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

- **20,000** 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
- Animal models

Development of national clinical and molecular genetics networks

*The Scientific Context*
I. THE FRENCH PLAN FOR RARE DISEASES

25 million European Citizen
3.5 million French Citizen

French population: 65,026,885
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

The National Organization
IB. CREATION OF A NATIONAL NETWORK OF MOLECULAR GENETICS LABORATORIES

- **110 molecular genetics laboratories**
- **1250 monogenic disorders**
- **1343 genes analyzed**
- **416,767 genetic analyses/year**

**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**

The National Organization

Ministry of Health and Solidarity

National Association of Molecular Geneticists

2012: Targeted NGS
IC. THE FRENCH FOUNDATION FOR RARE DISEASES

Promoting Research on rare diseases

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

www.fondation-maladiesrares.org
Nicolas Levy

6 major areas of intervention

February 2012

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

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

- **Biogenouest genomic platform, Nantes**
- **Imagine Institut Necker, Paris**
  - [http://www.necker.fr/irnem](http://www.necker.fr/irnem)
- **IGBMC, Strasbourg**
  - [http://www.igbmc.fr/technologies](http://www.igbmc.fr/technologies)
- **Integragen, Evry**
  - [http://www.integragen.com](http://www.integragen.com)
- **Genomic Institut Evry**

2 open calls 2012, 2013
77 funded projects
**1130 exomes**
II. THE FRENCH PLAN FOR CANCER

Plan cancer

2009 - 2013

University Hospitals
Comprehensive Cancer Centres

Organization of Cancer Genetics

Ministry of Health and Solidarity

Ministry of Higher Education and Research

Institut National du Cancer

Inserm

National Alliance for Life and Health Sciences

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

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

The National Organization

25 laboratories

73 genes analyzed
60,000 genetic analyses/year
IIC. STRUCTURING NEXT GENERATION SEQUENCING FOR DIAGNOSTIC IN CANCER

December 2013

9 NGS and bioinformatics facilities:
- Genomic analyses
- Training to bioinformatic analyses

Fabien Calvo
THE NEED TO DEVELOP HIGH THROUGHPUT NGS FACILITY

I. Targeted analyses
- Capture/amplicons
  - Exonic alterations of genes involved in monogenic disorders

II. Exome analyses
- Private and new exonic alterations

III. Exome and genome analyses
- Genetic bases of diseases
- New types of alterations (ncRNA, structural rearrangements...)
  - Genome analysis
  - Epigenetic alterations

National network of molecular genetics laboratories

Inter-Regional NGS Platforms

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

Jean-François Deleuze
NATIONAL AND STRATIFIED DEVELOPMENT OF GENOMIC MEDICINE

National networks of clinical centers
Phenotypic expertise

National networks of medical molecular genetics laboratories
Targeted analyses

National networks of inter-regional platforms:
Exome sequencing, analyses and training

National Platform:
Exome /genome sequencing and analyses

Genetic variations

Biological validation and medical interpretation

Bioinformatic analyses
NATIONAL AND STRATIFIED DEVELOPMENT OF GENOMIC MEDICINE

National networks of clinical centers
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National networks of medical molecular genetics laboratories
Targeted analyses

National networks of inter-regional platforms:
Exome sequencing, analyses and training

Genomic Research

Genomic Medicine

Ministry of Health and Solidarity
Ministry of Higher Education and Research

Genetic determinism
✓ Molecular bases
✓ Bioinformatics
✓ Biostatistics

Genetic variations

Biological validation and medical interpretation

Bioinformatic analyses