MITOMATCHER DB, a French clinical-biological national database to aid in mitochondrial variant prioritization

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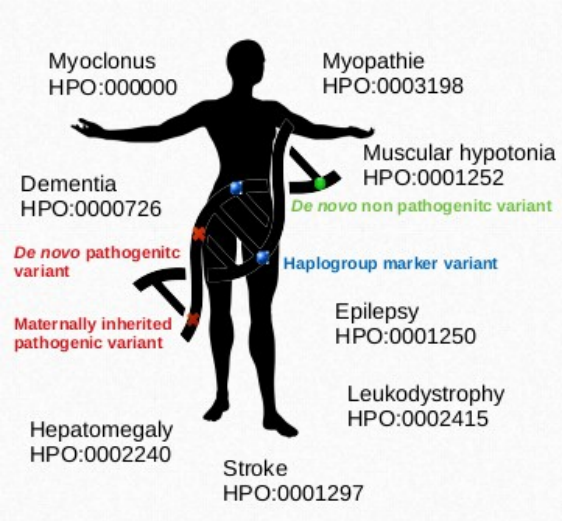
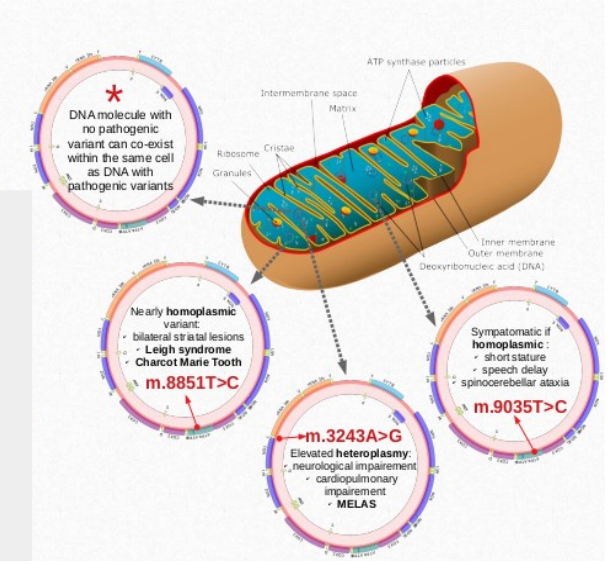
CONTEXT & GOALS

Mitochondrial diseases affect 1 in 4,300 live births. Mitomatcher DB aims at gathering phenotypic and genetic data to improve diagnostics and permit the search for co-occuring variation, interpretation of Variants of Uknown Significance and impact of mitochondrial haplogroup and heteroplasmy on pathogenicity.



Urgent need for a national database joining **genetical** and **phenotypical** data in a comprehensive manner.



- Clinical data
  - Age, age of onset
  - Cosanguinity
  - **HPO terms**
- Sampling
  - tissue
  - Sequencing technique
  - analysis metadata
- Reference center
  - laboratory
  - medical staff (user)

- Mitochondrial DNA
  - 16,5 kbp
  - 37 genes, 15 proteins
  - **heteroplasmy** *
- Nuclear DNA
  - 1500 proteins involved in mitochondrial functions
- Annotations
  - Pathogeneicity scores
  - Frequencies
  - Conservation scores

Setting a secure environnement and enabling complex querying through an user friendly interface.

Genetic data **Phenotypic data**

DATABASE & QUERYING

- Samples
  - 3k patients
  - 51k genbank
- Secure hosting environement
  - Dynamic Virtual Machine
  - Double authentication
  - Indirect querying (elasticsearch)
- Complex querying
  - Variant co-occurence
  - Similar phenotypes
- User friendly interface
  - Cafe Variome

Mitomatcher DB

TABLE_NAME	TABLE_ROWS
Analysis	56041
Annotation	14505
Clinical	548
Clinical_Sample	548
Gene	37
Gene_Variant	12355
Laboratory	13
Ontology	63
Ontology_Sample	10013
Sample	50051
Technique	5
User	18
Variant	14438
Variant_Call	1757403

Data is gathered from mitochondrial rare disease reference centers.

Visit → **mitodiag.fr/network**

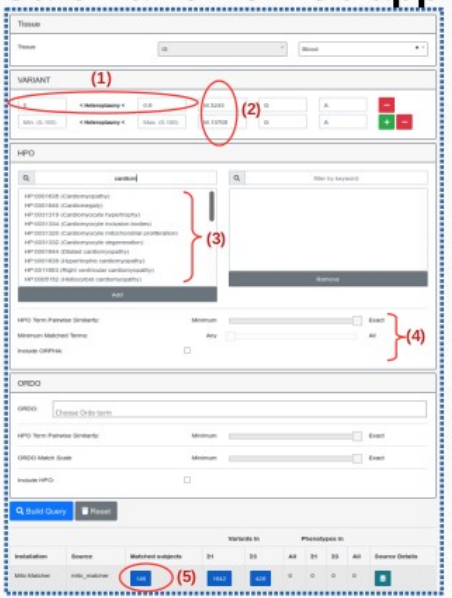
MySQL, python
PHP, CodeIgniter

display

The web app permits complex queries.

(1) Heteroplasmy filtering
(2) Co-occuring variants (mt/mt or mt/nucl.)
(3) Human Phenotype Ontology search
(4) HPO similarity
(5) Extracting query results in .csv or .xls format

Cafe Variome web app

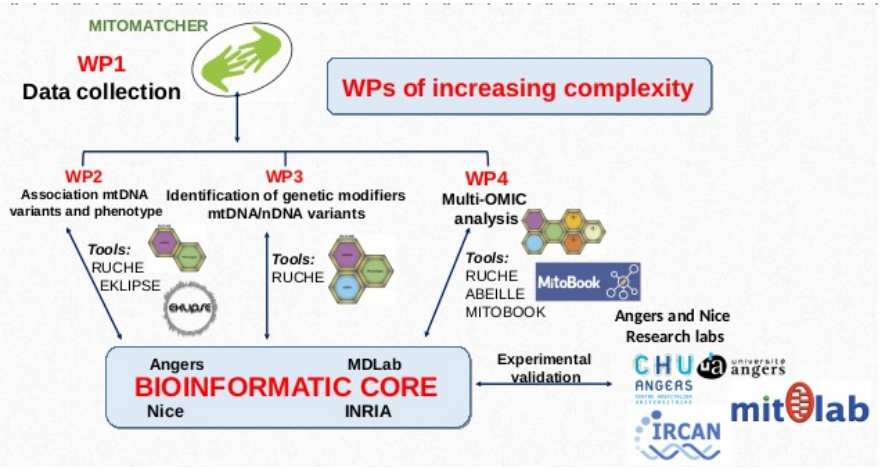


Video DEMO:
https://drive.google.com/file/d/1yyN0a-Qp87XWdw9igf3wYyboIPR7PGgM/view?usp=sharing

PROSPECTS

Better understanding of the molecular mechaisms responsible for the **clinical-genetic heterogeneity of mitochondrial diseases** by building Work Packages of increasing complexity.
Societal and ethical implications → *Social Science Humanities, Nantes University, Pr Tirard*

Mitomics – Mitomatcher project received national **PIA4 funding**.
Pending data sharing authorization (CNIL).



→ Pathologies liées à des mutations de l'ADN (Bris et al. 2018)
→ Prevalence of rare mitochondrial DNA mutations in mitochondrial disorders (Bannwarth et al. 2013)
→ Peculiar combinations of individually non-pathogenic missense mitochondrial DNA variants cause low penetrance Leber's hereditary optic neuropathy. (Caporali et al. 2018)