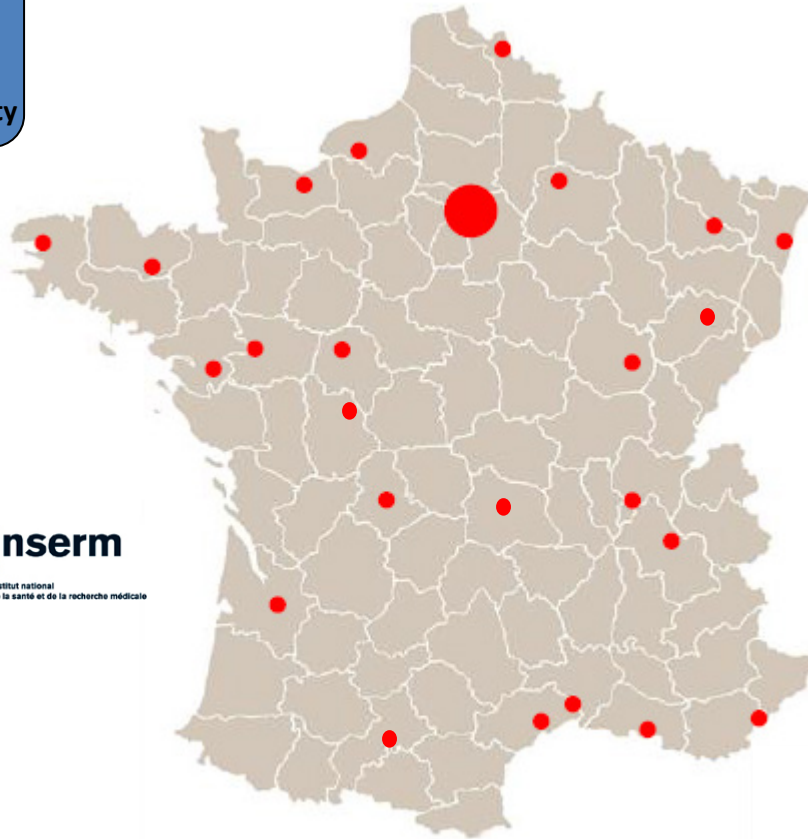
National
Association
of Molecular
Geneticists

Inserm

Institut national
de la santé et de la recherche médicale



2012 :
Targeted NGS



110 molecular genetics
laboratories

1. Cystic fibrosis
2. Muscular – Neuromuscular
3. Neurogenetics
4. Intellectual Deficiency
5. Cardiomyopathies
6. Mitochondrial diseases
7. Metabolism
8. Endocrinology
9. Development
10. Hematology
11. Immune Deficiency
12. Cardiovascular - Renal

✓ **1250** monogenic disorders
✓ **1343** genes analyzed
✓ **416.767** genetic analyses/year

IC. THE FRENCH FOUNDATION FOR RARE DISEASES



FRENCH FOUNDATION FOR
rare diseases

www.fondation-maladiesrares.org

Nicolas Levy

6 major areas of intervention

**Promoting Research
on rare diseases**



**Ministry of
Higher Education
and Research**

**Creating links
between
research and
healthcare
professionals**

**Improving the
access to
resources :**
- Expertise
- Technologies
- Funding

**Promoting
clinical and
biological data
collection**

**Supporting
early stages
of clinical
trials**

**Encouraging
research on
social and
human
sciences**

**Contributing
to national
and
international
policies**

*a non-profit private structure that
coordinates, federates and funds rare diseases research
to accelerate scientific, medical and social innovations*

February 2012

The National Organization

IC. BOOSTING ACCESS TO INTER-REGIONAL PLATFORMS OF HIGH THROUGHPUT NGS FOR EXOME ANALYSES

Biogenouest genomic platform, Nantes
<http://www.pf-genomique.univ-nantes.fr>

Imagine Institut Necker, Paris
<http://www.necker.fr/irnem>

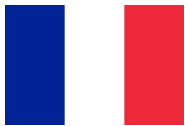
2 open calls 2012,2013
77 funded projects
1130 exomes

Integragen, Evry
<http://www.integragen.com>

IGBMC, Strasbourg
<http://www.igbmc.fr/technologies>

Genomic Institut
Evry <http://www.cng.fr/>





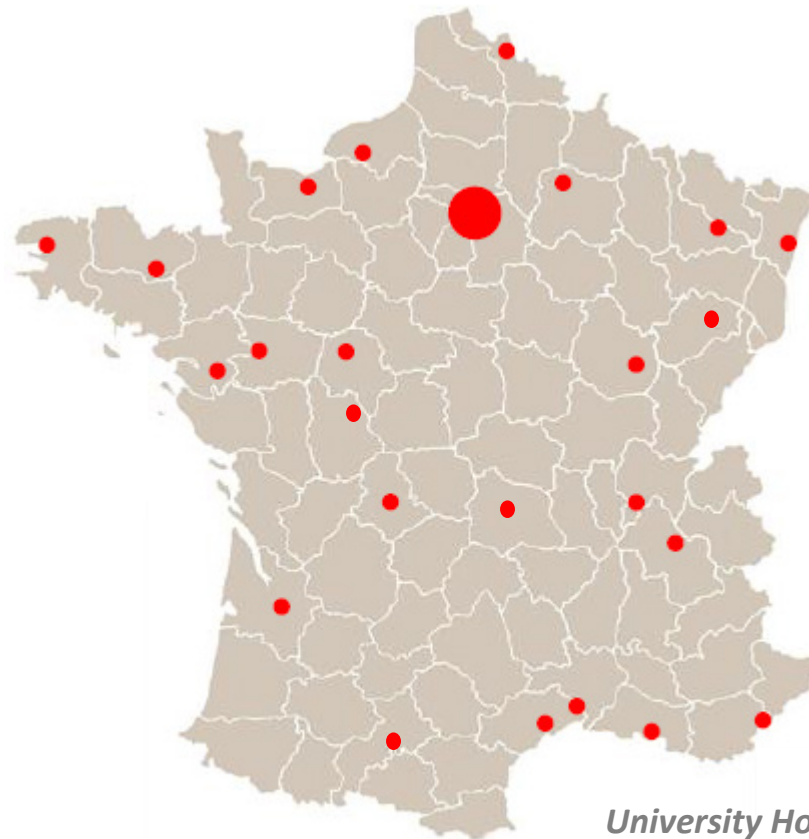
II. THE FRENCH PLAN FOR CANCER



2009

2013

Plan cancer



*University Hospitals
Comprehensive Cancer Centres*



Organization of **Cancer Genetics**



The National Organization

IIA. CREATION OF A NATIONAL NETWORK OF CLINICAL CANCER GENETICS CENTERS FOR INHERITED FORMS OF CANCER

Plan cancer

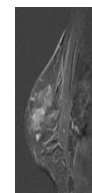
2009

2013

Plan cancer



INSTITUT NATIONAL DU CANCER



60
clinical cancer genetics centers



44.000 /year

Main clinical cancer genetics centres

Secondary clinical cancer genetics centres

The National Organization

IIB. CREATION OF A NATIONAL NETWORK OF MOLECULAR GENETICS LABORATORIES FOR INHERITED FORMS OF CANCER

Plan cancer

2009

2013

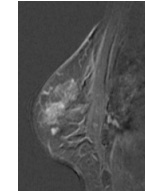
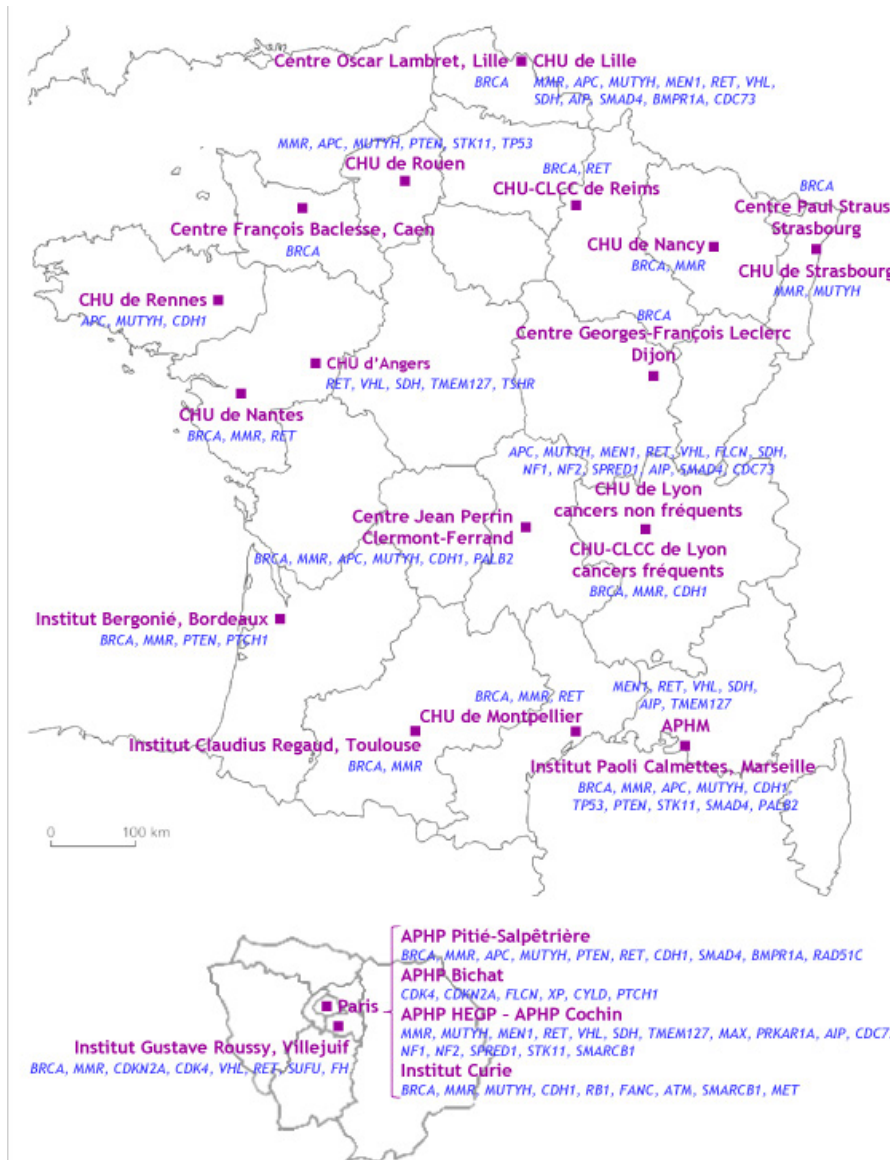
Plan cancer



INSTITUT NATIONAL DU CANCER

Laboratories

Tested genes



25
laboratories



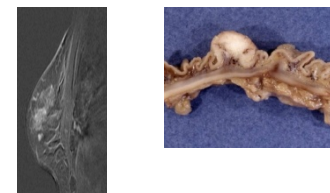
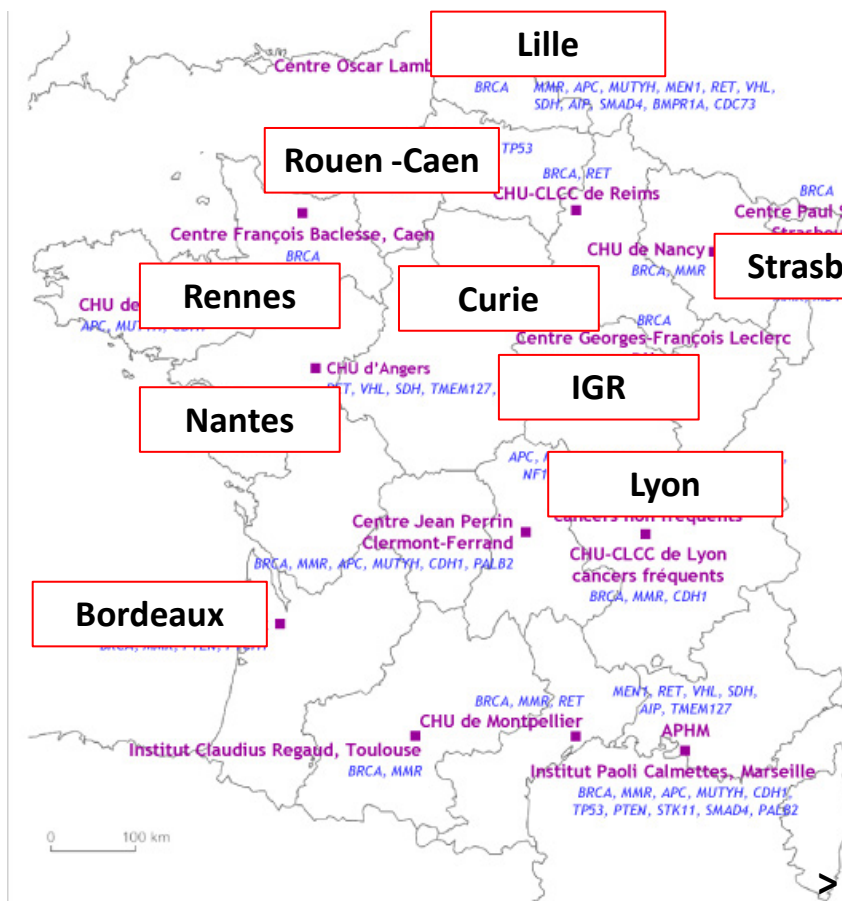
73 genes analyzed
60.000 genetic analyses/year

The National Organization

IIC. STRUCTURING NEXT GENERATION SEQUENCING FOR DIAGNOSTIC IN CANCER



Fabien Calvo



December 2013

9 NGS and bioinformatics facilities :

- > Genomic analyses
- > Training to bioinformatic analyses



THE NEED TO DEVELOP HIGHTROUGHPUT NGS FACILITY

Diagnosis

Research

Mean throughput

High throughput

Very high throughput

I. Targeted analyses Capture/amplicons

Exonic alterations
of genes involved
in monogenic disorders



National network
of molecular genetics
laboratories

II. Exome analyses

Private and new
exonic alterations



Inter-Regional
NGS Platforms

III. Exome and genome analyses

- ✓ Genetic bases of diseases
- ✓ New types of alterations
(ncRNA, structural rearrangements...)
- ✓ Genome analysis
- ✓ Epigenetic alterations



National NGS Platform
10 000 - 50 000 exomes /year

The Future Development

HIGH THROUGHPUT CAPACITY OF THE NATIONAL CENTER OF GENOMICS - EVRY

2nd European sequencing facility



> **3** HiSeq 2500

> **8 + 6** HiSeq 2000

> **1** Proton

> **11** Miseq

✓ **6600** Gb (raw data) in 2 weeks

✓ **440** Gb *per day*

✓ **30x** Whole Genome = 100 Gb

CEA world class

High Performance Computing Center

Total capacity

> **120 000** computing cores

~ **2-3** Petaflops

Dedicated to Genomics

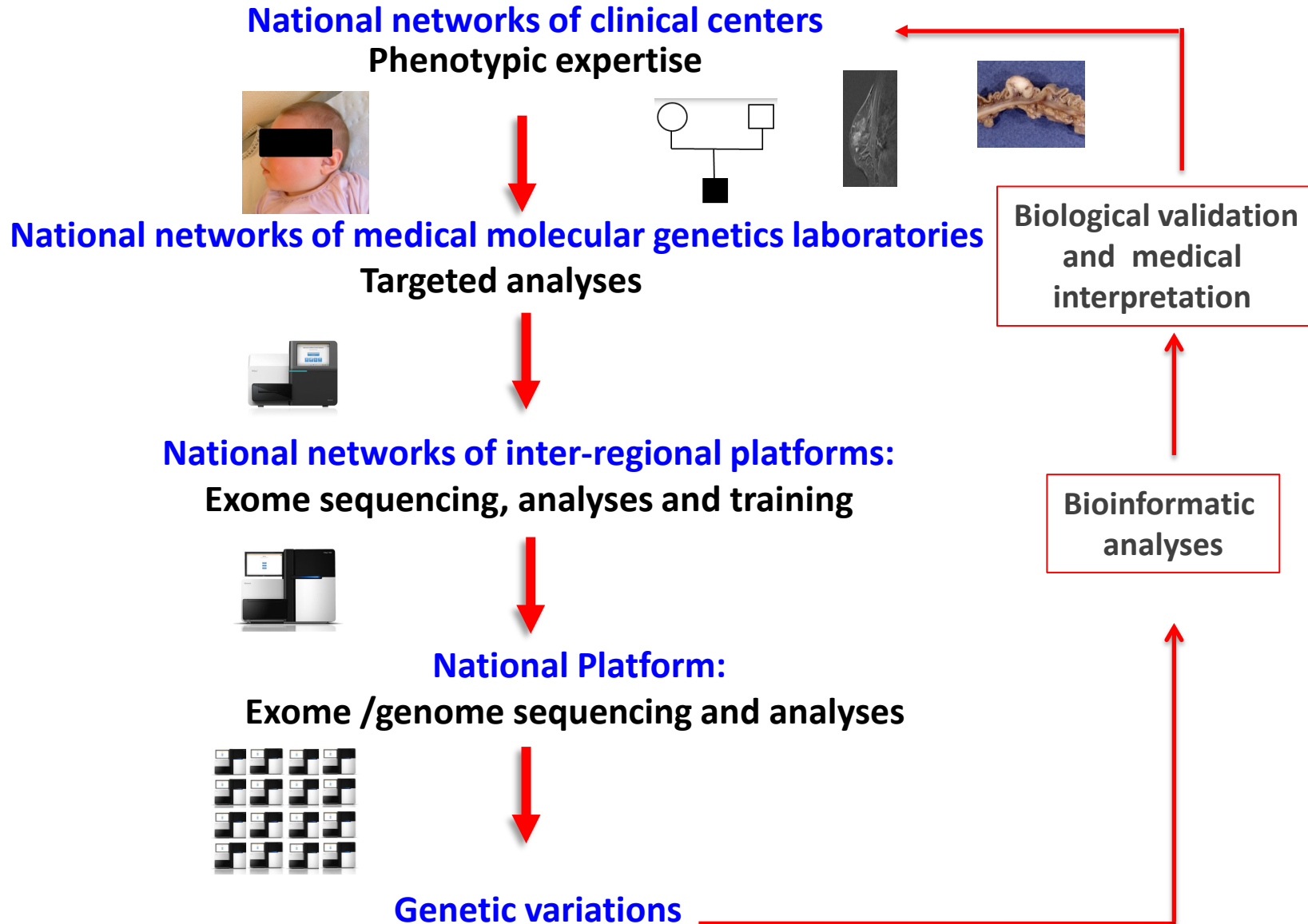
✓ **3000** cores

✓ **5** petabytes

✓ Exome and WGS analysis



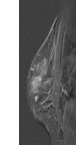
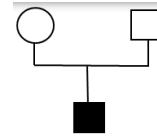
NATIONAL AND STRATIFIED DEVELOPMENT OF GENOMIC MEDICINE



NATIONAL AND STRATIFIED DEVELOPMENT OF GENOMIC MEDICINE

Genomic Medicine

National networks of clinical centers
Phenotypic expertise



National networks of medical molecular genetics laboratories

Biological validation and medical interpretation

Genomic Research

Targeted analyses



Inserm

Institut national de la santé et de la recherche médicale

National networks of inter-regional platforms:

Exome sequencing, analyses and training



aviesan

alliance nationale pour les sciences de la vie et de la santé

Bioinformatic analyses



National Platform:

Exome /genome sequencing and analyses



- ✓ Genetic determinism
- ✓ Molecular bases
- ✓ Bioinformatics
- ✓ Biostatistics

Genetic variations

