FORUM
DE LA RECHERCHE EN
CANCÉROLOGIE

# Génomique et IA, vers une médecine de précision

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CHU GRENOBLE ALPES

AURAGEN

FRANCE MÉDECINE GÉNOMIQUE 2025
aviesan

UNIVERSITÉ Grenoble Alpes

iAB
EPIGENETICS
CHRONIC DISEASES
CANCER

# 2003 – Fin du Human Genome Project

**Human Genome Project**

13 ans
> 3 milliards $

articles

## Initial sequencing and analysis of the human genome

**International Human Genome Sequencing Consortium***

** A partial list of authors appears on the opposite page. Affiliations are listed at the end of the paper.*

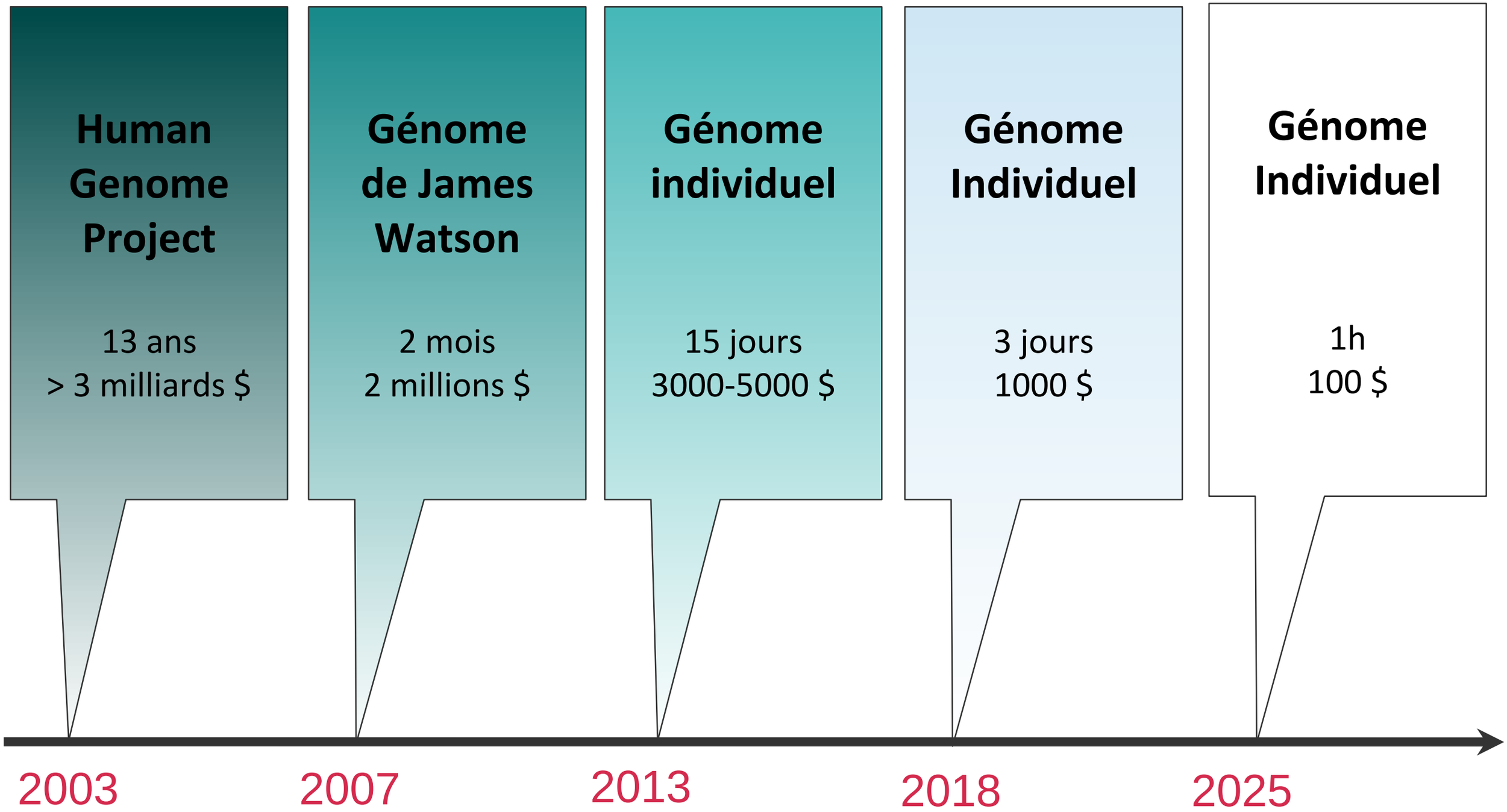
**The human genome holds an extraordinary trove of information about human development, physiology, medicine and evolution. Here we report the results of an international collaboration to produce and make freely available a draft sequence of the human genome. We also present an initial analysis of the data, describing some of the insights that can be gleaned from the sequence.**

Science
AAAS

**The Sequence of the Human Genome**
J. Craig Venter *et al.*
*Science* **291**, 1304 (2001);
DOI: 10.1126/science.1058040

2003

# Vers le séquençage en routine de génomes entiers



aviesan

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

# FRANCE MÉDECINE GÉNOMIQUE 2025

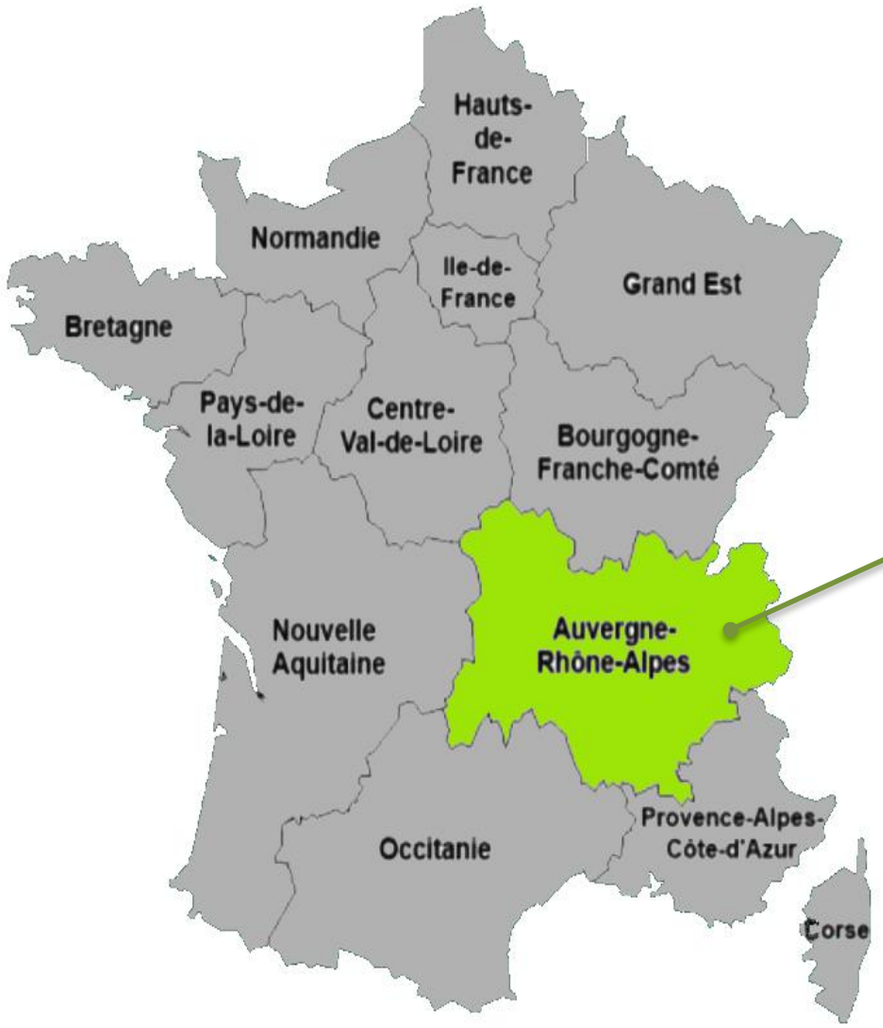
## Objectifs du PFMG2025:

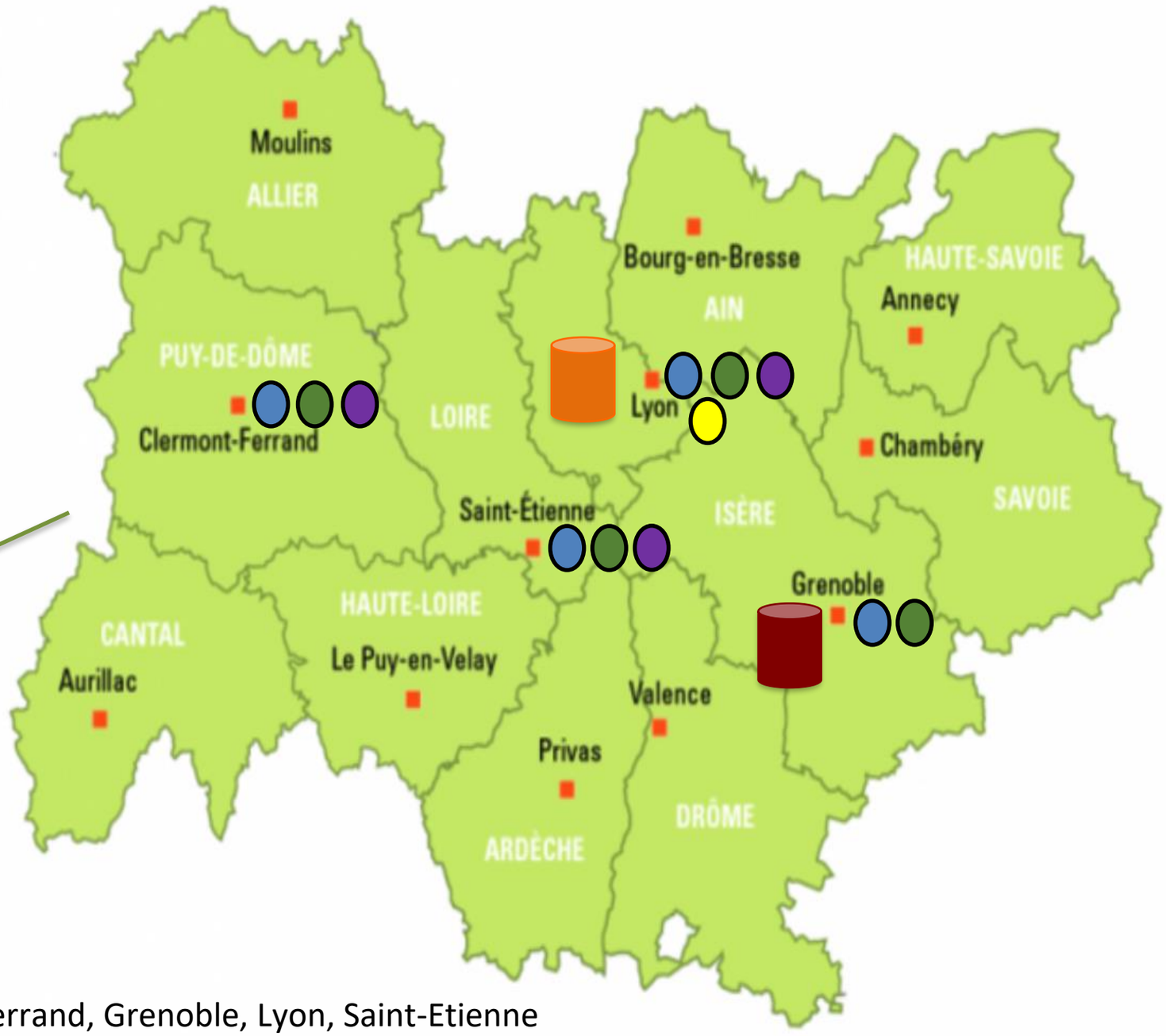
- Mise en oeuvre du parcours de soins génomique

- Déploiement opérationnel et montée en puissance, cadre technique et éthique sécurisé

- Outils de suivi, pilotage et adaptations; assurer l'adhésion du public

# Consortium régional AURAGEN




GCS (HCP)

- **Hôpital** : Clermont-Ferrand, Grenoble, Lyon, Saint-Etienne
- **CLCC-IC**: Centre Léon Bérard, Centre Jean Perrin, Inst. Cancérologie Loire

Partenaires

- **Universités** : Clermont-Ferrand, Grenoble, Lyon, Saint-Etienne
- **Partenaires académiques** : Ecole de mines, Fondation Synergie Lyon-Cancer

Infrastructures

- **Centre de séquençage**: HCL
- **Centre de calcul**: CHU Grenoble-Alpes

# Parcours de soins génomique proposé

centre de référence maladies rares

filière de santé maladies rares

INSTITUT NATIONAL DU CANCER

H

H

Pré-analytique
Données patient

Production des données de séquençage

Curation/Interprétation « Maladies rares »

Curation/Interprétation « Cancer »

Archivage
Analyse des données

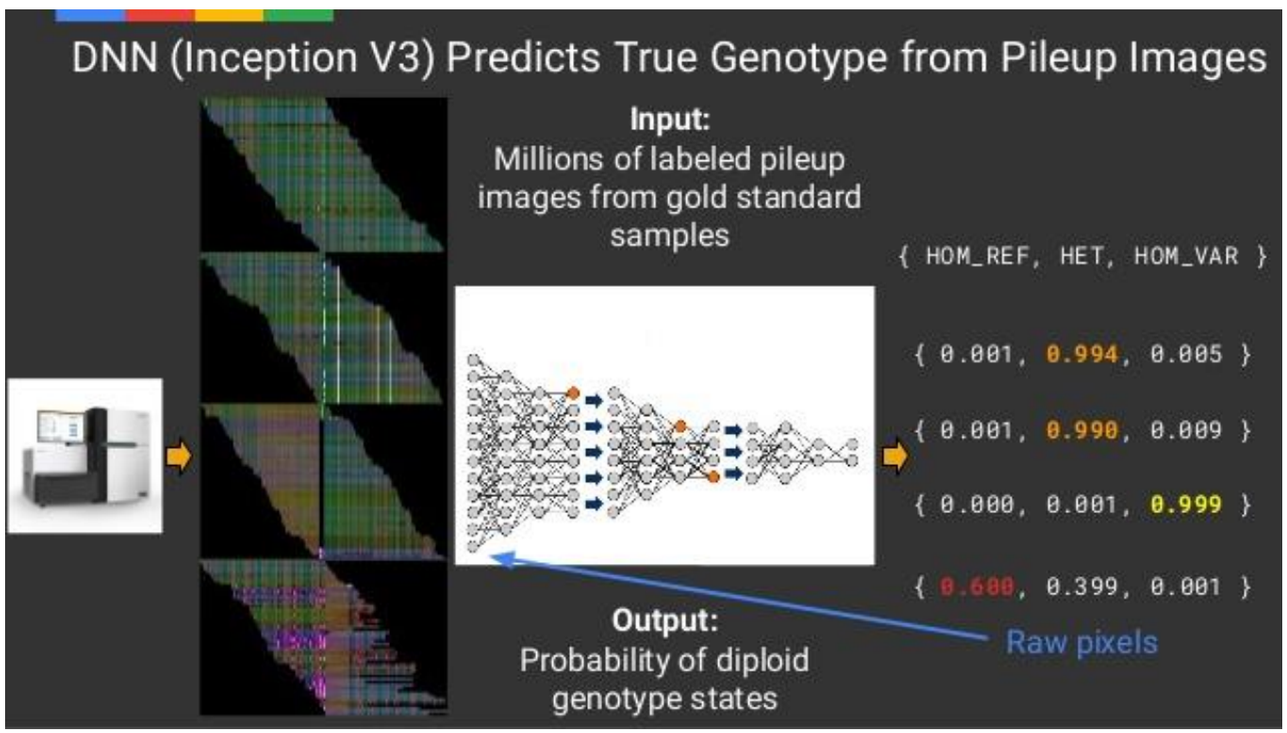
**CAD**

**CReflX**

**CAD**

# Perspectives d’application de l’IA en génomique

## Depuis le traitement du signal de séquençage


## A l’identification précises de variations génomiques

# Organisation de l'interprétation des données

## Variations génomiques germinales

**Table 2. SNPs Identified through Whole-Genome Sequencing of DNA from the Proband.***

| SNP Type | No. of SNPs |
|---|---|
| Nongene | 2,255,102 |
| Gene | 1,165,204 |
| Intron | 1,064,655 |
| Promoter | 60,075 |
| 3′ UTR | 16,350 |
| 5′ UTR | 3,517 |
| Splice regulatory site | 2,089 |
| Splice site | 112 |
| Synonymous | 9,337 |
| Stop→stop | 17 |
| Nonsynonymous | 9,069 |
| Stop→gain | 121 |
| Stop→loss | 27 |
| Total | 3,420,306 |

* Stop→stop refers to synonymous substitutions within a stop codon that maintain the stop codon, stop→gain refers to nonsense mutations, and stop→loss refers to nonsynonymous substitutions that change a stop codon to any other codon. SNP denotes single-nucleotide polymorphism, and UTR untranslated region.

*Lupski et al., 2010 NEJM*

**Table 2. Variant Categories in Clinical Reports of Whole-Exome Sequencing.***

| Category | No. of Variants† |
|---|---|
| **Focused report** | |
| Deleterious mutation related to the disease phenotype | 0–2 |
| VUS related to the disease phenotype | 4–9 |
| Medically actionable mutation‡ | 0 or 1 |
| Autosomal recessive carrier status§ | 0 or 1 |
| Pharmacogenetic variant¶ | 0–4 |
| **Expanded report** | |
| Deleterious mutation unrelated to the disease phenotype | 1–3 |
| VUS unrelated to the disease phenotype | 17–41 |
| Truncating mutation in genes with no known association with disease | 17–25 |
| **Not included in report** | |
| VUS unrelated to the disease phenotype in which only one mutant allele was identified in a gene associated with a recessive disorder | 26–64 |
| VUS in gene with no known association with disease | 300–600 |

*Yang et al., 2013 NEJM*

# Organisation de l'interprétation des données

## Variations génomiques germinales

Curation/interprétation experte et manuelle de 300-600 variations = 1 h de praticien

AURAGEN = 20000 WGS/an

20000 heures d'interprétation
~10 emplois à temps plein

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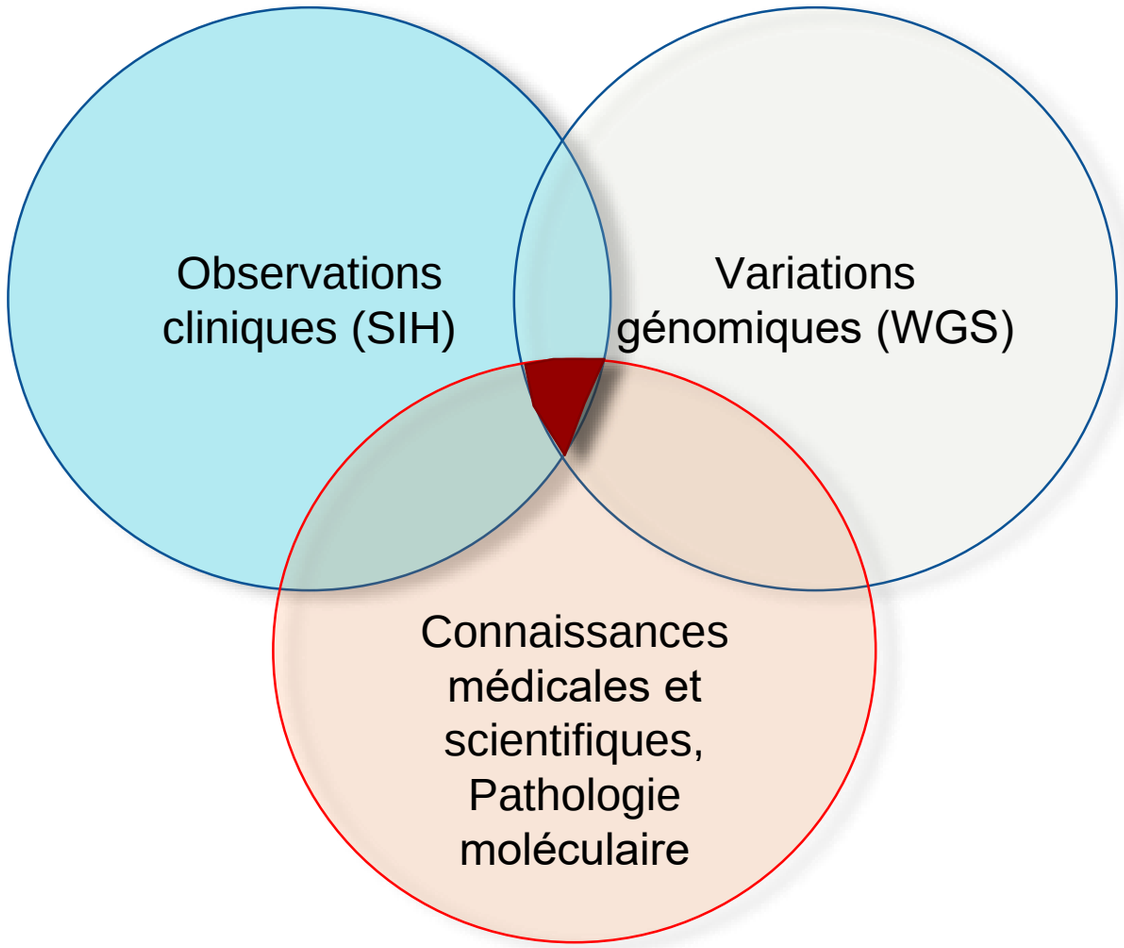
*Yang et al., 2013 NEJM*

# Intégration des contextes cliniques et génomiques

Thésaurus cliniques

*HP:0000xxx*
*HP:0000xxx*
*HP:0000xxx*
*HP:0000xxx*
*HP:0000xxx*
*HP:0000xxx*




VCF

*Variant N – gène X*
*Variant N – gène X*
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*Variant N – gène X*

Mécanismes moléculaires
Modes de transmission
Règles d'interprétation métier

**« Automatisation » de la curation des variations génomiques**

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# Merci pour votre attention

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