Genomic Medicine in France

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Advancing Disease Modeling in Animal-Based research in Support of Precision Medicine: a Workshop

ILAR Roundtable, October 5-6, 2017
**Genomic Medicine: A Reality Revolutionizing Healthcare Pathways**

- Will this immunotherapy be effective at this stage of the disease?
- What rare disease does this patient have?
- Can we predict the evolution of diabetes in this individual?
- What treatment is best suited for this patient?
- Will this treatment be tolerated?
The Prime Minister entrusted Aviesan with the task of examining the current landscape for incorporating genome sequencing in the context of the healthcare pathway by touching on the following four points in his mission statement:

1. Defining the presence and importance of genomic sequencing in current medical practices as well as expected future developments in the coming 10 years.

2. Evaluating France’s positioning in the field of genomic research and its role in current health plans and priorities to be implemented in line with national strategies for health and research.

3. Evaluating the issues related to innovation and technology transfer and economic growth, taking into account technological aspects, management of large data sets and ethical implications.

4. Proposing a long-term medico-economic model integrating coverage by medical insurance and the establishment of an industrial sector to support such an initiative.
A Co-Constructed National Plan

More than 160 people mobilized under an Aviesan presidency

- Institutional representatives
- Transversal competences across fields of research, health and industry
- Research and health agencies
- Central administrations of ministries
- Representatives from the industry (Ariis, IT,...)
- CNAM and HAS
- CGI,
- Toulouse School of Economics...
STATE OF THE ART IN FRANCE

- An existing Genomics program (60M€) funded by Equipex, Labex
- Genopole Evry, CEA: CNG, CNS: 2nd European sequencing center (17 machines): sequencing of 3 whole genomes/day costing 3k€
- Informatic storage capabilities
- 28 INCa genomic platforms dedicated to cancer care

The Report showed...

- **A favorable environment for development of personalized medicine** (structured health system, clinical link – long-term research, research competitiveness, presence of industrial sector, ...)
- The definition of a French National Strategy needs a strong governmental commitment
Ambition of the French Genomic Medicine Plan 2025

- Integrate sequencing in the routine and clinical practice
  Implement a general healthcare pathway for all French patients with cancer, rare diseases or common diseases that includes access to genomic medicine for all those concerned (patients and eventually family members depending on diagnosis) by 2025

- Develop a national genomic medicine sector
  Place France amongst the leading countries in the field of genomic medicine in the next ten years in order to export its expertise developed in this area and establish a medical and industrial sector of genomic medicine.
Ambition of the French Genomic Medicine Plan 2025

- Integrate sequencing in the routine and clinical practice

- Develop a national genomic medicine sector

The proposition should lead to a long term medico-economic model
Integrating:
  - coverage by medical insurance
  - The establishment of an industrial sector to support such an initiative.
INTEGRATE SEQUENCING INTO A GENERIC HEALTHCARE PATHWAY

Request for exam, pre-analytic, analytic, biological interpretation, returned

Patient/doctor dialogue
Shared decisions

Request for exam Agreement

Pre-analytic sampling

Clinical data

Genomic data

Support tools for analysis

Sequences analyzed

Technical validation

Research

Support for the diagnostic decision

Support for the therapeutic decision

National database of Clinico-biological Meta-data

“Diagnostic Laboratory”

Biological validation and interpretation
Challenges on the 2020 horizon

**Patient: personalized treatments**
- A diagnosis based on the integration of genomic data with all classical clinical data
- Adequate care by the health care system (information, consent, secondary findings, return of results, and sharing and security of data, ethics).

**Healthcare system: Equal access to sequencing** (110,000 patients 310,000 analyses) rare diseases, cancers (~60,000 patients per year)

**Economics: an integrated industry sector dedicated to precision medicine**

**Practitioner: Diagnostics and therapeutics adjusted on validated indications**
- A set of validated indications
- A digital file associated with each patient (genomic data + clinical data)
- Identification of variants for a particular pathology, good practices related to secondary findings
- Tools for exploring data and elaborating therapeutic strategies

**A hybrid system of care/research**
To overcome scientific and technical hurdles, molecular exploration of pathologies, matching of heterogeneous databases, interpretation of large scale data, etc.
3 OBJECTIVES – 14 ACTIONS

Implement the tools for a genomic healthcare pathway (Actions 1 to 3)
Ensure operational implementation and growth (Actions 4 to 8)
Implement monitoring and management tools (Actions 9 to 14)
A plan organized around 3 Major Objectives – 14 actions

SET UP THE TOOLS FOR A GENOMIC HEALTHCARE PATHWAY

Action 1  Creation of a network of sequencing platforms
Action 2  Creation of a Central Analyser of Data (CAD) to process and use the volume of data generated
Action 3  Allow the integration and use of patient data in the healthcare pathway

ENSURE THESE DEVELOPMENTS IN A SAFE TECHNICAL & ETHICAL FRAMEWORK

Action 4  Set up a center of reference, innovation, expertise and transfer (CREFIX)
Action 5  Overcome technological, clinical and regulatory barriers encountered along the pathway
Action 6  Set up an evaluation and validation system of new indications for access to genomic diagnosis
Action 7  Foster new skills and personnel capable of meeting the challenge of analyzing and interpreting the data
Action 8  Integrate ethical aspects related to the processing of clinical & genomic data

IMPLEMENT MONITORING AND MANAGEMENT TOOLS

Action 9  Mobilize industry stakeholders around the project
Action 10  Guide sector activities to address industry issues in the genomic healthcare pathway
Action 11  Monitor the developments at the international level
Action 12  Implement a program dedicated to health economic aspects
Action 13  Organize information, consultation, and involvement of concerned stakeholders in society
Action 14  Governance of the Plan
A plan organized around 3 Major Objectives – 14 actions

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Funding: 670 M€

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PILOT PROJECTS: OVERCOMING BARRIERS IN THE GENOMIC HEALTHCARE PATHWAY

Clinical data

Collection of consents

Modes and types of sampling

Transport and transfer to sequencing centers

Elaboration, validation & transmission of summaries

Quality control

Laboratoire d’analyse

Putting in place staff for sequencing, varient extraction, analysis and interpretation

Types of sequencing, analysis and data linking

Types of data transfer to CAD
CRefIX: ensure technological and informatic development

CRefIX:
- Center of Reference
  - Innovation
  - Expertise

Research

Sequences analyzed

Technical validation

Laboratoire d’analyse
CAD (action 2) : services

**Services for industry**
- Feasibility of specific genotype clinical trials
- Assistance in recruiting patients
- Pharmacogenetics: longitudinal studies

**Services for patients**
- Consent
- Access to data

**Services for the clinic**
- Tools to support therapeutic decisions
- Tools to support analysis, tools of comparison
- Data manipulation training

**Services for research**
- Validation of therapeutic hypotheses
- **Biological research**: cross analysis of different pathologies, access to raw data extraction
- **Clinical research**: virtual studies, validation of companion tests, biomarkers,…
- **Epidemiological research**

**Other services**
- Access to or interconnection with other databases
- Methodological support
- Analysis tools allowing the integration of other omics data

« Laboratoire d’analyse »
Advancing Disease Modeling Animal-Based research in Support of Precision Medicine

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MISSION STATEMENT
The primary mission of the Alliance of Genome Resources (AGR, or the Alliance) is to develop and maintain sustainable genome information resources that facilitate the use of diverse model organisms in understanding the genetic and genomic basis of human biology, health and disease.

Animal models:
- for deciphering the physiopathology pathways
- Suitable to enhance our knowledge in molecular mechanism
  - these Knowledge can be translated to human studies

Have access to different models with their own specificity give the means to explore biological issues with different lighting.

Services for research
- Validation of therapeutic hypotheses
- Biological research: cross analysis of different pathologies, access to raw data extraction
- Clinical research: virtual studies, validation of companion tests, biomarkers,...
- Epidemiological research
Impact of animal research on personalized medicine

**PRO**
- To get knowledge on gene function from the KO mutant animal (ex mouse from IMPC)
- To generate additional knowledge about SNVs and CNVs (ex CrispR/Cas9 revolution and precision modelling)
- To understand the variations in the genome and environmental conditions at the origin of diseases
- To approach the organismal level (complementary to cellular and organoid approach)
- To control environmental parameters that could affect the expression of a variant (ex: microbiota, diet, infection, pollution,...)
- Performed with clear regulation and rules (ethic, welfare, 3R,...)

**CONS**
- Primate specific genes
- Variation in human genes with alternative consequence in models (ex coevolution of proteins involved in large complex)
- Limits of animal models (relevance, predictive value, cost, time,...)
- Which animal model for which purpose?
- Reproducibility of Animal research
- Society concerns about animal research
FRENCH GENOMIC MEDICINE PLAN
2025

- 670 M€ over 10 years

Thank you for your attention