# M1 SM THORAX ED TG: Recherche in silico.

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Team IIA

L'unité de recherche de l'institut du thorax
Inserm UMR 1087 / CNRS UMR 6291
Nantes, France

Nantes, 12 Octobre 2023

# 1. Les analyses bibliographiques

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# Que des sources scientifiques avérées …

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Le **Centre américain pour les informations biotechnologiques** (NCBI), en anglais National Center for Biotechnology Information, est un institut national américain pour l'information biologique moléculaire. Fondé en 1988 à Bethesda dans le Maryland, cet organisme fait partie de la Bibliothèque américaine de médecine, un des Instituts américains de la santé.


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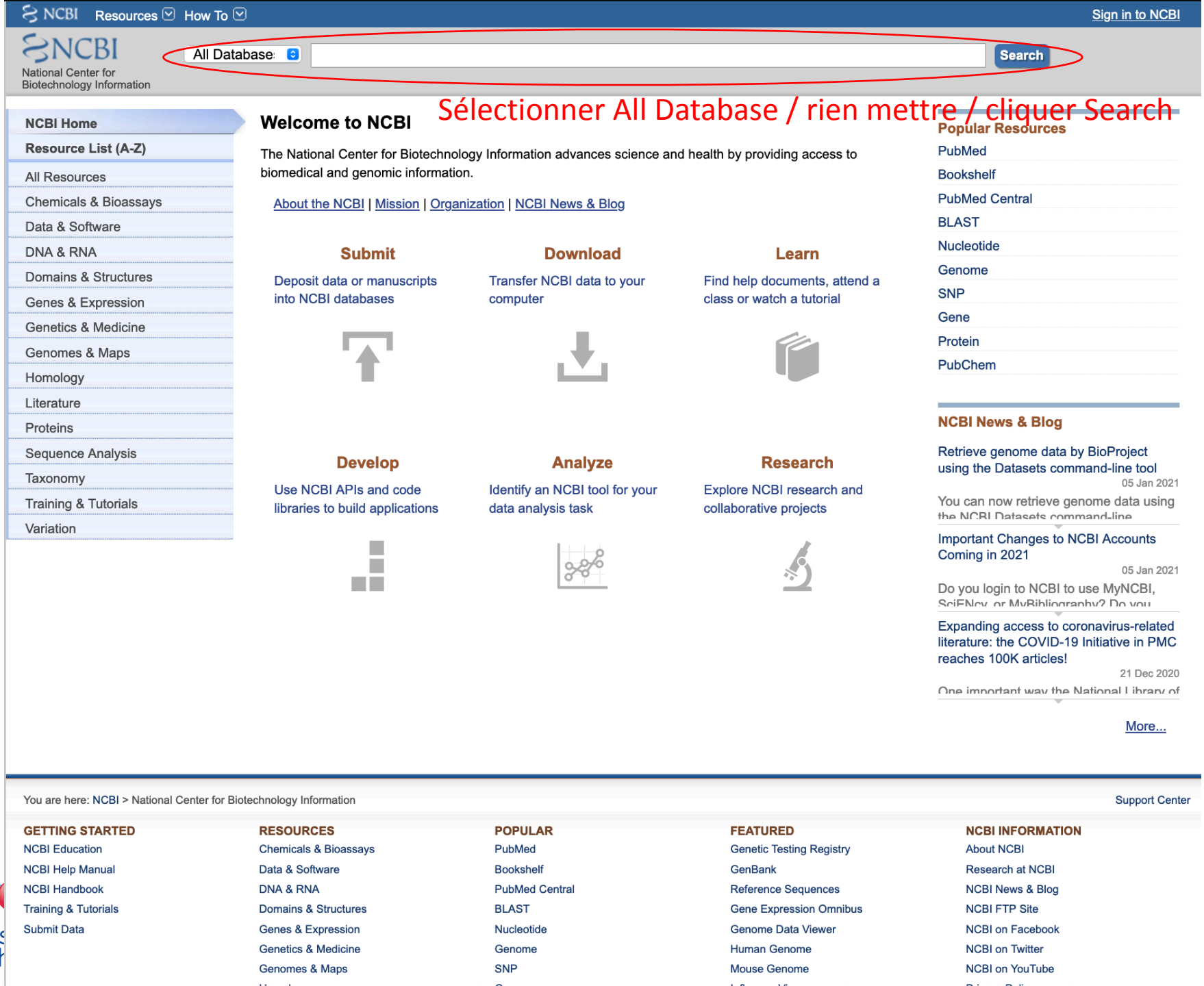
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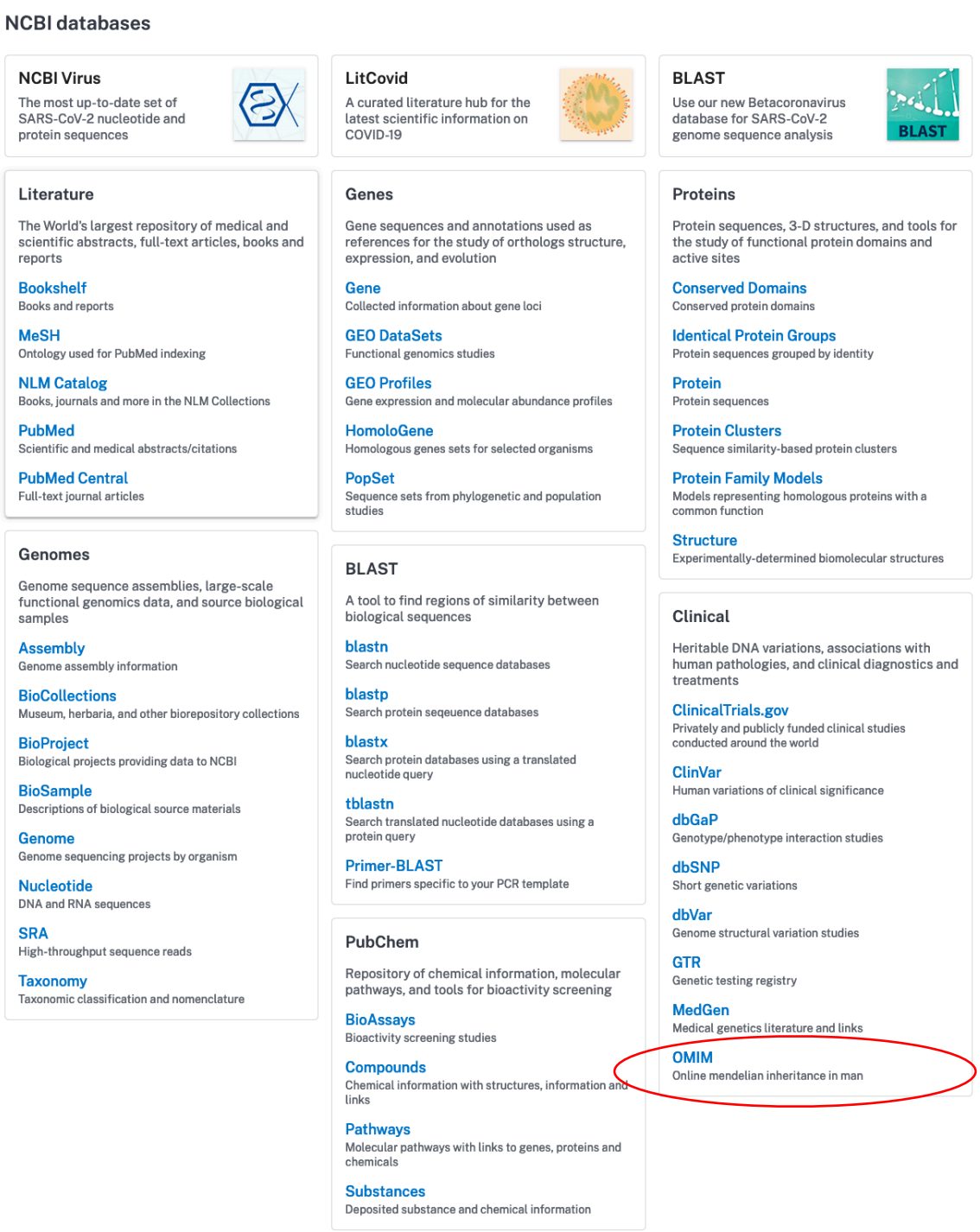


Le NCBI abrite une série de bases de données pertinentes pour la biotechnologie et la biomédecine et constitue une ressource importante pour les outils et services de bioinformatique.

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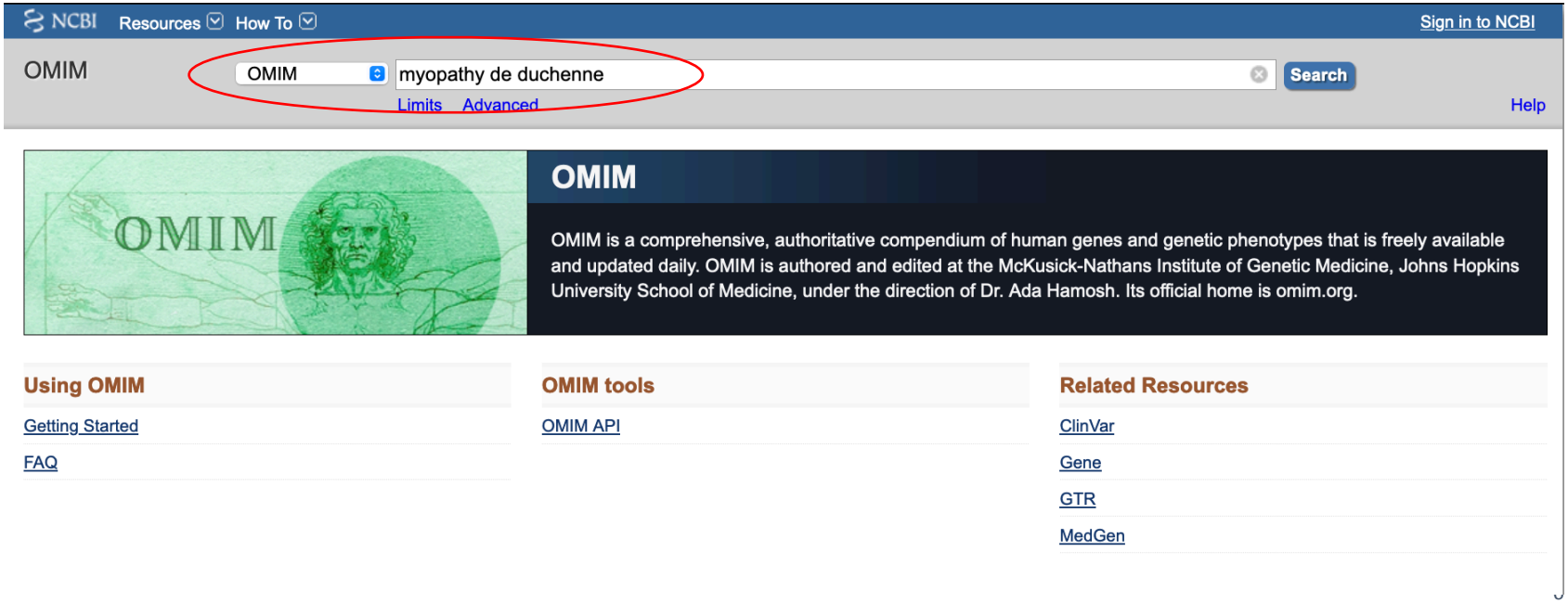
OMIM : Le projet Héritage mendélien chez l'humain (en anglais : Mendelian Inheritance in Man) est une base de données originellement compilée par Victor A. McKusick et qui dresse un catalogue de toutes les maladies connues qui relèvent de l'un ou l'autre composant génétique et — si possible — les relie aux gènes adéquats au sein du génome humain. Cette base de données est disponible sous forme d'un livre appelé Mendelian Inheritance in Man (MIM), qui en est à sa 13e édition.

La version en ligne est appelée Online Mendelian Inheritance in Man, OMIM, et peut être consultée à partir de la base de données Entrez1 de la National Library of Medicine2.

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   Cytogenetic locations: 13q12.12
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2. #608099 - MUSCULAR DYSTROPHY, LIMB-GIRDLE, AUTOSOMAL RECESSIVE 3; LGMDR3
   Cytogenetic locations: 17q21.33
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3. #310200 - MUSCULAR DYSTROPHY, **DUCHENNE** TYPE; DMD
   Cytogenetic locations: Xp21.2-p21.1
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ICD+

# 310200

# MUSCULAR DYSTROPHY, DUCHENNE TYPE; DMD

*Alternative titles; symbols*

DUCHENNE MUSCULAR DYSTROPHY
MUSCULAR DYSTROPHY, PSEUDOHYPERTROPHIC PROGRESSIVE, DUCHENNE TYPE

## Phenotype-Gene Relationships

| Location | Phenotype | Phenotype MIM number | Inheritance | Phenotype mapping key | Gene/Locus | Gene/Locus MIM number |
|---|---|---|---|---|---|---|
| Xp21.2-p21.1 | Duchenne muscular dystrophy | 310200 | XLR | 3 | DMD | 300377 |

Clinical Synopsis | PheneGene Graphics

## TEXT

A number sign (#) is used with this entry because Duchenne muscular dystrophy is caused by mutation in the gene encoding dystrophin (DMD; 300377).

## Description

Dystrophin-associated muscular dystrophies range from the severe Duchenne muscular dystrophy (DMD) to the milder Becker muscular dystrophy (BMD; 300376). Mapping and molecular genetic

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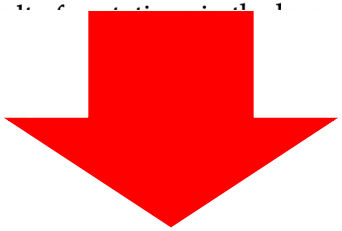

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## Description

Dystrophin-associated muscular dystrophies range from the severe Duchenne muscular dystrophy (DMD) to the milder Becker muscular dystrophy (BMD; 300376). Mapping and molecular genetic studies indicate that both are the result of mutations in the huge gene that encodes dystrophin, also symbolized DMD. Approximately two-thirds of the mutations in both forms are deletions of one or many exons in the dystrophin gene. Although there is no clear correlation found between the extent of the deletion and the severity of the disorder, DMD deletions usually result in frameshift. Boland et al. (1996) studied a retrospective cohort of 33 male patients born between 1953 and 1983. The mean age at DMD diagnosis was 4.6 years; wheelchair dependency had a median age of 10 years; cardiac muscle failure developed in 15% of patients with a median age of 21.5 years; smooth muscle dysfunction in the digestive or urinary tract occurred in 21% and 6% of the patients, respectively, at a median age of 15 years. In this cohort, death occurred at a median age of 17 years. The authors commented that the diagnosis of DMD is being made at an earlier age but survival has not changed.

## Clinical Features

### *Skeletal Muscle*

The most distinctive feature of Duchenne muscular dystrophy is a progressive proximal muscular dystrophy with characteristic pseudohypertrophy of the calves. The bulbar (extraocular) muscles are spared but the myocardium is affected. There is massive elevation of creatine kinase levels in the blood, myopathic changes by electromyography, and myofiber degeneration with fibrosis and fatty infiltration on muscle biopsy.The onset of Duchenne muscular dystrophy usually occurs before age 3 years, and the victim is chairridden by age 12 and dead by age 20. The onset of Becker muscular dystrophy is often in the 20s and 30s and survival to a relatively advanced age is frequent.


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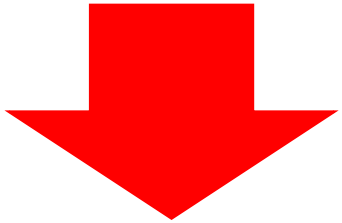

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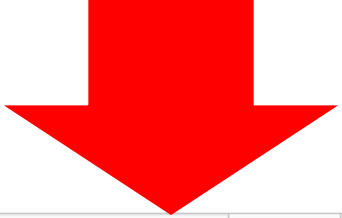

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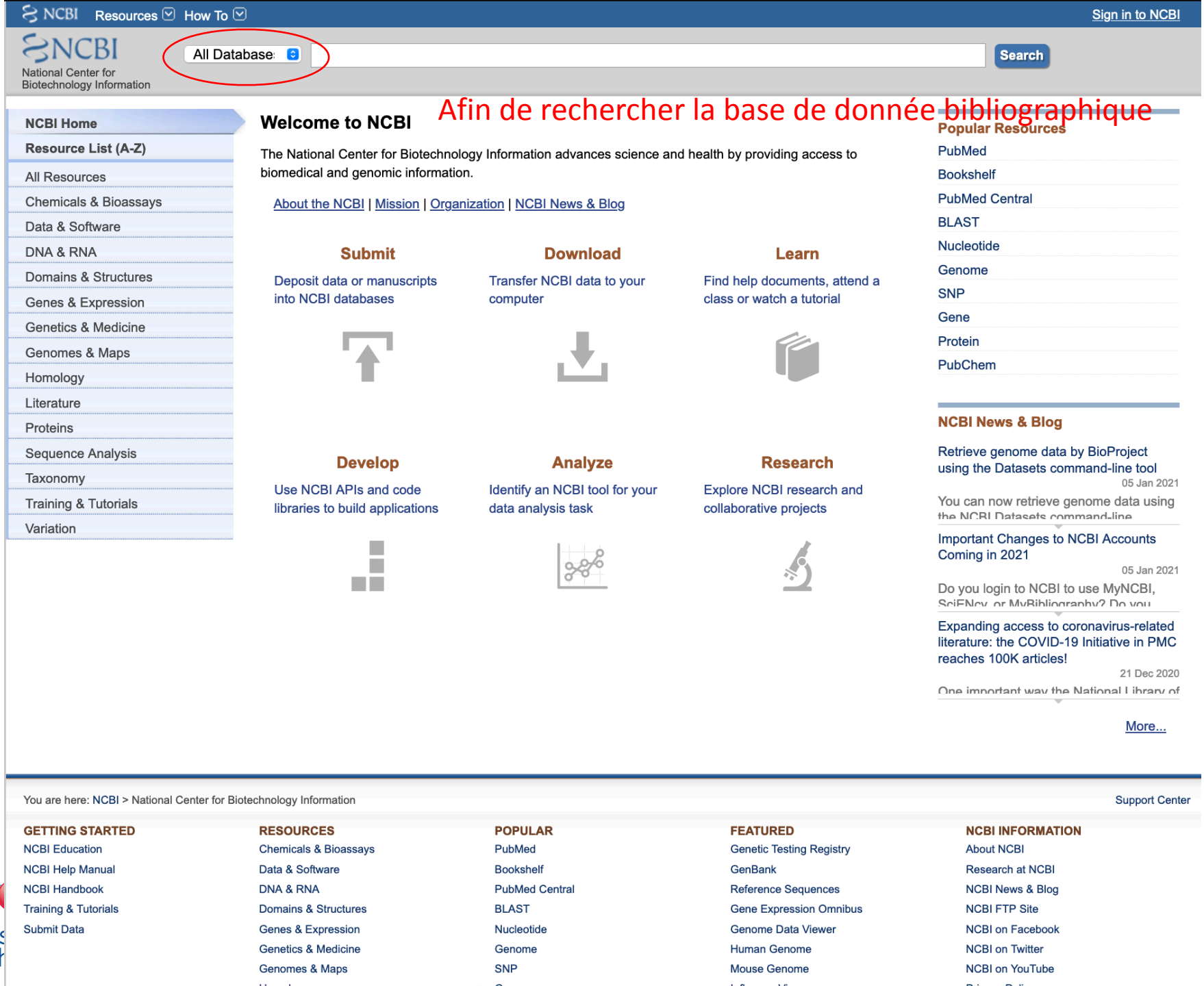
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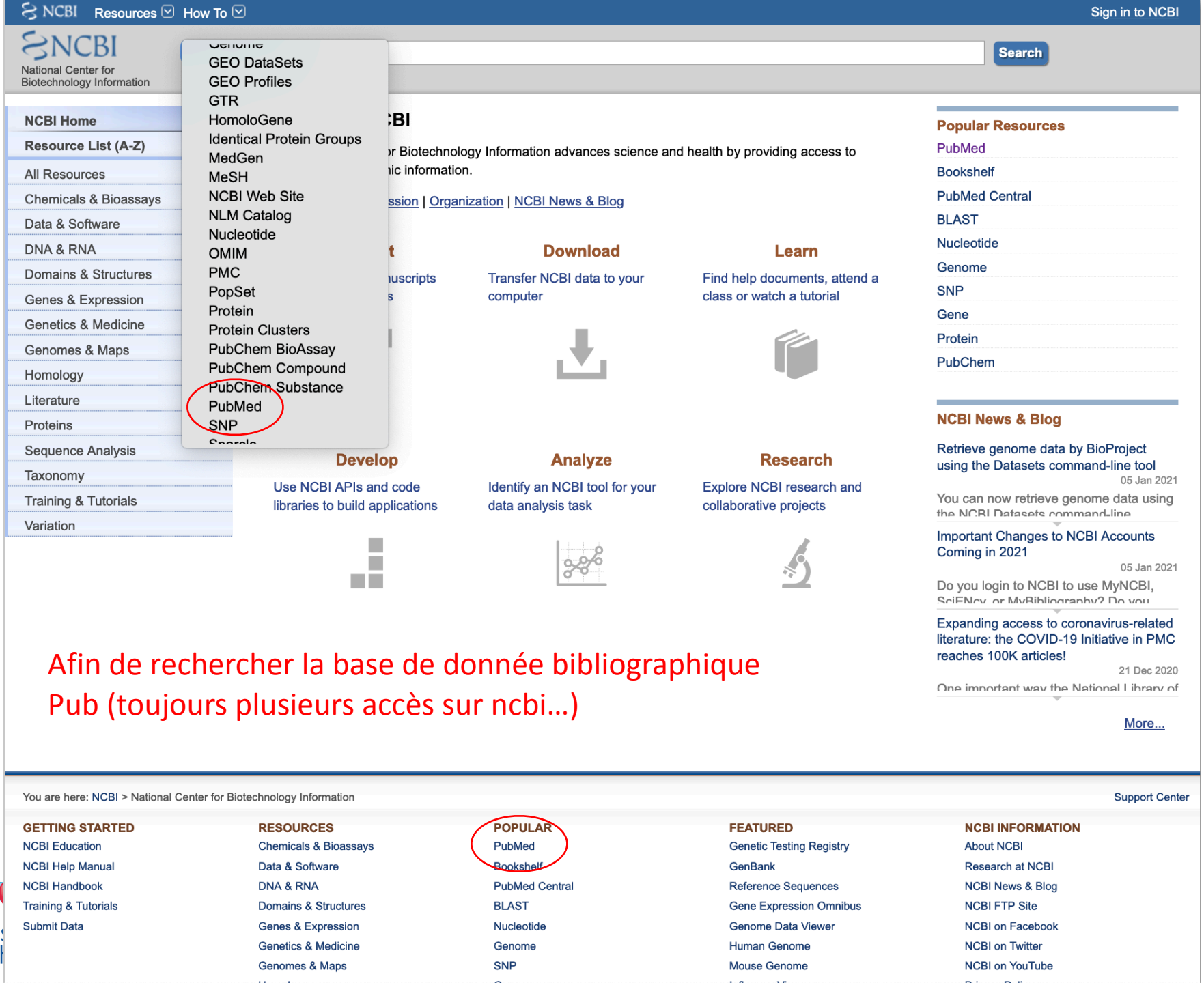


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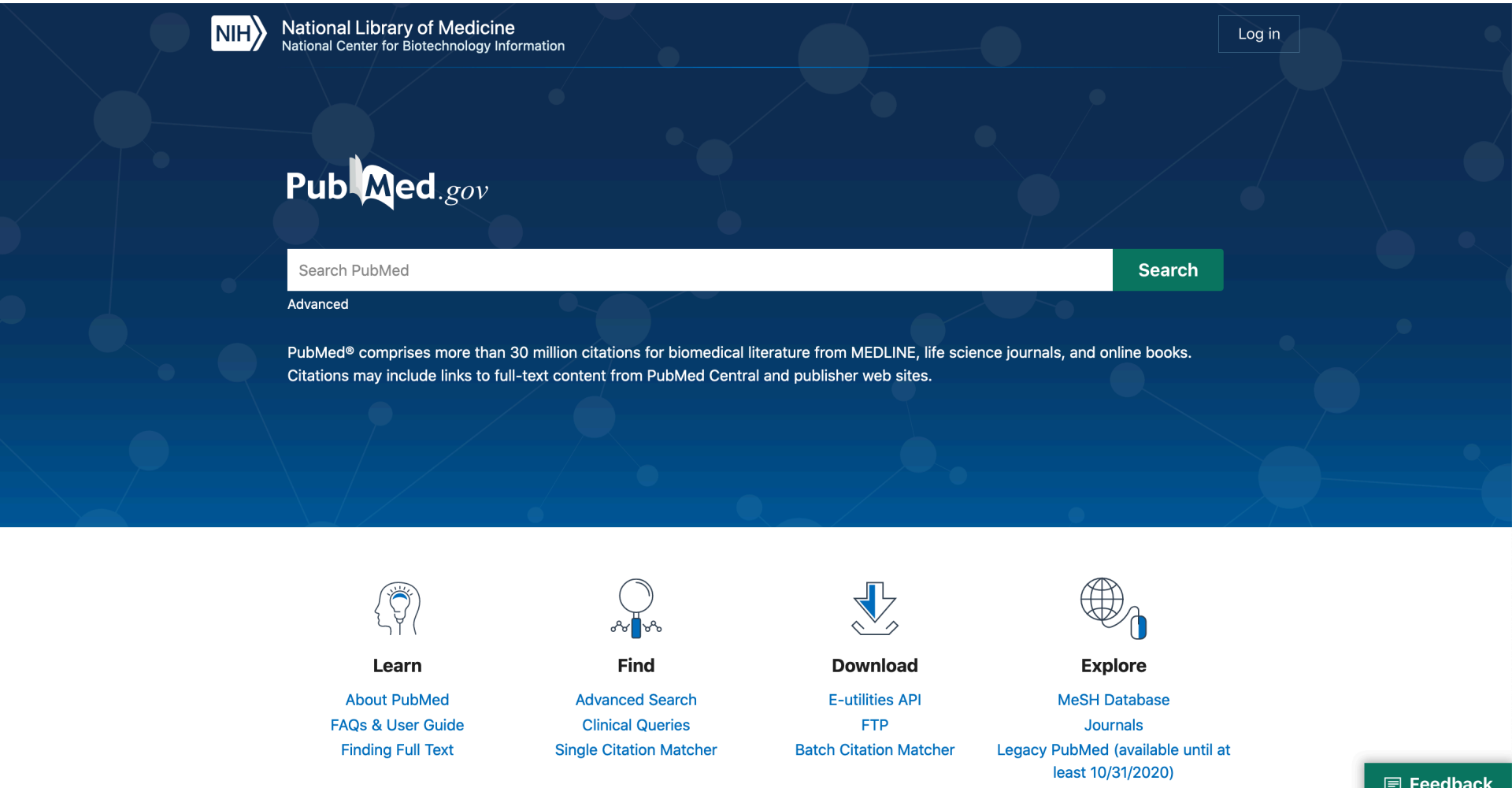


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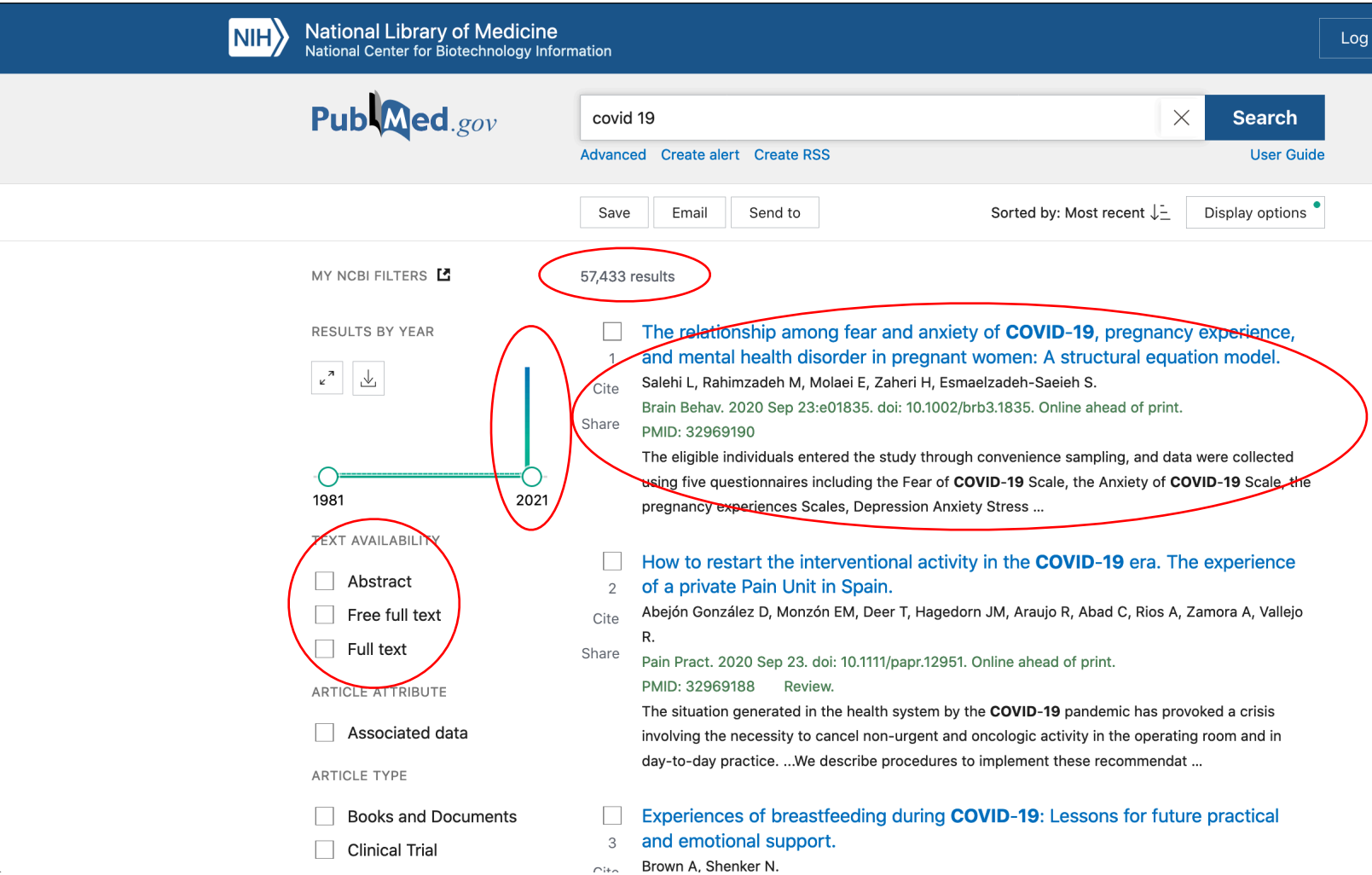


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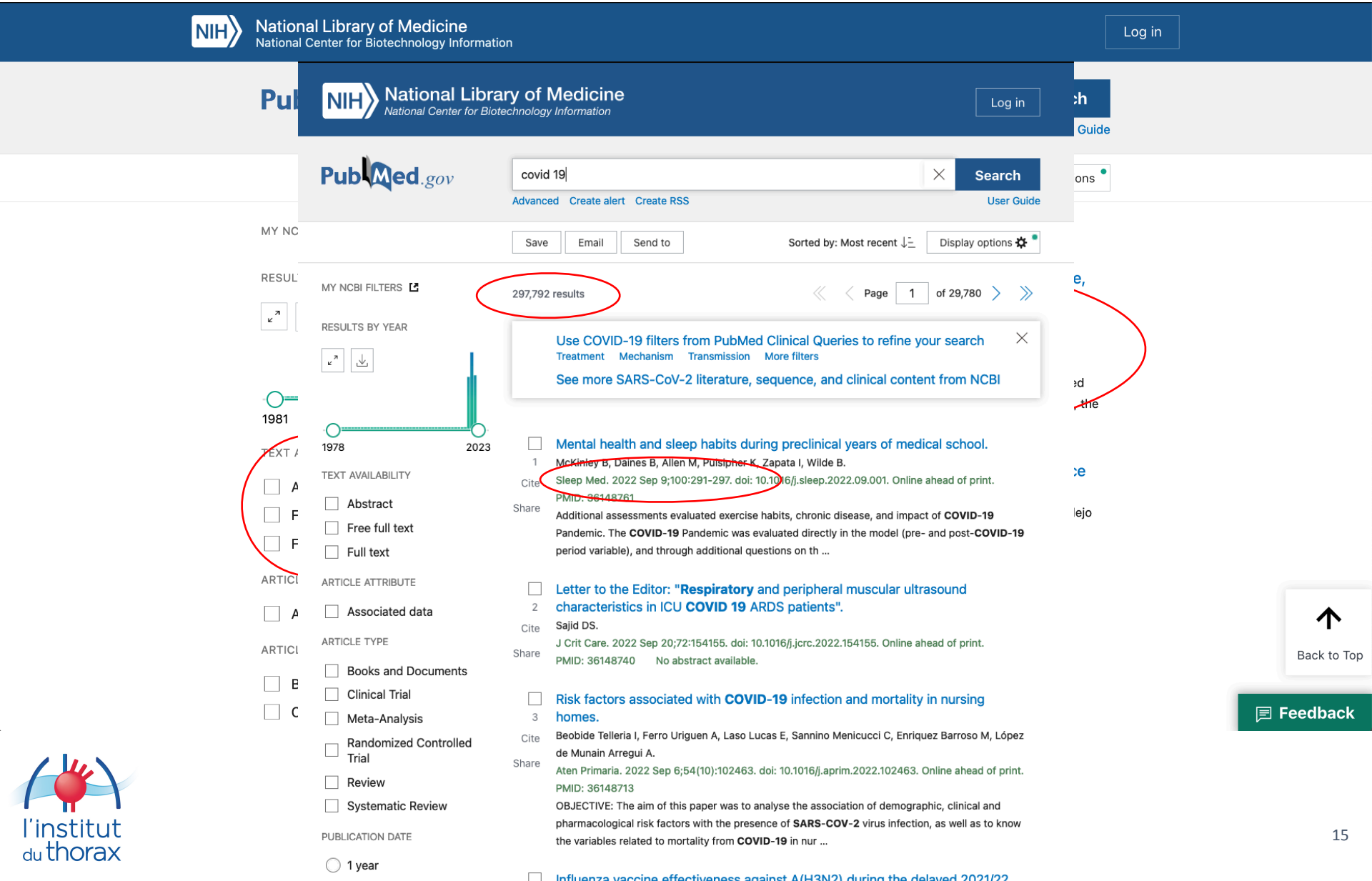


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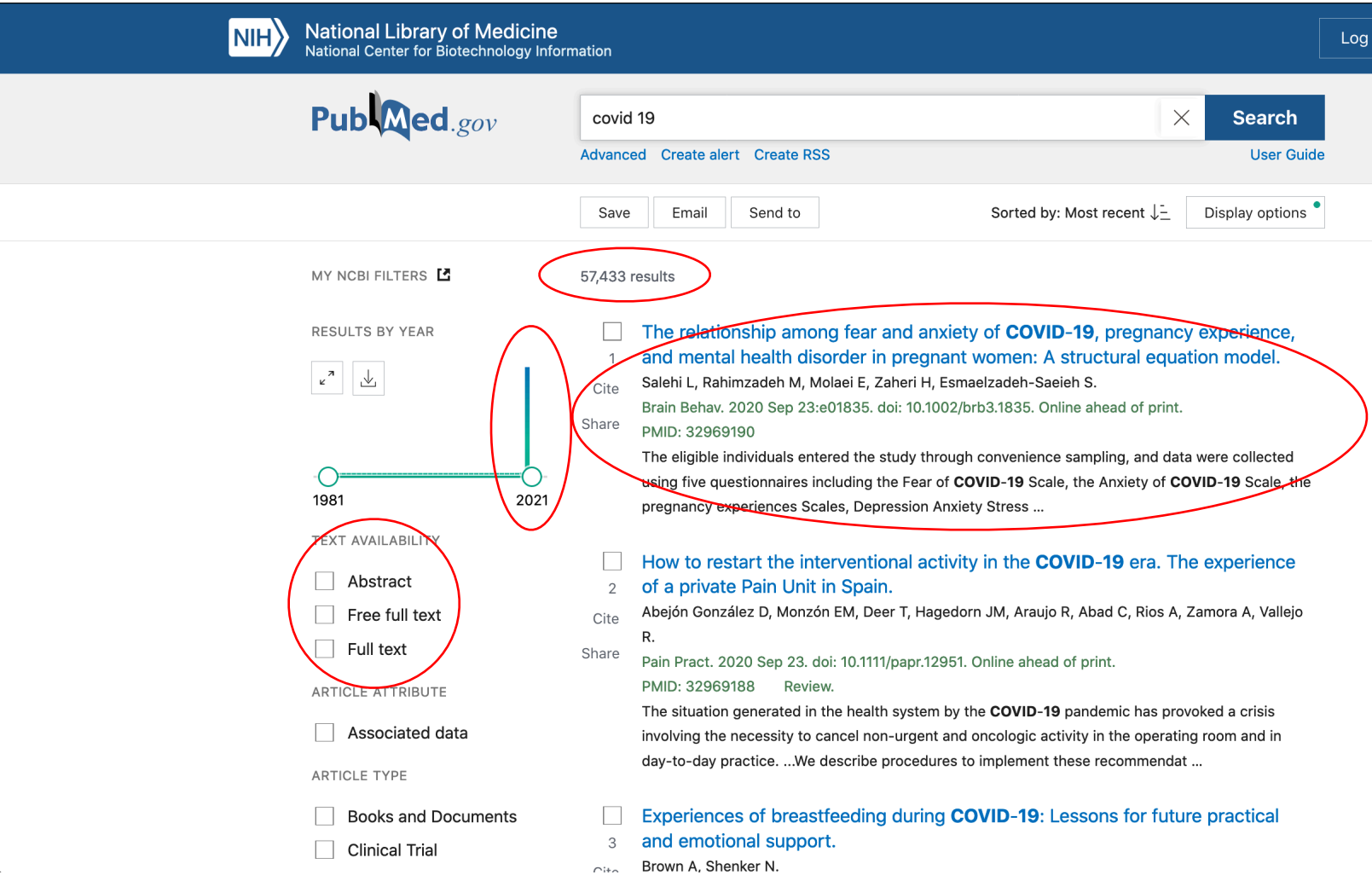


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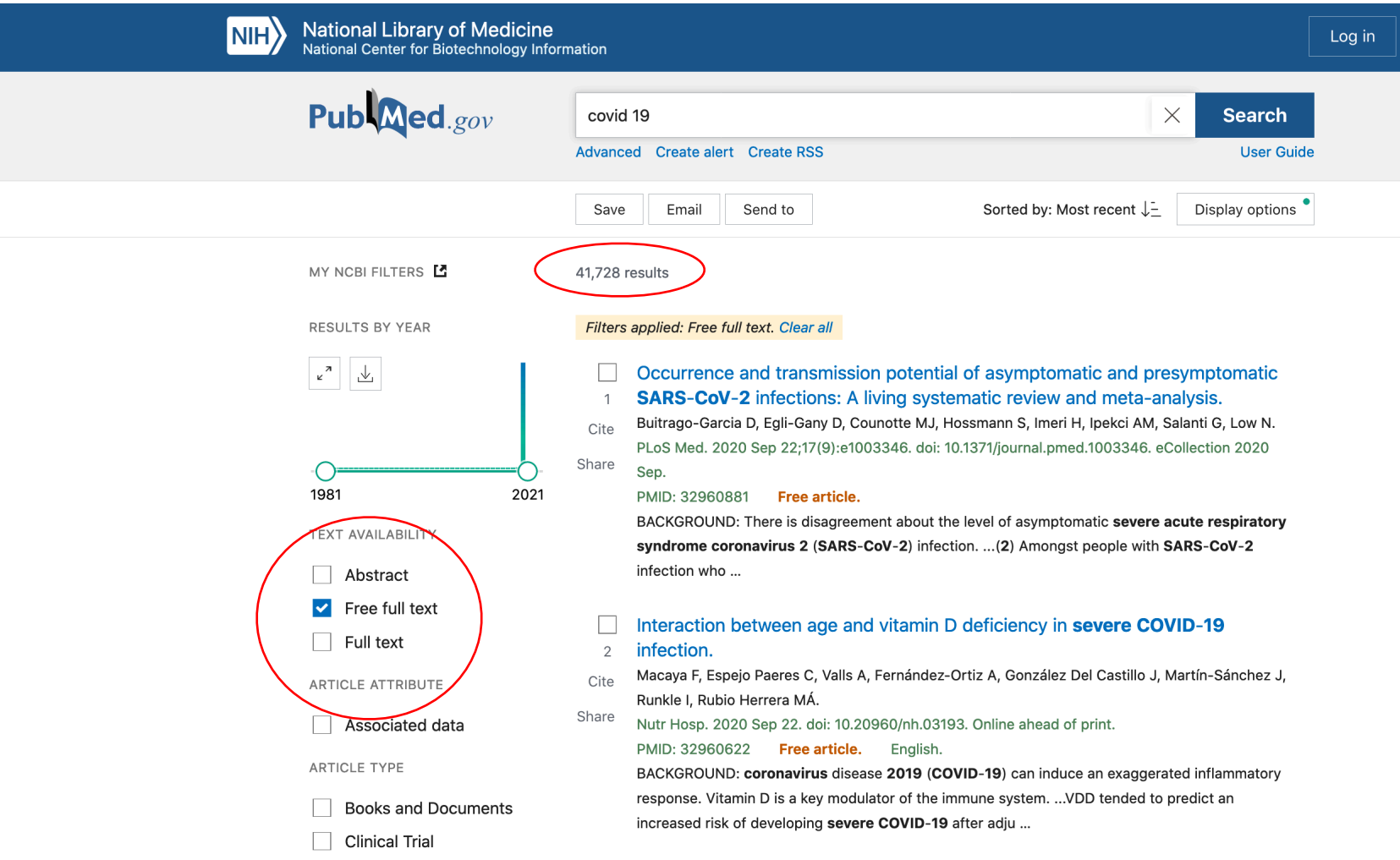


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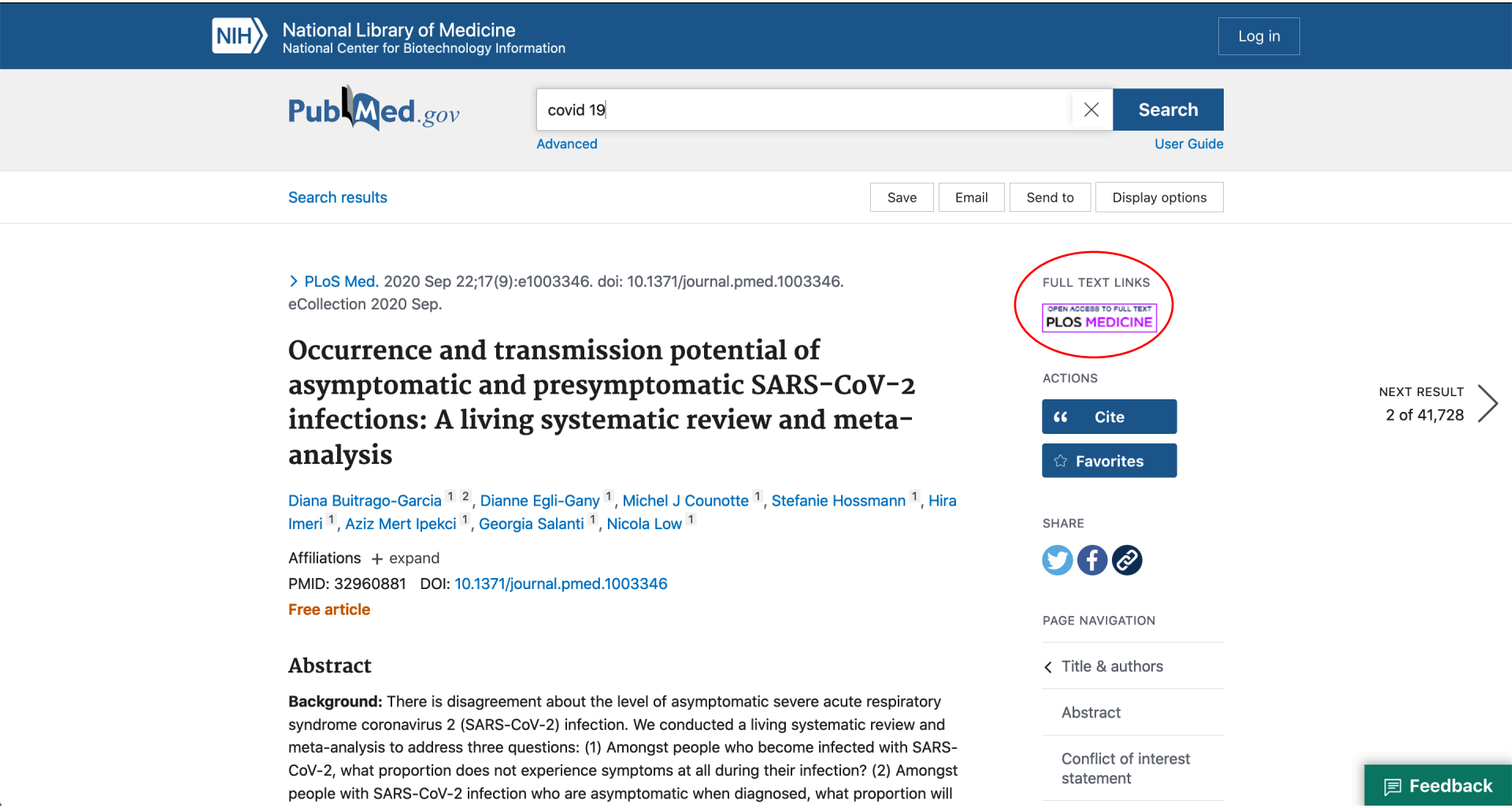


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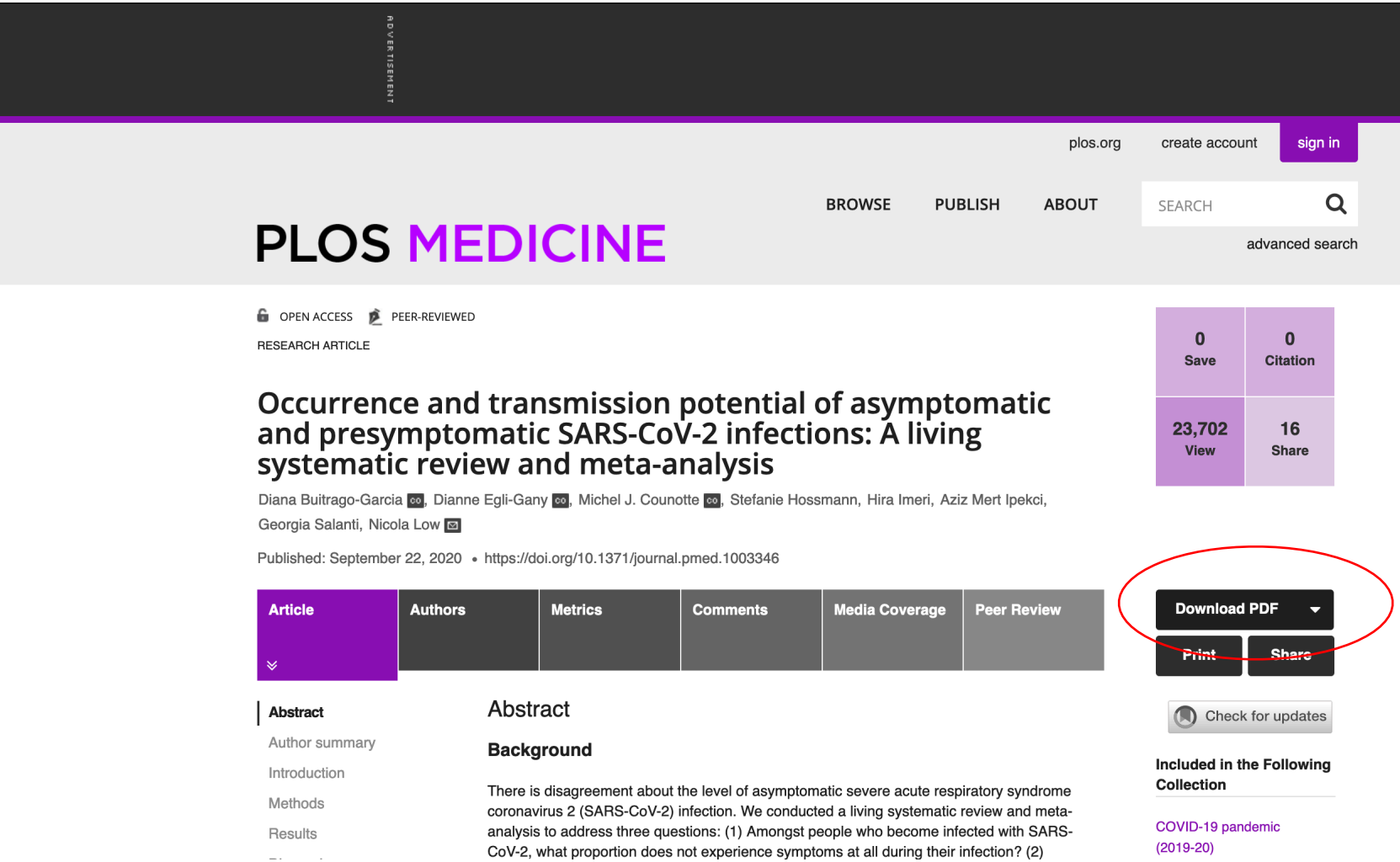


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PLOS MEDICINE

RESEARCH ARTICLE

## Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis

**Diana Buitrago-Garcia[1,2☯], Dianne Egli-Gany[1☯], Michel J. Counotte[1☯], Stefanie Hossmann[1], Hira Imeri[1], Aziz Mert Ipekci[1], Georgia Salanti[1], Nicola Low[1]***

1 Institute of Social and Preventive Medicine, University of Bern, Bern, Switzerland, 2 Graduate School of Health Sciences, University of Bern, Bern, Switzerland

☯ These authors contributed equally to this work.
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**Citation:** Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, et al. (2020) Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis. PLoS Med 17(9): e1003346. https://doi.org/10.1371/journal.pmed.1003346

**Academic Editor:** Nathan Ford, World Health Organization, SWITZERLAND

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**Published:** September 22, 2020

**Peer Review History:** PLOS recognizes the benefits of transparency in the peer review process; therefore, we enable the publication of all of the content of peer review and author responses alongside final, published articles. The editorial history of this article is available here: https://doi.org/10.1371/journal.pmed.1003346



**Data Availability Statement:** The file listing all included studies and files used for all analyses are available from the Harvard Dataverse database.

## Abstract

### Background

There is disagreement about the level of asymptomatic severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. We conducted a living systematic review and meta-analysis to address three questions: (1) Amongst people who become infected with SARS-CoV-2, what proportion does not experience symptoms at all during their infection? (2) Amongst people with SARS-CoV-2 infection who are asymptomatic when diagnosed, what proportion will develop symptoms later? (3) What proportion of SARS-CoV-2 transmission is accounted for by people who are either asymptomatic throughout infection or presymptomatic?

### Methods and findings

We searched PubMed, Embase, bioRxiv, and medRxiv using a database of SARS-CoV-2 literature that is updated daily, on 25 March 2020, 20 April 2020, and 10 June 2020. Studies of people with SARS-CoV-2 diagnosed by reverse transcriptase PCR (RT-PCR) that documented follow-up and symptom status at the beginning and end of follow-up or modelling studies were included. One reviewer extracted data and a second verified the extraction, with disagreement resolved by discussion or a third reviewer. Risk of bias in empirical studies was assessed with an adapted checklist for case series, and the relevance and credibility of modelling studies were assessed using a published checklist. We included a total of 94 studies. The overall estimate of the proportion of people who become infected with SARS-CoV-2 and remain asymptomatic throughout infection was 20% (95% confidence interval [CI] 17–25) with a prediction interval of 3%–67% in 79 studies that addressed this review question. There was some evidence that biases in the selection of participants influence the estimate. In seven studies of defined populations screened for SARS-CoV-2 and then





**Table 1. Characteristics of studies reporting on proportion of asymptomatic SARS-CoV-2 infections.**

| Author | Country, location | Total SARS-CoV-2, *n* | Asymptomatic SARS-CoV-2, *n* | Sex of asymptomatic people | Age of asymptomatic people, years, median | Follow-up method[a] |
|---|---|---|---|---|---|---|
| Contact investigation, single | | | | | | |
| Tong, ZD [44] | China, Zhejiang | 5 | 3 | 2 F, 3 M | 28 IQR 12–41 | 1, 3 |
| Huang, R [74] | China, Suqian | 2 | 1 | 1 F, 0 M | 54 | 3 |
| Jiang, XL [76] | China, Shandong | 8 | 3 | 3 F, 0 M | 35 IQR 0–53 | 3 |
| Jiang, X [75] | China, Chongqing | 3 | 1 | 1 F, 0 M | 8 | 2 |
| Liao, J [22] | China, Chongqing | 12 | 3 | NR | NR | 1, 2 |
| Hu, Z [21] | China, Nanjing | 4 | 1 | 0 F, 1 M | 64 | 2, 3 |
| Luo, SH [23] | China, Anhui | 4 | 1 | 1 F, 0 M | 50 | 1, 2, 3 |
| Chan, JF [18] | China, Guangdong | 5 | 1 | 0 F, 1 M | 10 | 1 |
| Ye, F [49] | China, Sichuan | 5 | 1 | 0 F, 1 M | 28 | 1, 2 |
| Bai, Y [17] | China, Anyang | 6 | 1 | 1 F, 0 M | 20 | 1 |
| Luo, Y [85] | China, Wuhan | 6 | 5 | NR | 37 IQR 7–62 | 1 |
| Zhang, J [50] | China, Wuhan and Beijing | 5 | 2 | 1 F, 1 M | NR | 2 |
| Zhang, B [110] | China, Guangdong | 7 | 2 | 0 F, 2 M | 13.5 IQR 13–14 | 3 |
| Huang, L [73] | China, Gansu | 7 | 2 | 2 F, 0 M | 44 IQR 38.5–49.5 | 2 |
| Qian, G [26] | China, Zhejiang | 8 | 2 | 1 F, 1 M | 30.5 IQR 1–60 | 1, 2 |
| Gao, Y [70] | China, Wuxi | 15 | 6 | 3 F, 3 M | 50 IQR 48–51 | 1, 2 |
| Contact investigation, aggregated | | | | | | |
| Hijnen, D [72] | Germany | 11 | 1 | 0 F, 1 M | 49 | 1 |
| Brandstetter, S [62] | Germany | 36 | 2 | NR | NR | 2 |
| Zhang, W2 [111] | China, Guiyang | 12 | 4 | NR | NR | 1, 2, 3 |
| Cheng, HY [66] | Taiwan | 22 | 4 | NR | NR | 1 |
| Wang, Z [47] | China, Wuhan | 47 | 4 | NR | NR | 1 |
| Wu, J [105] | China, Zhuhai | 83 | 8 | NR | NR | 1, 2 |
| Luo, L [36] | China, Guangzhou | 129 | 8 | NR | NR | 1, 2, 3 |
| Bi, Q [60] | China, Shenzhen | 87 | 17 | NR | NR | 2, 3 |
| Yang, R [108] | China, Wuhan | 78 | 33 | 22 F, 11 M | 37 IQR 26–45 | 3 |
| Outbreak investigation | | | | | | |
| Danis, K [32] | France | 13 | 1 | NR | NR | 1, 2 |
| Böhmer, MM [61] | Germany | 16 | 1 | NR | NR | 1 |
| Roxby, AC [94] | USA | 6 | 3 | NR | NR | 1 |
| Yang, N [48] | China, Xiaoshan | 10 | 2 | 1 F, 1 M | NR | 1, 2 |
| Schwierzeck, V [95] | Germany | 12 | 2 | NR | NR | 2 |
| Arons, MM [58] | USA | 47 | 3 | NR | NR | 2 |
| Park, SY [90] | South Korea | 97 | 4 | NR | NR | 2 |
| Dora, AV [68] | USA | 19 | 6 | 0 F, 6 M | 75 IQR 72–75 | 3 |
| Tian, S [43] | China, Shandong | 24 | 7 | NR | NR | 3 |
| Solbach, W [97] | Germany | 97 | 10 | NR | NR | 2 |
| Graham, N [71] | United Kingdom | 126 | 46 | NR | NR | 2 |

(*Continued*)



Accès à la totalité de la publication en mode pdf...

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# Notion de sources et citations…



**S7 Fig. Assessment of credibility of mathematical modelling studies.**
(PDF)

**S1 Table. Types of study included in successive versions of the living systematic review, as of 10 June 2020.**
(DOCX)

**S2 Table. Location of studies contributing data to review questions 1 and 2.**
(DOCX)

## Author Contributions

**Conceptualization:** Diana Buitrago-Garcia, Dianne Egli-Gany, Nicola Low.

**Data curation:** Diana Buitrago-Garcia, Dianne Egli-Gany, Michel J. Counotte, Stefanie Hossmann, Hira Imeri, Nicola Low.

**Formal analysis:** Michel J. Counotte, Georgia Salanti.

**Investigation:** Aziz Mert Ipekci.

**Methodology:** Diana Buitrago-Garcia, Dianne Egli-Gany, Michel J. Counotte, Georgia Salanti, Nicola Low.

**Project administration:** Diana Buitrago-Garcia, Dianne Egli-Gany.

**Supervision:** Nicola Low.

**Validation:** Diana Buitrago-Garcia, Dianne Egli-Gany, Michel J. Counotte, Stefanie Hossmann, Hira Imeri, Aziz Mert Ipekci, Nicola Low.

**Writing – original draft:** Diana Buitrago-Garcia, Nicola Low.

**Writing – review & editing:** Diana Buitrago-Garcia, Dianne Egli-Gany, Michel J. Counotte, Stefanie Hossmann, Hira Imeri, Aziz Mert Ipekci, Georgia Salanti, Nicola Low.

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# Figures pour vos rapports ou oraux.

Notion de citation



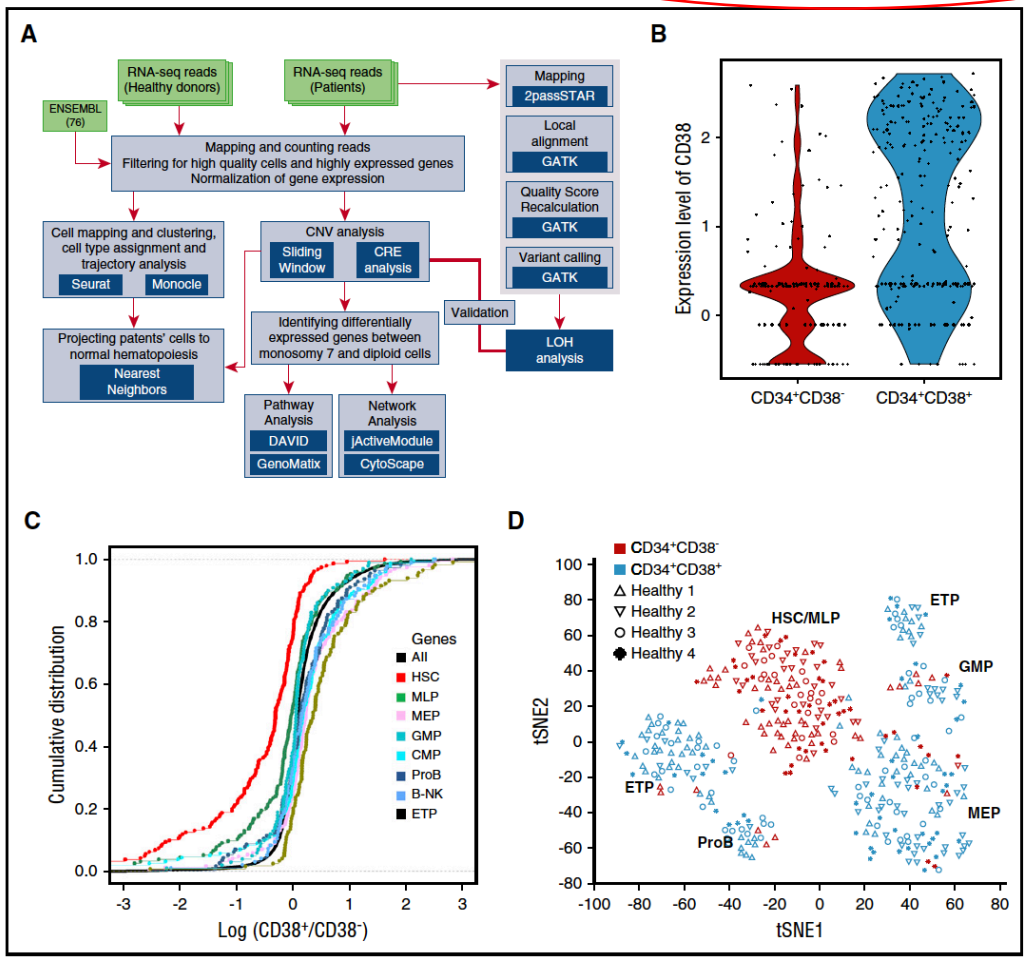


**Figure 1. Hematopoietic heterogeneity in healthy donors quantified by scRNA-seq.** $CD34^+CD38^-$ and $CD34^+CD38^+$ cells from 4 healthy donors (healthy 1-4) were sorted by surface-membrane markers and subjected to analyses. (A) The schematic pipeline consisting of 3 major analytic components: differentiation analysis with cells from healthy donors, identification and characterization of monosomy 7 cells with gene expression, and validation of monosomy identification with loss of reterozygosity (LOH). CNV, copy-number variation; CRE, chromosome relative expression; GATK, Genome Analysis Toolkit. (B) CD38 expression levels in $CD34^+CD38^-$ and $CD34^+CD38^+$ cells. Each dot represents a single cell. y-axis, batch-corrected gene expression levels. (C) Cumulative distribution of fold changes of expression of hematopoietic cell type signature genes between $CD34^+CD38^-$ and $CD34^+CD38^+$ cells. Each dot represents a gene. B-NK, B cell–natural killer cell precursor; CMP, common myeloid progenitor; ETP, earliest thymic progenitor; GMP, granulocyte-monocyte progenitor; MEP, megakaryocytic-erythroid progenitor; MLP, multilymphoid progenitor; ProB, pro–B cell. y-axis, cumulative distribution; x-axis, log (marker gene expression levels in $CD34^+CD38^+$ cells/marker gene expression levels in $CD34^+CD38^-$ cells). (D) t-distributed stochastic neighbor embedding (tSNE) plot of single-cell gene expression data. Single cells from 4 healthy donors (healthy 1-4) are represented by different symbols. Highly variable genes (1024) across all healthy donors were used in tSNE analysis.

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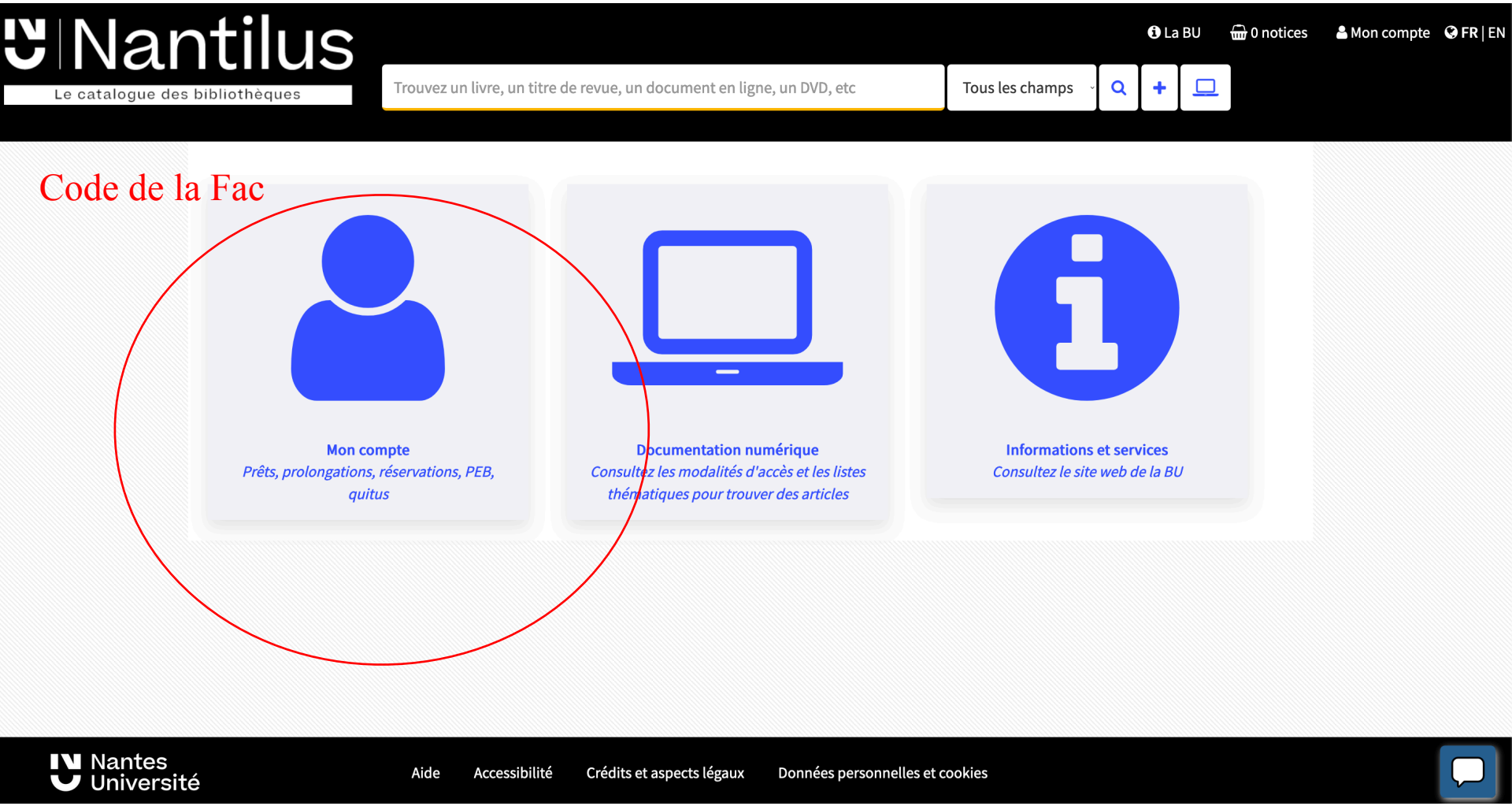
# Un exemple de recherche: Covid19 ?

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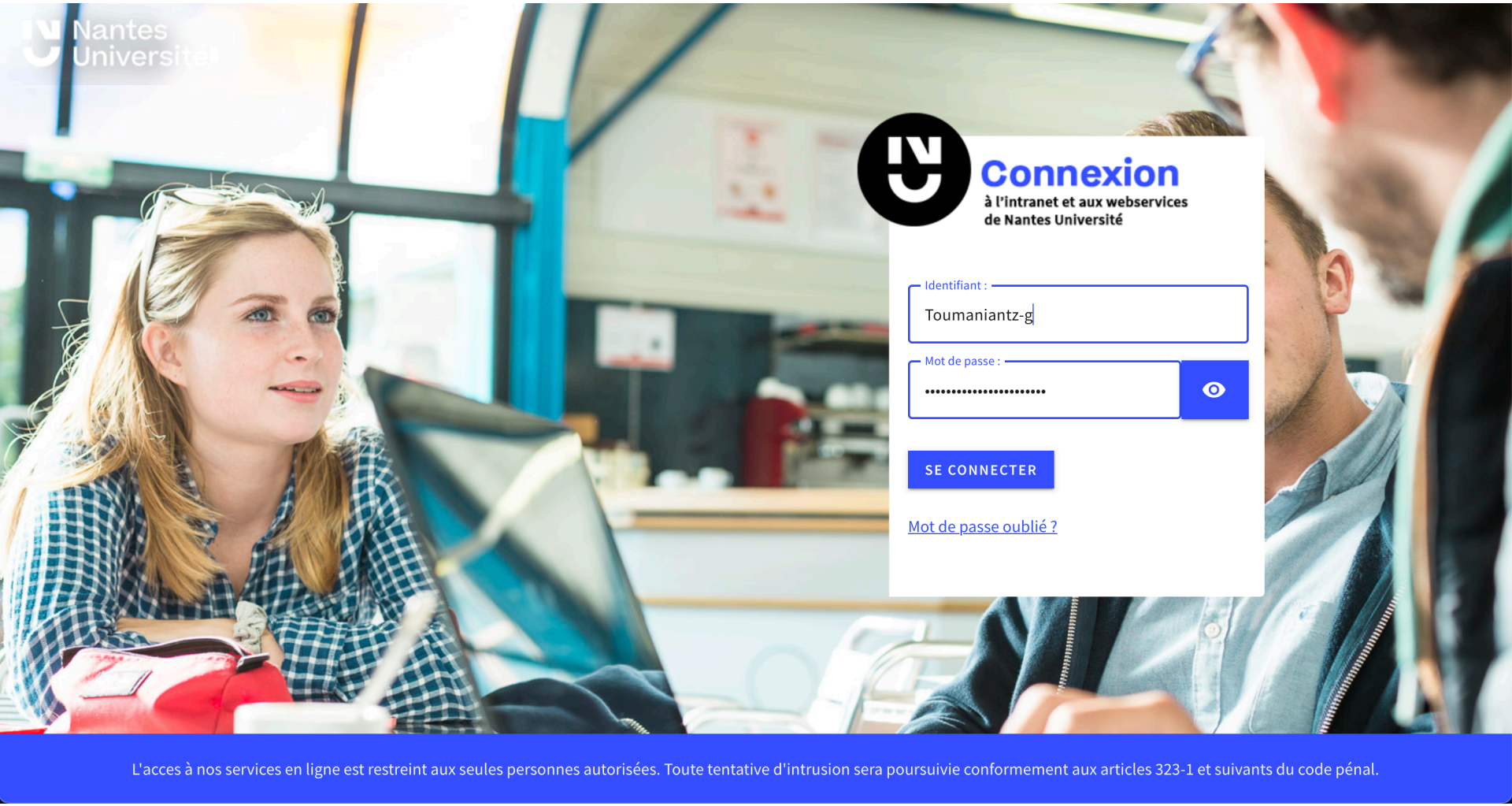
# Un exemple de recherche: Covid19 ?

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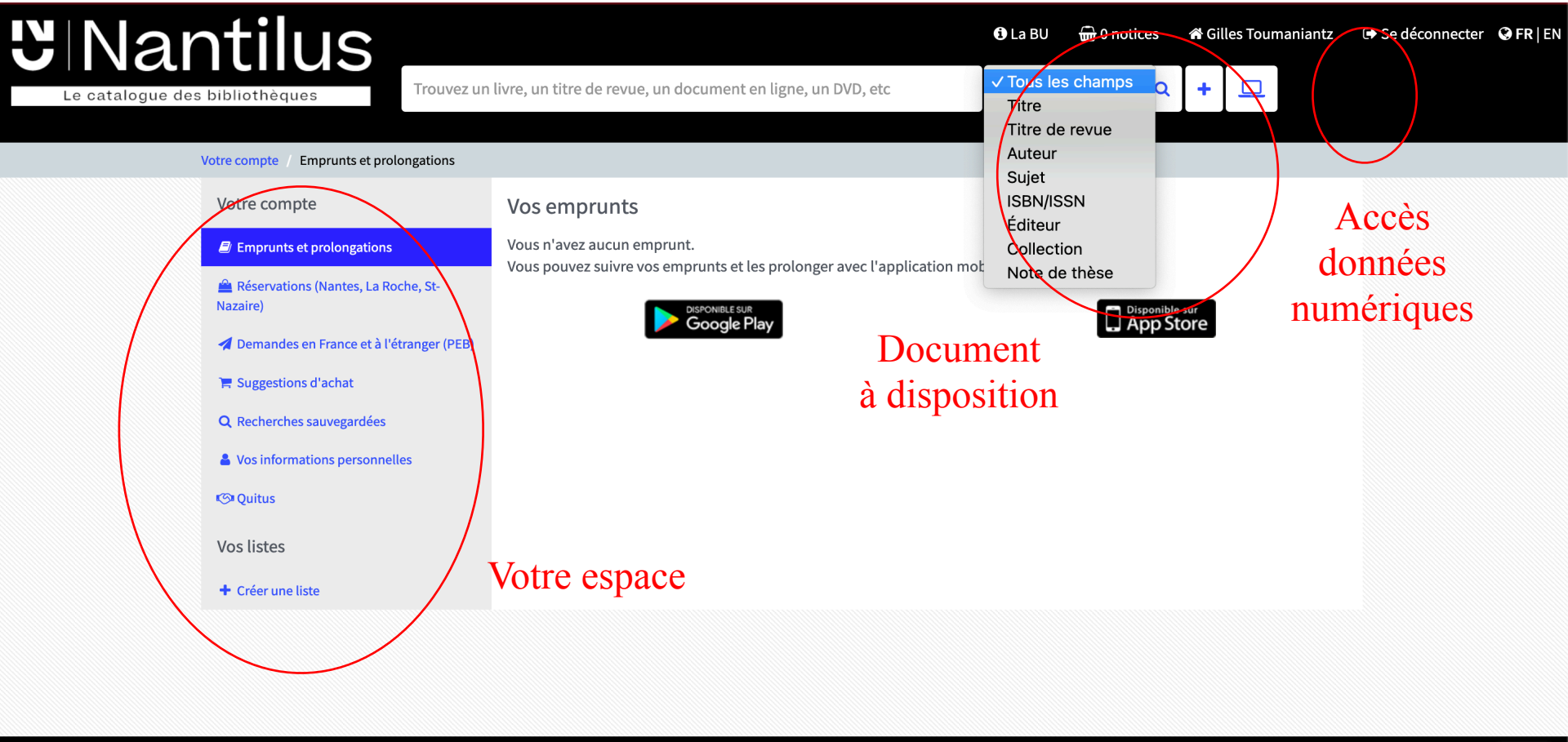
# Un exemple de recherche: Covid19 ?

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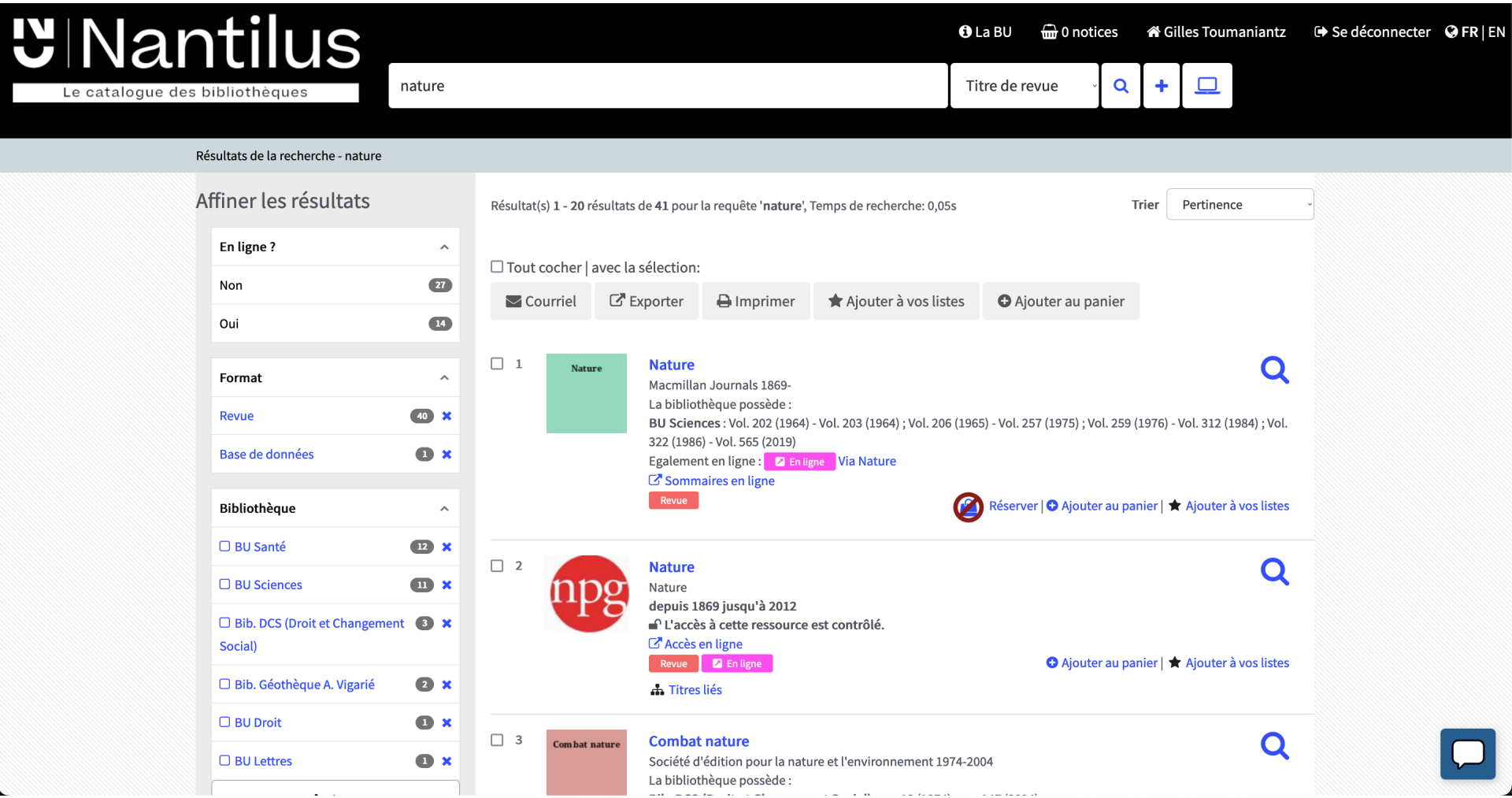
# Un exemple de recherche: Covid19 ?



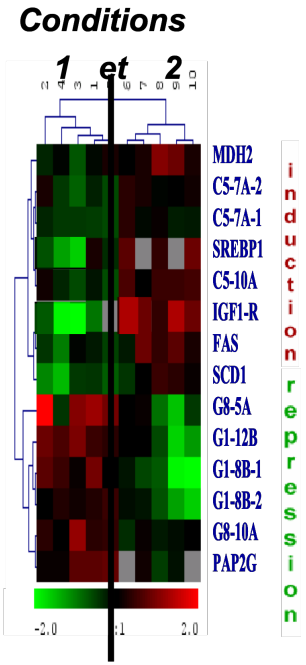

Mode d'emploi en ligne.
Attention pas Pub Med… Vous savez ce que vous cherchez.

# Au labo : analyse à haut débit de cette bibliographie.

**Les données expérimentales (en « omique ») => Biblio à au débit...**

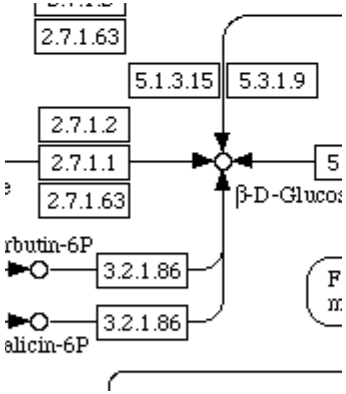
**sont-elles cohérentes/incohérentes**

**avec les connaissances du moment ?**




**littérature**


**Les modèles intégrés**




→ *Construire **un modèle intégré de connaissance***

→ *Développer des méthodes pour comparer données expé et modèle permettant de trouver les cohérences/incohérences*

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# 2. Les analyses nucléotidiques

***Question à étudier:***

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# 2. Les analyses nucléotidiques

## *Question à étudier:*

**Suite à un protocole de puce à ADN cet ARNm a été décrit comme étant différentiel dans des préparations de coeur issues d'un modèle d'insuffisance cardiaque par ligature de coronaire chez le rat. Il est en effet sous-exprimé. Déterminez la nature de ce messager.**

**tcgctgctgcctccagccagcgagggctcagcgccgctgtcgcagcagtggaccgcgggtatgggccta**
**ctcctggcgctcatcgtgctgctcatcgtagtgggcaacgtgttggtgatcgtggccatcgccaagacccc**
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**ccccgcgccctcgcc**

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# 2. Les analyses nucléotidiques


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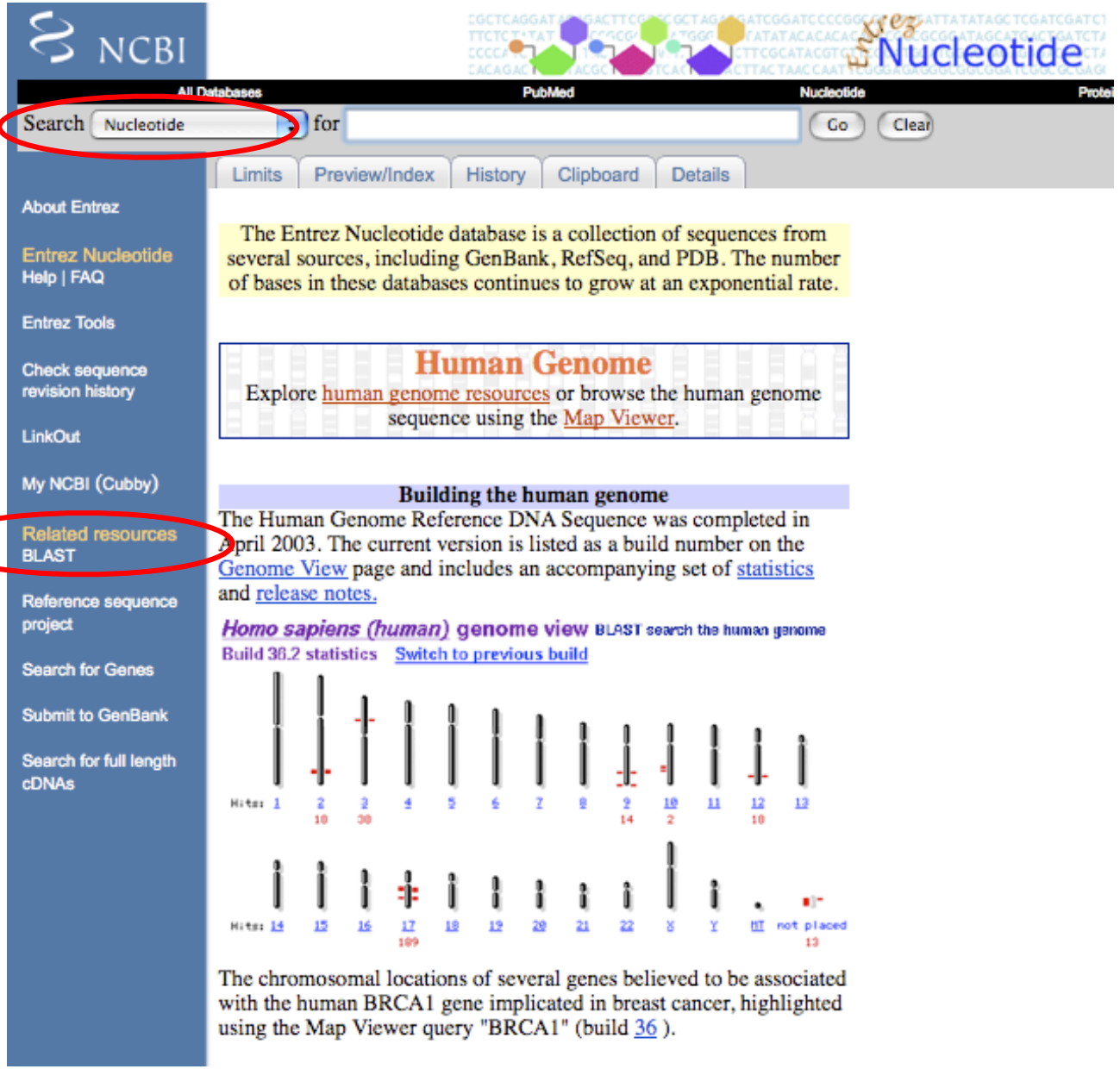
# 2. Les analyses nucléotidiques

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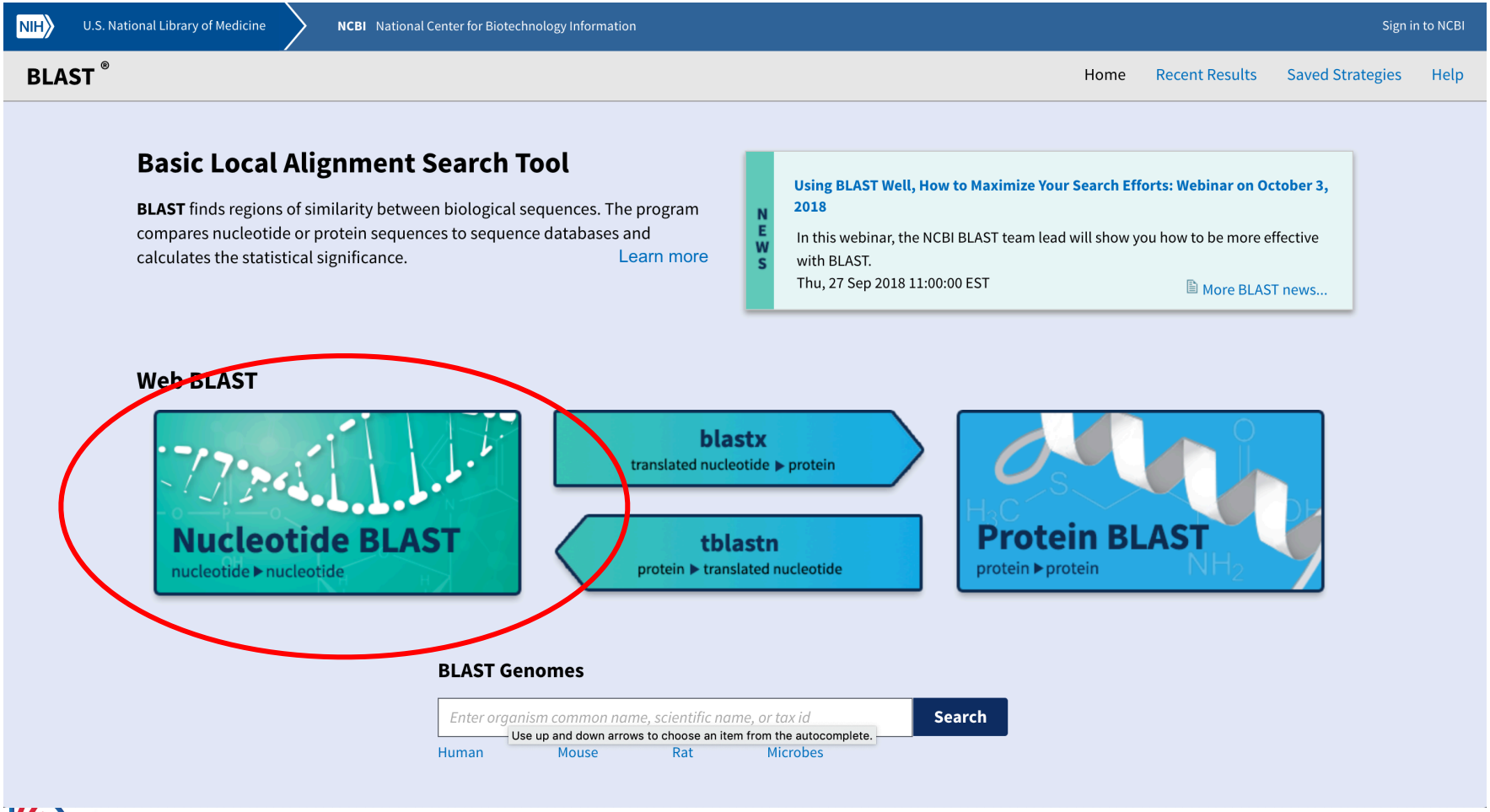
# 2. Les analyses nucléotidiques

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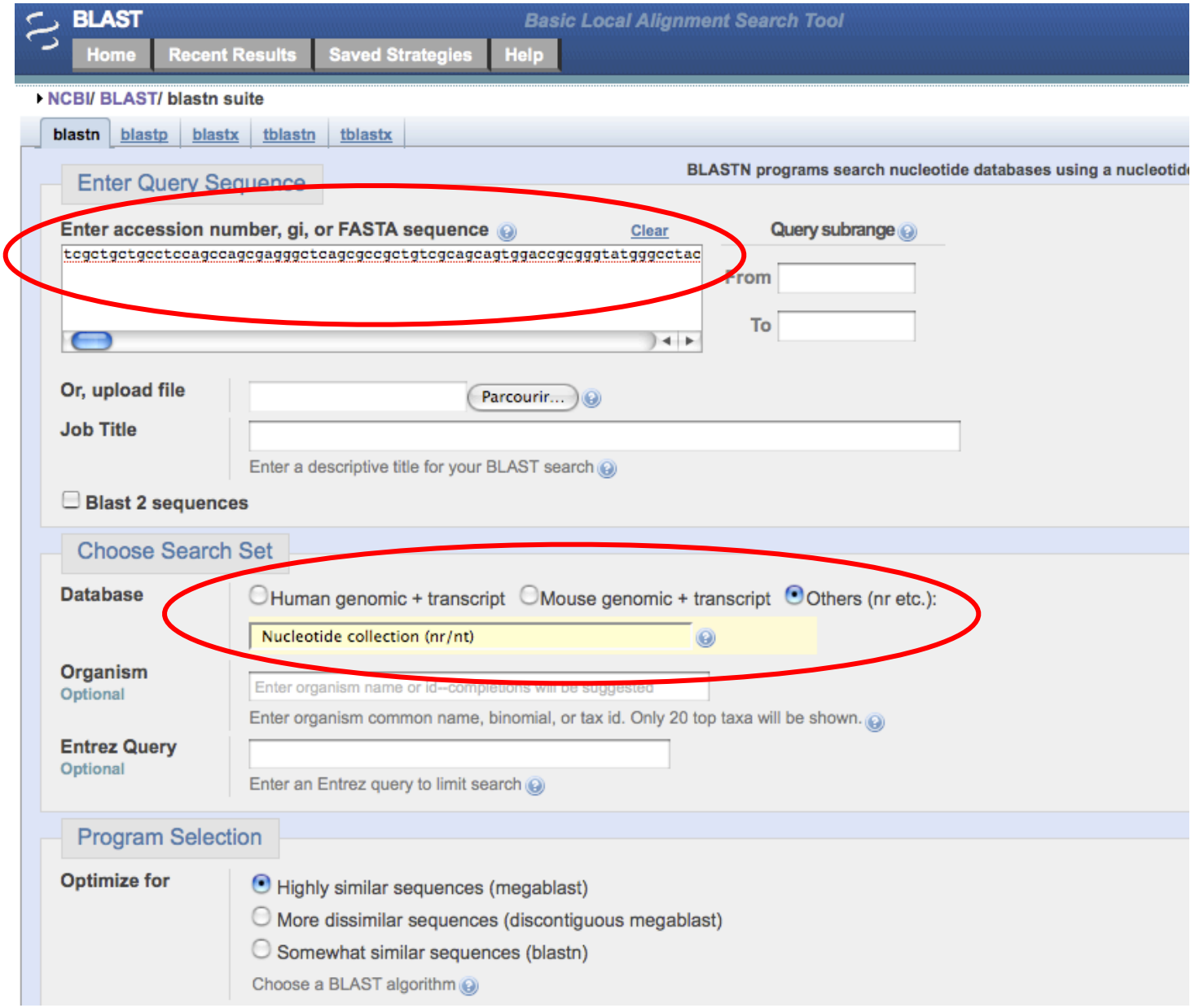
# 2. Les analyses nucléotidiques

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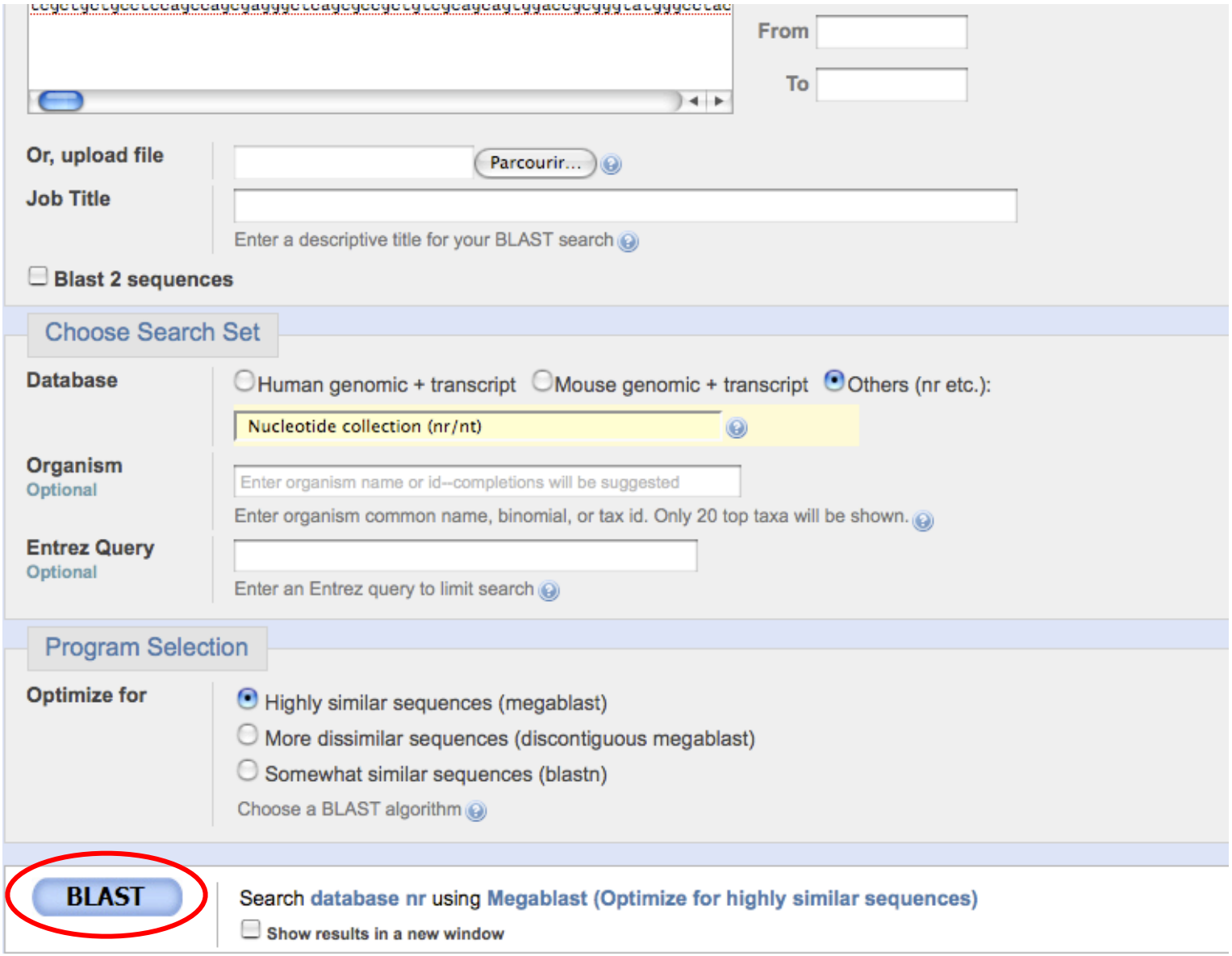
# 2. Les analyses nucléotidiques

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# 2. Les analyses nucléotidiques

BLAST Basic Local Alignment Search Tool

Home | Recent Results | Saved Strategies | Help

My NCBI [Sign In] [Register]

NCBI/ BLAST/ blastn suite/ **Formatting Results - HRDEGBVV01R**

Edit and Resubmit | Save Search Strategies | ▷Formatting options | ▷Download

## Nucleotide Sequence (716 letters)

**Query ID** lcl|27220
**Description** None
**Molecule type** nucleic acid
**Query Length** 716

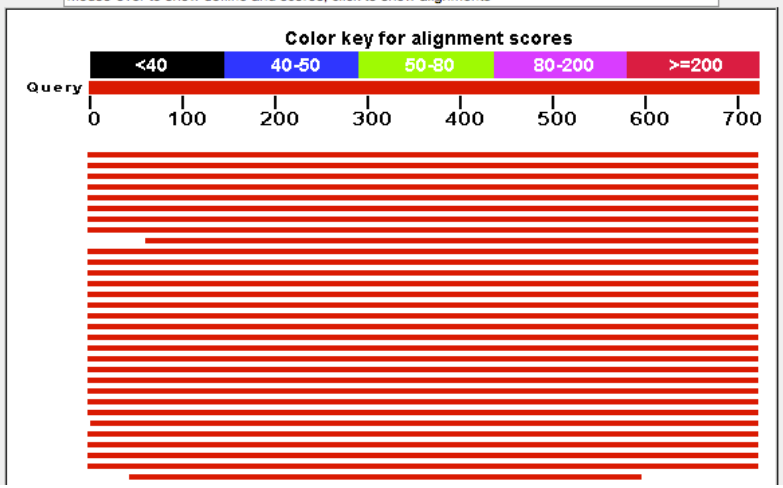
**Database Name** nr
**Description** All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS,environmental samples or phase 0, 1 or 2 HTGS sequences)
**Program** BLASTN 2.2.18+ ▷Citation

Other reports: ▷Search Summary [Taxonomy reports] [Distance tree of results]

▼ Graphic Summary

Distribution of 45 Blast Hits on the Query Sequence

Mouse-over to show defline and scores, click to show alignments

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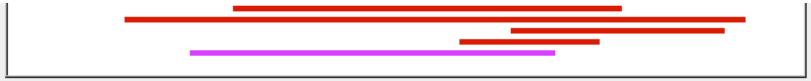
# 2. Les analyses nucléotidiques



## Descriptions

Legend for links to other resources: U UniGene E GEO G Gene S Structure M Map Viewer

**Sequences producing significant alignments:**
(Click headers to sort columns)

| Accession | Description | Max score | Total score | Query coverage | E value | Max ident | Links |
|---|---|---|---|---|---|---|---|
| NM_012701.1 | Rattus norvegicus adrenergic, beta-1-, receptor (Adrb1), mRNA | 1317 | 1317 | 100% | 0.0 | 99% | U E G |
| J05561.1 | R.norvegicus beta-1-adrenergic receptor gene, complete cds | 1317 | 1317 | 100% | 0.0 | 99% | G |
| D00634.1 | Rattus norvegicus gene for beta-1 adrenergic receptor, complete cds | 1295 | 1295 | 100% | 0.0 | 99% | E G |
| BC147435.1 | Mus musculus adrenergic receptor, beta 1, mRNA (cDNA clone MGC:182135 IMAC | 1157 | 1157 | 100% | 0.0 | 95% | U G |
| NM_007419.2 | Mus musculus adrenergic receptor, beta 1 (Adrb1), mRNA | 1157 | 1157 | 100% | 0.0 | 95% | U E G |
| AC158549.8 | Mus musculus chromosome 19, clone RP24-216K4, complete sequence | 1157 | 1157 | 100% | 0.0 | 95% | |
| L10084.1 | Mus musculus beta-1 adrenergic receptor gene, complete cds | 1157 | 1157 | 100% | 0.0 | 95% | E G |
| X75540.1 | M.mullata beta 1 adrenergic receptor gene | 1057 | 1057 | 100% | 0.0 | 93% | |
| AK018378.1 | Mus musculus 16 days embryo lung cDNA, RIKEN full-length enriched library, clor | 1037 | 1037 | 91% | 0.0 | 95% | U E G |
| AF169006.1 | Homo sapiens beta-1-adrenergic receptor (ADRB1) gene, complete cds | 1029 | 1029 | 100% | 0.0 | 92% | G |
| NM_001009375.1 | Felis catus adrenergic, beta-1-, receptor (ADRB1), mRNA >gb\|AF192344.1\|AF192 | 1029 | 1029 | 100% | 0.0 | 92% | G |
| EU332832.1 | Homo sapiens adrenergic, beta-1-, receptor (ADRB1) gene, complete cds | 1024 | 1024 | 100% | 0.0 | 92% | |
| XM_521608.2 | PREDICTED: Pan troglodytes beta-1-adrenergic receptor (ADRB1), mRNA | 1024 | 1024 | 100% | 0.0 | 92% | G |
| NM_000684.2 | Homo sapiens adrenergic, beta-1-, receptor (ADRB1), mRNA | 1024 | 1024 | 100% | 0.0 | 92% | U E G |
| AY567837.1 | Homo sapiens adrenergic, beta-1-, receptor (ADRB1) gene, complete cds | 1024 | 1024 | 100% | 0.0 | 92% | |
| AF169007.1 | Homo sapiens beta-1-adrenergic receptor (ADRB1) gene, complete cds | 1024 | 1024 | 100% | 0.0 | 92% | G |
| AL355543.13 | Human DNA sequence from clone RP11-86E10 on chromosome 10 Contains the A | 1024 | 1024 | 100% | 0.0 | 92% | |
| J03019.1 | Human beta-1-adrenergic receptor mRNA, complete cds | 1024 | 1024 | 100% | 0.0 | 92% | U E G |
| AC005886.2 | b240g16, complete sequence | 1018 | 1018 | 100% | 0.0 | 92% | |
| AB334518.1 | Sus scrofa ADRB1 gene for beta-1 adrenergic receptor, complete cds, breed: Lanc | 1013 | 1013 | 100% | 0.0 | 92% | G |
| AB334517.1 | Sus scrofa ADRB1 gene for beta-1 adrenergic receptor, complete cds, breed: Jinh | 1009 | 1009 | 100% | 0.0 | 92% | G |
| NM_001123074.1 | Sus scrofa adrenergic, beta-1-, receptor (ADRB1), mRNA | 1003 | 1003 | 100% | 0.0 | 92% | U G |
| AF042454.1 | Sus scrofa beta-1 adrenergic receptor gene, complete cds | 1003 | 1003 | 100% | 0.0 | 92% | G |
| NM_001008713.1 | Canis lupus familiaris adrenergic, beta-1-, receptor (ADRB1), mRNA | 979 | 979 | 100% | 0.0 | 91% | U G |
| U73207.1 | Canis familiaris beta1 adrenergic receptor (dogbeta1) gene, complete cds | 979 | 979 | 100% | 0.0 | 91% | E G |
| EU332753.1 | Cavia porcellus beta-1 adrenergic receptor (ADRB1) gene, complete cds | 935 | 935 | 99% | 0.0 | 90% | |
| DQ538524.1 | Bos taurus beta 1 adrenergic receptor gene, complete cds | 907 | 907 | 100% | 0.0 | 89% | G |

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# 2. Les analyses nucléotidiques

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| M14379.1 | Turkey beta-adrenergic receptor mRNA, complete cds | 501 | 501 | 89% | 2e-138 | 81% | U |
| AF055349.1 | Meriones unguiculatus beta-1-adrenergic receptor mRNA, partial cds | 364 | 364 | 30% | 2e-97 | 96% | |
| BC169226.1 | Homo sapiens cDNA clone IMAGE:9093418, partial cds | 261 | 261 | 24% | 3e-66 | 93% | |
| AF041457.1 | Cervus dama beta 1 adrenergic receptor mRNA, partial cds | 228 | 228 | 20% | 3e-56 | 95% | |
| U51098.1 | Cavia porcellus beta3-adrenergic receptor mRNA, partial cds | 132 | 132 | 52% | 3e-27 | 74% | G |

▼ Alignments ☐ Select All Get selected sequences Distance tree of results

☐ ref|NM_012701.1| UEG Rattus norvegicus adrenergic, beta-1-, receptor (Adrb1), mRNA
Length=1401

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(Over 10 PubMed links)

Score = 1317 bits (713), Expect = 0.0
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**Position 470/début séquence référencée**

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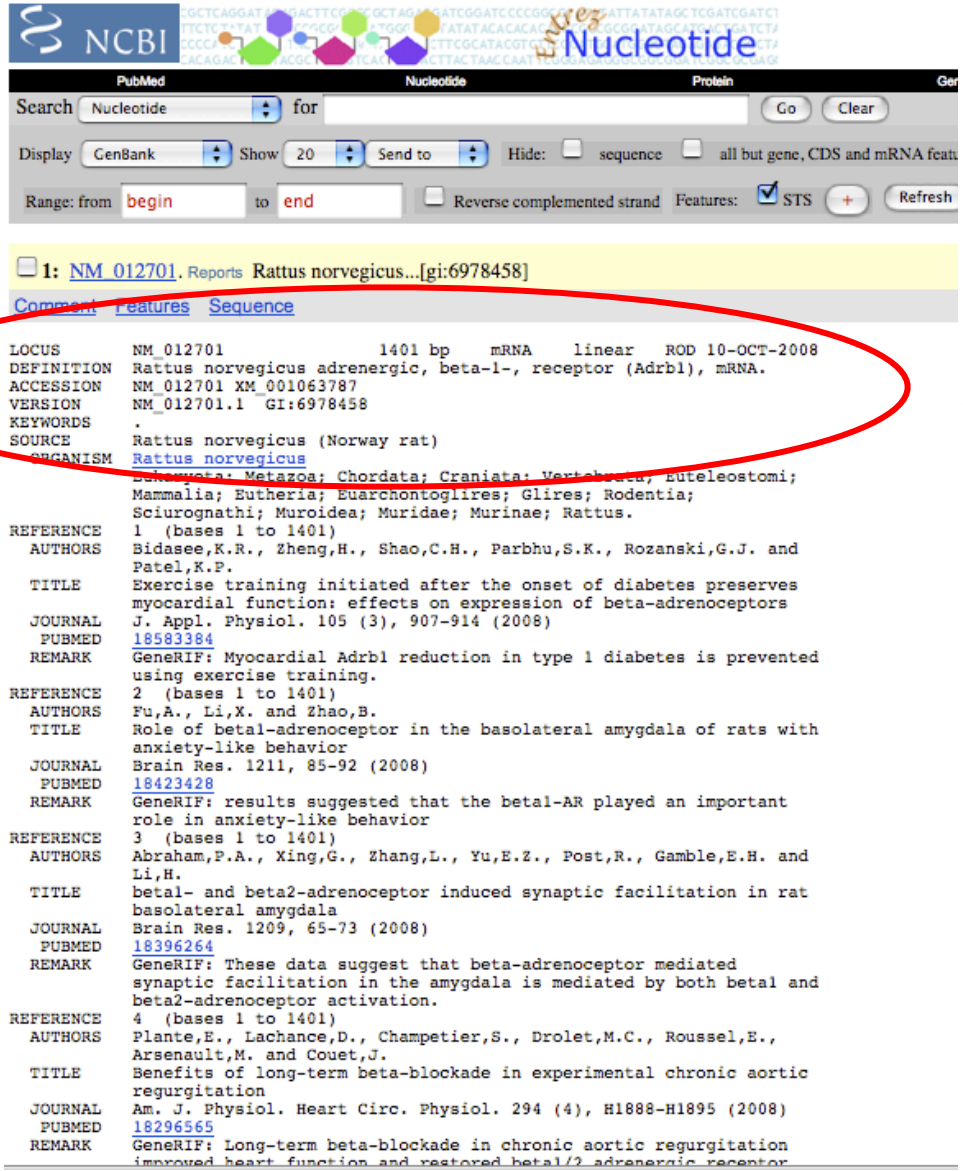
# 2. Les analyses nucléotidiques




**Identité**

**Bibliographie**

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# 2. Les analyses nucléotidiques

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**Défaut en position 470/début séquence référencée**

**Phase ouverte de lecture**

**Protéine**

**Séquence nucléotidique**

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# 2. Les analyses nucléotidiques

## *Question à étudier:*

**Mutation silencieuse, faux-sens ou non-sens chez mon patient ?**

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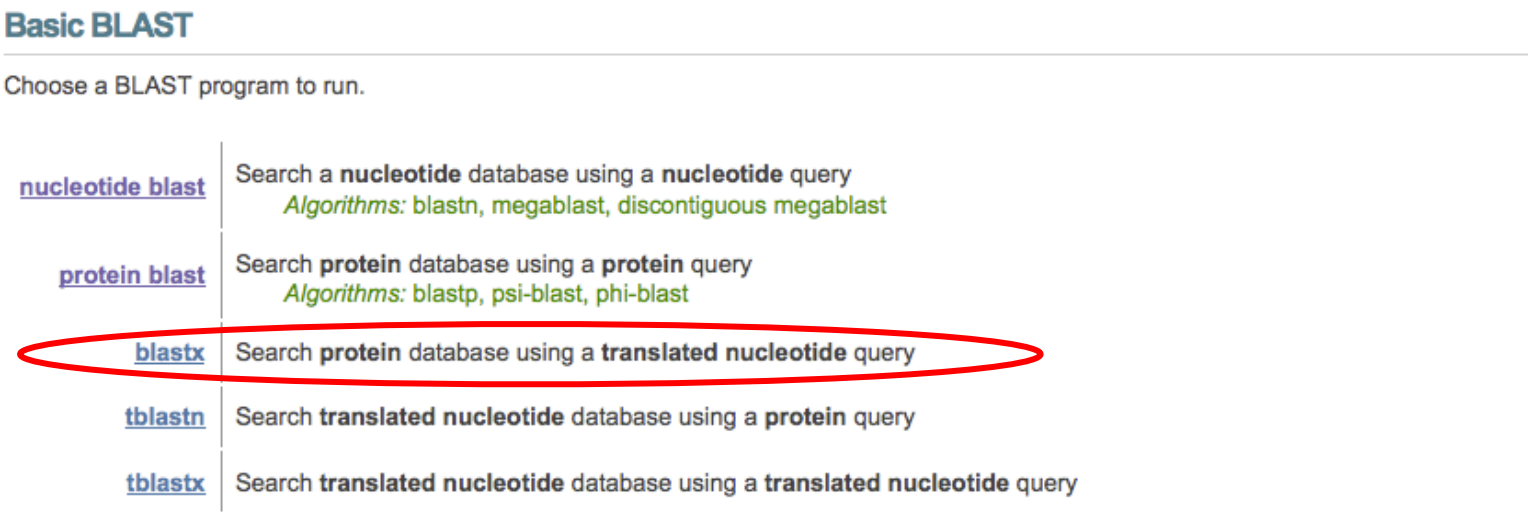
# 2. Les analyses nucléotidiques

## *Question à étudier:*

**Mutation silencieuse, faux-sens ou non-sens chez mon patient ?**

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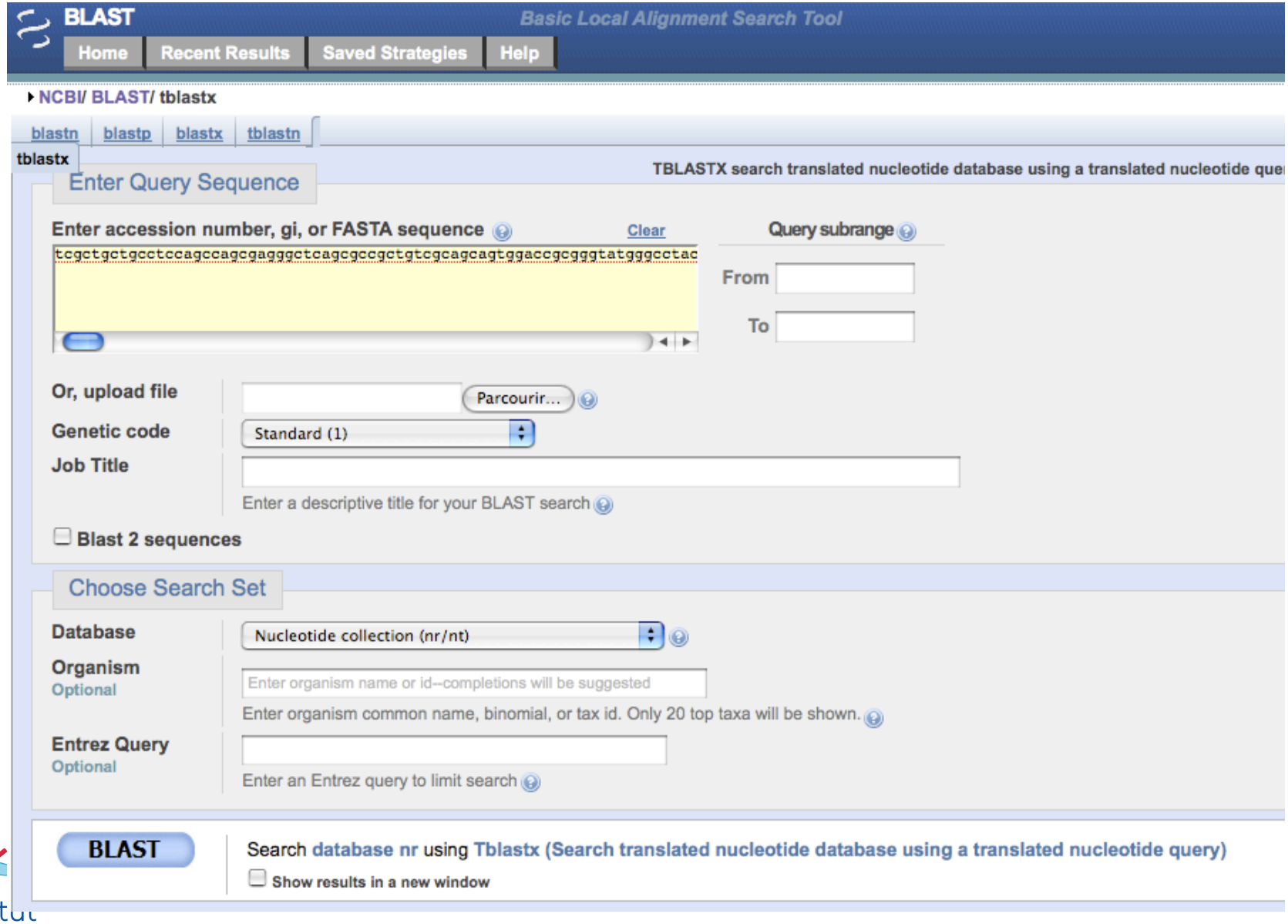
# 2. Les analyses nucléotidiques

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# 2. Les analyses nucléotidiques

BLAST Basic Local Alignment Search Tool

Home | Recent Results | Saved Strategies | Help

My NCBI [Sign In] [Register]

NCBI/ BLAST/ tblastx/ Formatting Results - HRFE3ZC7015

Edit and Resubmit | Save Search Strategies | ▷Formatting options | ▷Download

## Nucleotide Sequence (716 letters)

**Query ID** lcl|22459
**Description** None
**Molecule type** nucleic acid
**Query Length** 716

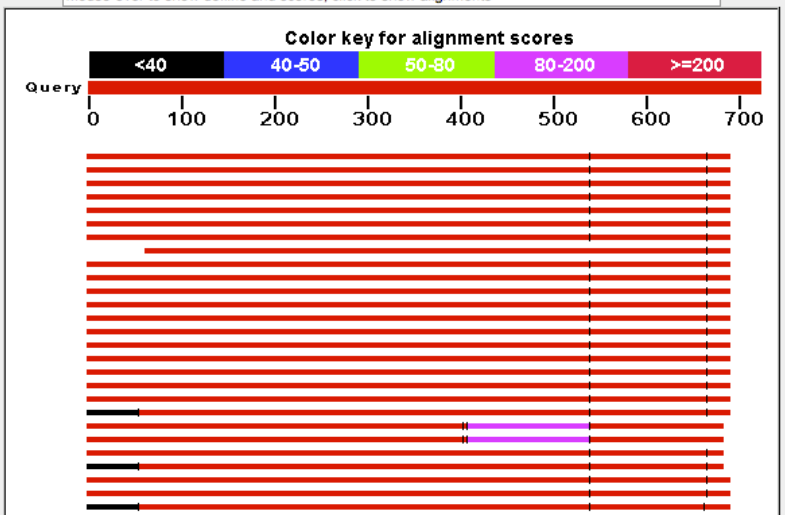
**Database Name** nr
**Description** All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS,environmental samples or phase 0, 1 or 2 HTGS sequences)
**Program** TBLASTX 2.2.18+ ▷Citation

Other reports: ▷Search Summary [Taxonomy reports]

### Graphic Summary

Distribution of 1000 Blast Hits on the Query Sequence

Mouse-over to show defline and scores, click to show alignments

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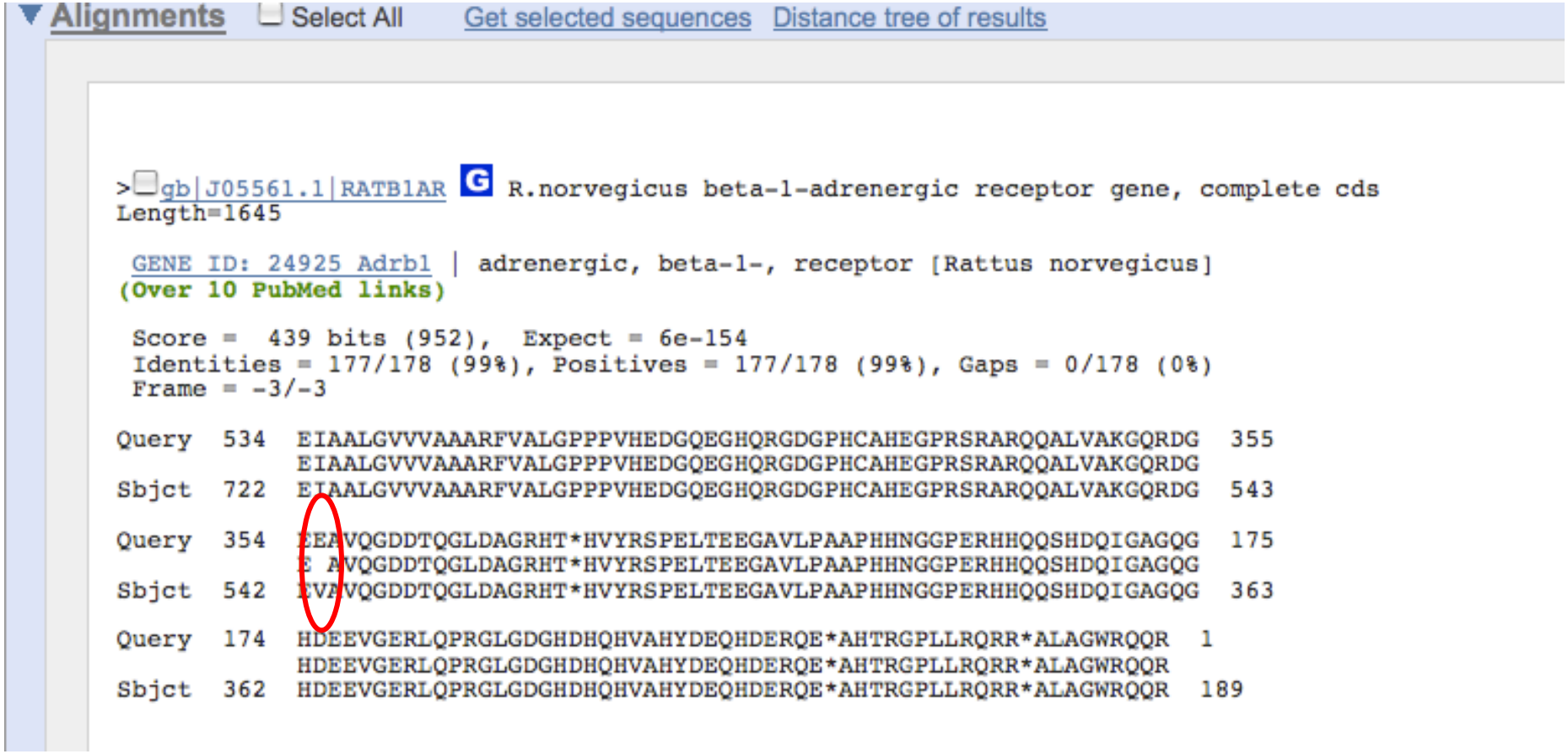
# 2. Les analyses nucléotidiques



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(Over 10 PubMed links)

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# 2. Les analyses nucléotidiques


**Position sur le génome ???**

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# 2. Les analyses nucléotidiques

Legend for links to other resources: U UniGene E GEO G Gene S Structure M Map Viewer

**Position sur le génome ???**

NCBI Entrez Gene

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | OMIM | PMC | Journals | Books

Search Gene for 6978458[NUID] Go Clear Save Search

Limits | Preview/Index | History | Clipboard | Details

Display Full Report Show 20 Sort by Relevance Send to

All: 1 | Current Only: 1 | Genes Genomes: 1 | SNP GeneView: 0

**1: Adrb1 adrenergic, beta-1-, receptor [ *Rattus norvegicus* ]**

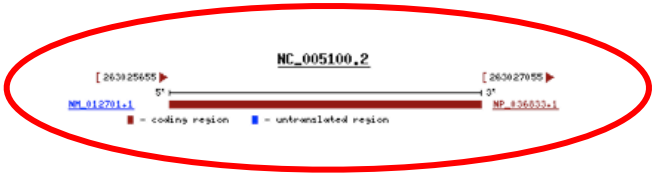
GeneID: 24925 updated 15-Oct-2008

**Summary**

| | |
|---|---|
| **Official Symbol** | Adrb1 provided by RGD |
| **Official Full Name** | adrenergic, beta-1-, receptor provided by RGD |
| **Primary source** | RGD:2059 |
| **See related** | Ensembl:ENSRNOG00000017002; RATMAP:34960 |
| **Gene type** | protein coding |
| **RefSeq status** | PROVISIONAL |
| **Organism** | *Rattus norvegicus* |
| **Lineage** | *Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Rattus* |
| **Also known as** | B1AR; RATB1AR; Adrb1 |
| **Summary** | binds beta-adrenergic receptor agonists isoproterenol, norepinephrine, and epinephrine; mediates adenylylcyclase induction; involved in regulation of calcium current [RGD] |

**Genomic regions, transcripts, and products**

Go to reference sequence details Try our new Sequence Viewer




Entrez Gene Home

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- Summary
- Genomic regions, transcripts...
- Genomic context
- Bibliography
- Interactions
- General gene information
- General protein information
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- HomoloGene
- Map Viewer
- Nucleotide
- PubChem Compound
- PubChem Substance
- Full text in PMC
- Probe
- Protein
- PubMed
- PubMed (GeneRIF)
- Taxonomy
- UniSTS
- Ensembl
- Evidence Viewer
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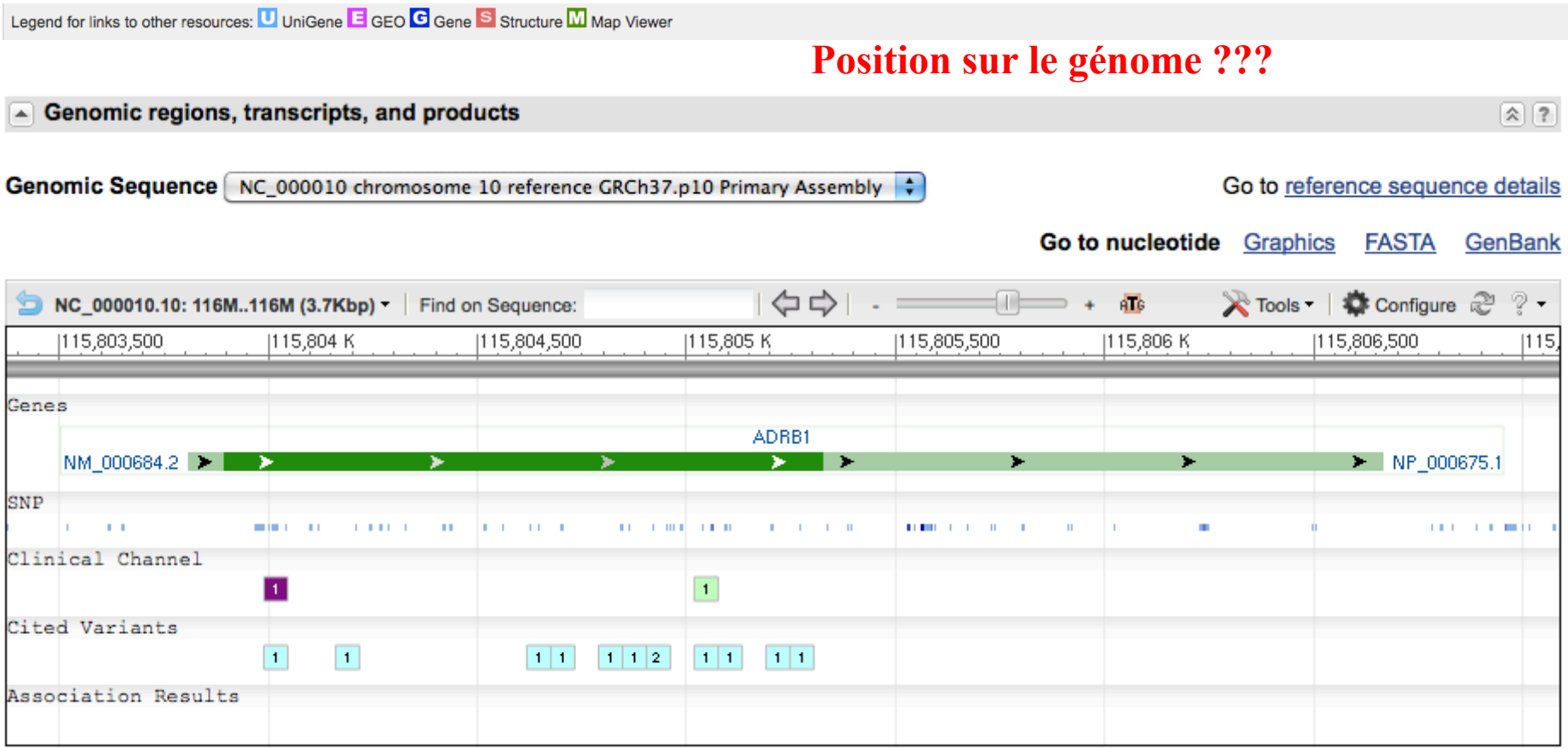
- LinkOut

Entrez Gene Info

# 2. Les analyses nucléotidiques

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# 2. Les analyses nucléotidiques


=> *Accès à toute séquence des génomes séquencés…*

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# 2. Les analyses nucléotidiques

# *3. Les pathologies héréditaires*

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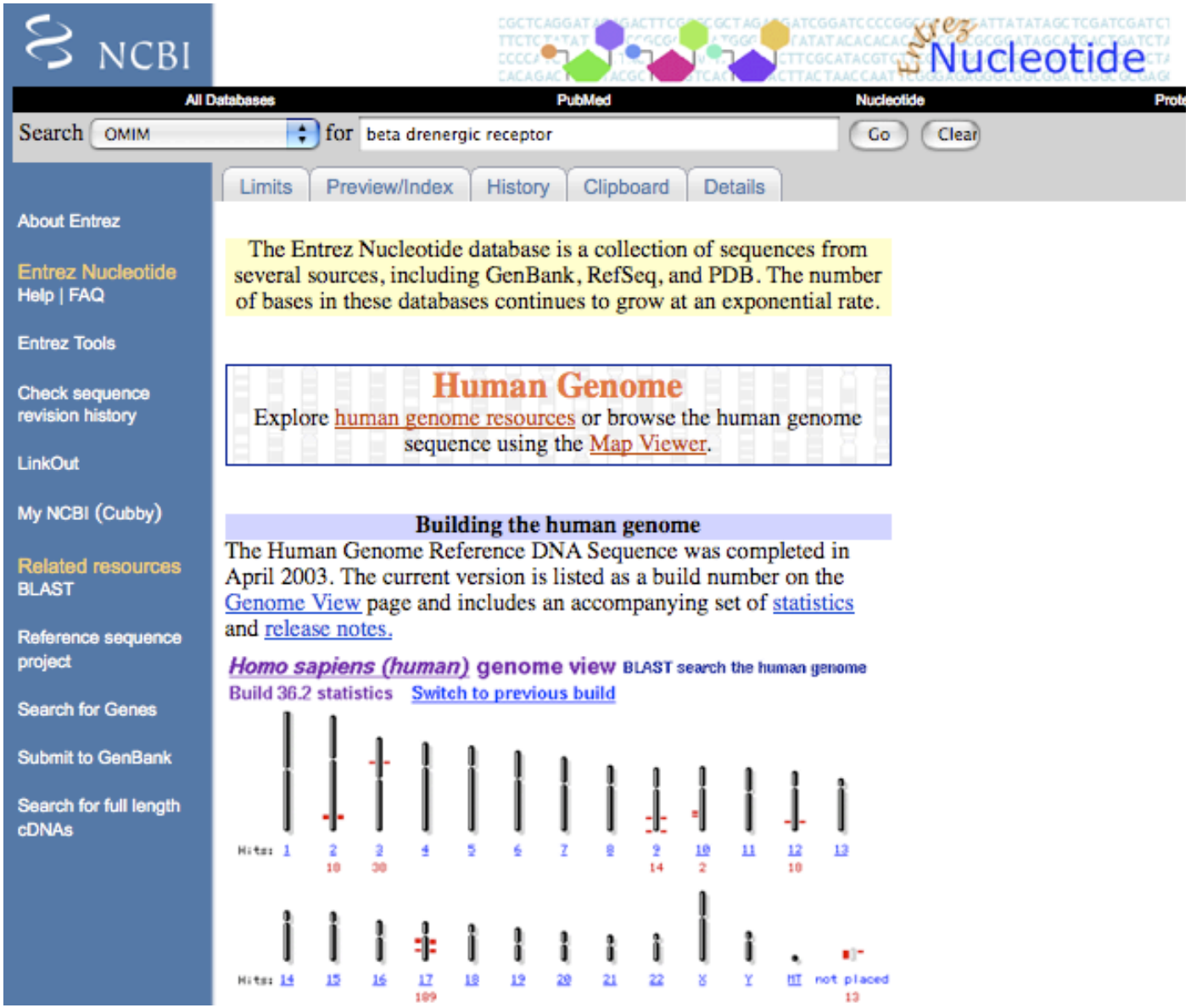
# 3. Les pathologies héréditaires

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# 3. Les pathologies héréditaires


**L'onglet OMIM est un outils de synthèse**

# 3. Les pathologies héréditaires

NCBI

OMIM
Online Mendelian Inheritance in Man
Johns Hopkins University

My NCBI [Sign In] [Register]

All Databases | PubMed | Nucleotide | Protein | Genome | Structure | PMC | OMIM

Search OMIM for [Go] [Clear]

Limits | Preview/Index | History | Clipboard | Details

Display Detailed Show 20 Send to

MIM *109691
Cloning
Gene Structure
Mapping
Molecular Genetics
Animal Model
Allelic Variants
• View List
References
Contributors
Creation Date
Edit History

• Gene map

Entrez Gene
N Nomenclature
R RefSeq
G GenBank
P Protein
U UniGene

LinkOut
HGVS
HGMD
GAD
MGI

Links

*109691
**BETA-3-ADRENERGIC RECEPTOR; ADRB3**

Gene map locus 8p12-p11.2

**TEXT**

**CLONING**

Emorine et al. (1989) isolated a third beta-adrenergic receptor, beta-3-adrenergic receptor (ADRB3). (See ADRB1 (109630) and ADRB2 (109690).) Exposure of eukaryotic cells transfected with this gene to adrenaline or noradrenaline promoted the accumulation of adenosine 3-prime,5-prime-monophosphate. The potency of beta-AR agonists and inhibitors was described.

Van Spronsen et al. (1993) demonstrated that the transcription start sites of the mouse and human ADRB3 mRNA are located in a region comprised between 150 and 200 nucleotides 5-prime from the ATG translation start codon. Motifs potentially implicated in heterologous regulation of ADRB3 expression by glucocorticoids and by beta-adrenergic agonists were identified upstream from these cap sites.

**GENE STRUCTURE**

Van Spronsen et al. (1993) described the exon/intron structure of the mouse and human ADRB3 genes. Their results suggested that utilization of alternate promoters and/or 3-prime untranslated regions may allow tissue-specific regulation of the expression of ADRB3.

**MAPPING**

Wilkie et al. (1993) presented a list of G protein-coupled receptor genes (their Table 3), indicating that the ADRB3 gene had been mapped to 8p12-p11.2 and the homologous gene to mouse chromosome 8.

**MOLECULAR GENETICS**

The beta-3-adrenergic receptor, located mainly in adipose tissue, is involved in the regulation of lipolysis and thermogenesis. The potential relevance of this receptor to obesity (see 601665) in humans led Clement et al. (1995) to screen obese patients for the mutation in the ADRB3 gene that results in replacement of tryptophan by arginine at position 64 (W64R; 109691.0001). They studied DNA extracted from leukocytes of 94 normal subjects and 185 unrelated patients with morbid obesity, as defined by a body-mass index (BMI; the weight in kilograms divided by the square of the height in meters) greater than 40. The mutation was detected by analysis of RFLPs with the restriction enzyme BstNI, which discriminates between the normal and mutant sequences. The frequency of the W64R variant was similar in the morbidly obese patients and the normal subjects: 0.08 and 0.10, respectively. However, patients with morbid obesity who were heterozygous for the allele had an increased capacity to gain weight: the mean weight in the 14 heterozygous patients was 140 kg, as compared with 126 kg in the 171 patients without the mutation ($P = 0.03$). There were no homozygotes in this sample. The cumulative 25-year change in weight (from the age of 20 years) was 67 kg in W64R heterozygotes, as compared with 51 kg in those without the mutation. The maximum weight differential (the maximal lifetime weight minus the weight at 20 years of age) in the heterozygotes was 74 kg, as compared with 59 kg in the patients without the mutation ($P = 0.02$). Clement et al. (1995) interpreted the findings as indicating that the ADRB3 gene mutation W64R increases the capacity to gain weight.

**ANIMAL MODEL**

To determine whether the sympathetic nervous system is the efferent arm of diet-induced thermogenesis, Bachman et al. (2002) created mice that lacked the beta-adrenergic receptors ADRB1, ADRB2, and ADRB3. Beta-less mice on a chow

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# 3. Les pathologies héréditaires



the allele had an increased capacity to gain weight: the mean weight in the 14 heterozygous patients was 140 kg, as compared with 126 kg in the 171 patients without the mutation (P = 0.03). There were no homozygotes in this sample. The cumulative 25-year change in weight (from the age of 20 years) was 67 kg in W64R heterozygotes, as compared with 51 kg in those without the mutation. The maximum weight differential (the maximal lifetime weight minus the weight at 20 years of age) in the heterozygotes was 74 kg, as compared with 59 kg in the patients without the mutation (P = 0.02). Clement et al. (1995) interpreted the findings as indicating that the ADRB3 gene mutation W64R increases the capacity to gain weight.

**ANIMAL MODEL**

To determine whether the sympathetic nervous system is the efferent arm of diet-induced thermogenesis, Bachman et al. (2002) created mice that lacked the beta-adrenergic receptors ADRB1, ADRB2, and ADRB3. Beta-less mice on a chow diet had a reduced metabolic rate and were slightly obese. On a high-fat diet, beta-less mice, in contrast to wildtype mice, developed massive obesity that was due entirely to a failure of diet-induced thermogenesis. Bachman et al. (2002) concluded that the beta-adrenergic receptors are necessary for diet-induced thermogenesis and that this efferent pathway plays a critical role in the body's defense against diet-induced obesity.

**ALLELIC VARIANTS**
**(selected examples)**

**.0001 OBESITY, SUSCEPTIBILITY TO [ADRB3, TRP64ARG]**

Using a candidate gene approach to study the genetics of obesity (601665), Clement et al. (1995) found evidence suggesting that the trp64-to-arg (W64R) variant of the ADRB3 gene increases the capacity to gain weight. Gagnon et al. (1996) failed to find an association between W64R and obesity in studies in 2 cohorts: the Quebec Family Study (QFS) and the Swedish Obese Subjects (SOS).

Walston et al. (1995) found that Pima Indians homozygous for the W64R ADRB3 mutation had an earlier onset of noninsulin-dependent diabetes mellitus (NIDDM; 125853) and tended to have a lower resting metabolic rate. The authors suggested that the mutation may accelerate the onset of NIDDM by altering the balance of energy metabolism in visceral adipose tissue.

Elbein et al. (1996) tested the hypothesis that the beta-3-adrenergic receptor locus affects diabetes susceptibility, obesity as measured by body mass index (BMI), and components of the insulin (176730) resistance syndrome, by examining ADRB3 allele sharing in families ascertained for 2 or more sibs with NIDDM. They found no evidence for linkage to NIDDM as a dichotomous trait and no evidence for linkage to BMI, waist/hip ratio, insulin levels, or glucose levels as quantitative traits or to reported age of onset among NIDDM individuals. The W64R mutation present in 11% of the population also did not show linkage or association. They concluded that the beta-3-adrenergic receptor locus does not play an important role in NIDDM susceptibility or in the insulin resistance syndrome among members of families with a strong predisposition to NIDDM.

Kim-Motoyama et al. (1997) examined the frequency of the W64R variant in 278 Japanese men in relation to visceral obesity assessed by computerized tomography. They found that the mutation was more frequent in subjects with higher BMI. In subjects with a moderate degree of obesity, the mutation (homozygotes and heterozygotes) was associated with visceral obesity (higher ratio of visceral to subcutaneous fat area). Furthermore, the W64R variant was more frequent in subjects with lower serum triglyceride levels, and homozygotes, but not heterozygotes, exhibited lower triglyceride levels. Kim-Motoyama et al. (1997) suggested that the mutation may describe a subset of subjects characterized by decreased lipolysis in visceral adipose tissue.

To examine the effect of W64R on body weight during adult life, the ADRB3 genotypes of 186 unselected Japanese men, most of whom had records of body weight measured yearly from 25 to 53 years of age, were determined by Nagase et al. (1997). Of these subjects, 26 were diagnosed as having noninsulin-dependent diabetes mellitus (NIDDM) and 41 as having impaired glucose tolerance. The results suggested that ADRB3 is not a major contributing factor to obesity or NIDDM in Japanese men.

Buettner et al. (1998) examined the prevalence of the 2 ADRB3 alleles in Germany and looked for associations between the ADRB3 genotype and obesity and NIDDM. The frequencies of the different genotypes in the examined cohort were as follows: trp64/trp64, 88.3%; trp64/arg64, 10.8%; and arg64/arg64, 0.8%. The authors found no significant differences between the different genotypes when comparing age, BMI, weight, total and high density lipoprotein, cholesterol, fasting insulin, HbA1c, and blood pressure. They concluded that the NIDDM phenotype did not differ significantly between the different genotype groups in terms of age of diabetes onset or HbA1c.

Using hyperinsulinemic/euglycemic clamp methodology, Garcia-Rubi et al. (1998) measured insulin sensitivity in 13 obese women heterozygous for the W64R ADRB3 variant and in 14 women homozygous for the normal gene. Exogenous glucose infusion during the clamp was significantly lower (P = 0.03) in W64R heterozygotes (241 +/- 135 mg/min) compared with normal homozygotes (379 +/- 172 mg/min). They concluded that obese postmenopausal women who are heterozygous for the W64R variant have greater insulin resistance than women homozygous for the normal gene matched for age, body composition, and physical activity.

Mitchell et al. (1998) detected an effect of the W64R variant on obesity in a Mexican-American population. They had previously identified a major quantitative trait locus (QTL) influencing the serum concentrations of leptin on 2p in a Mexican-American population in south Texas (Comuzzie et al., 1997). They studied 45 sib pairs who were concordant (identical by descent) for this locus on chromosome 2, which had been shown previously to be tightly linked to obesity in this population. The W64R variant, detected by PCR-RFLP analysis, was present in 1 sib within each of the 45 sib pairs. Presence of the variant was associated with a significantly higher values in body mass index, fat mass, and waist circumference. The paired-sib design enhanced their ability to detect the effects of this variant by allowing them to account for variation attributable to another obesity susceptibility locus and to background genes.

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# 4. Les analyses génomiques

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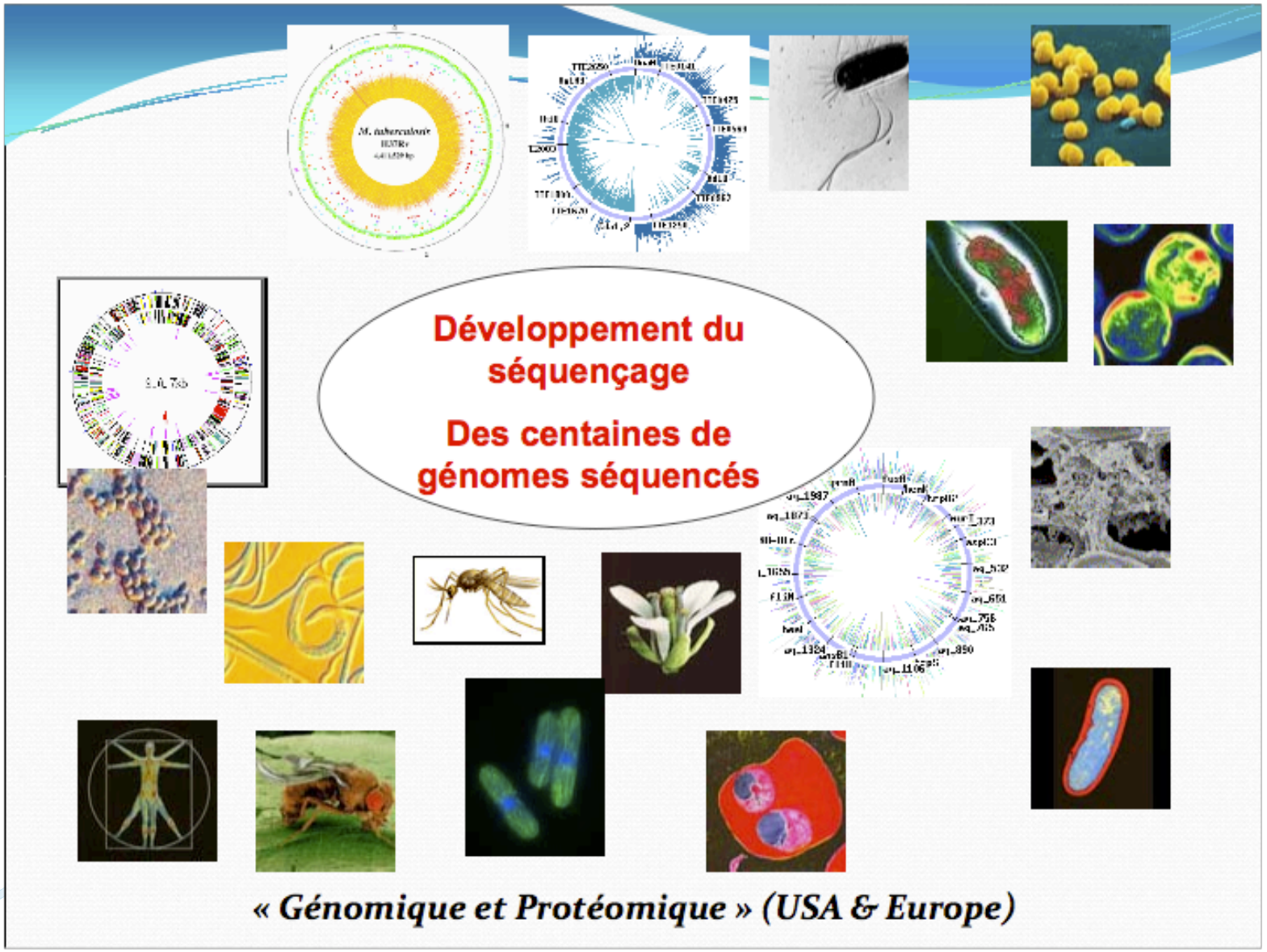
# 4. Les analyses génomiques

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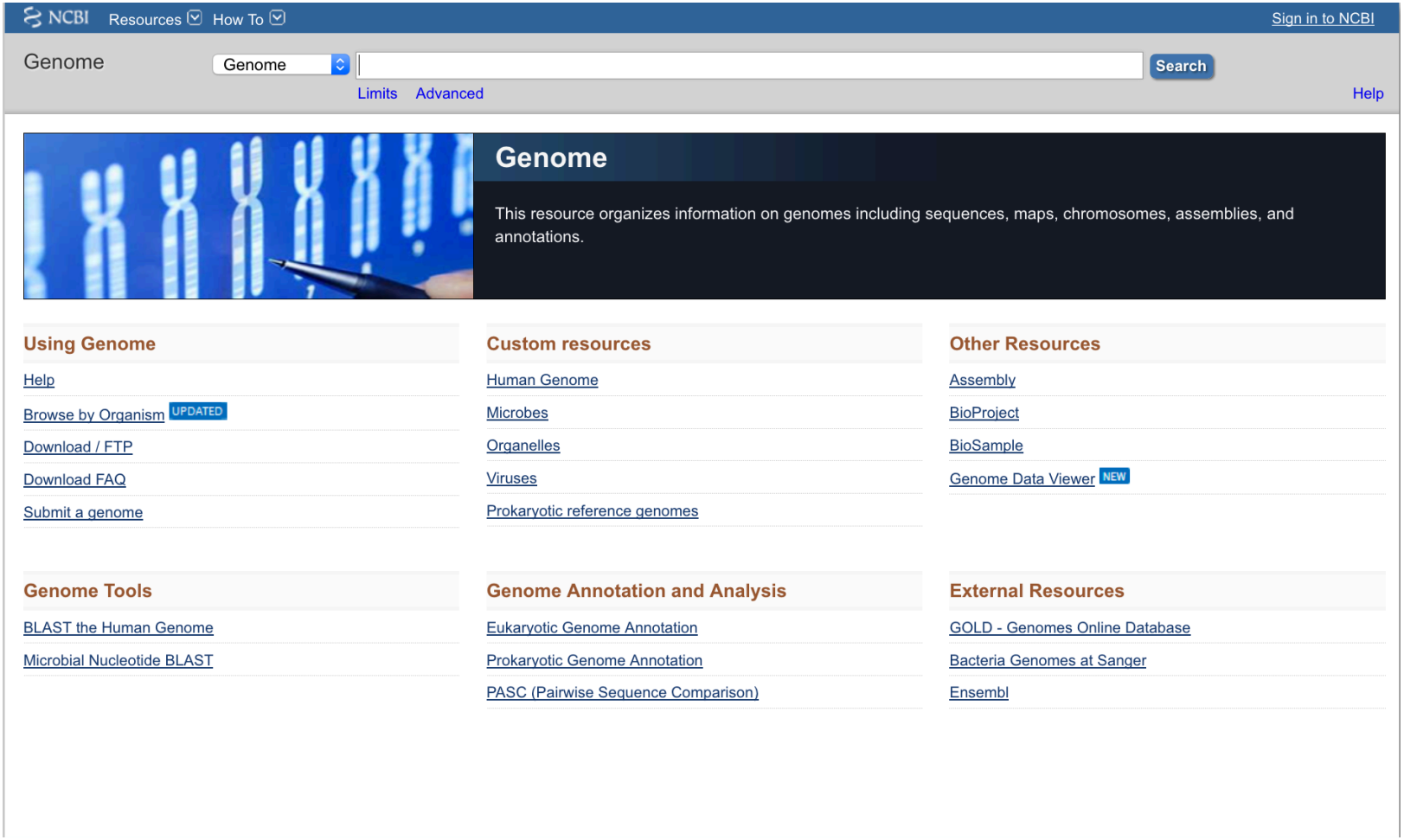
# 4. Les analyses génomiques

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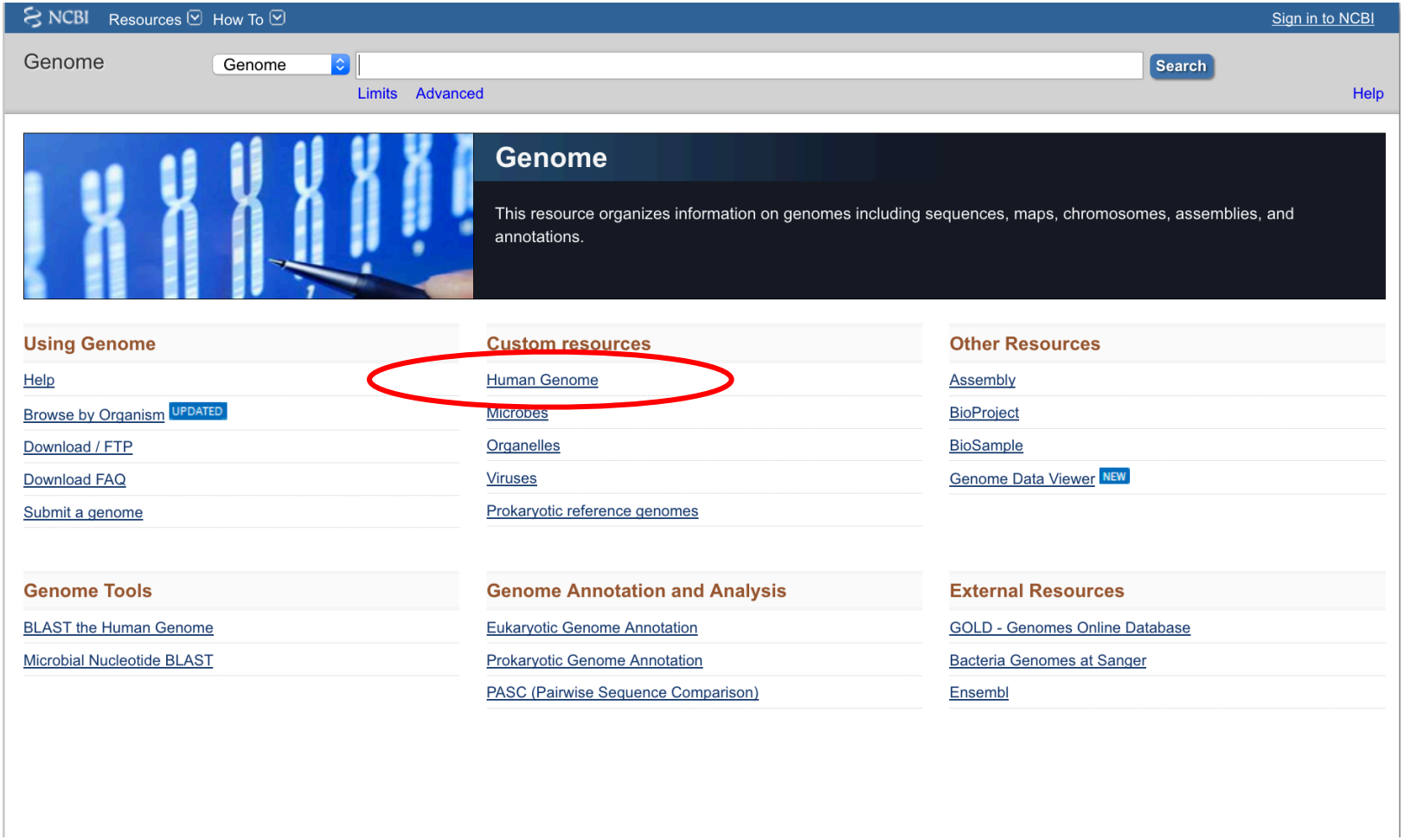
# 4. Les analyses génomiques

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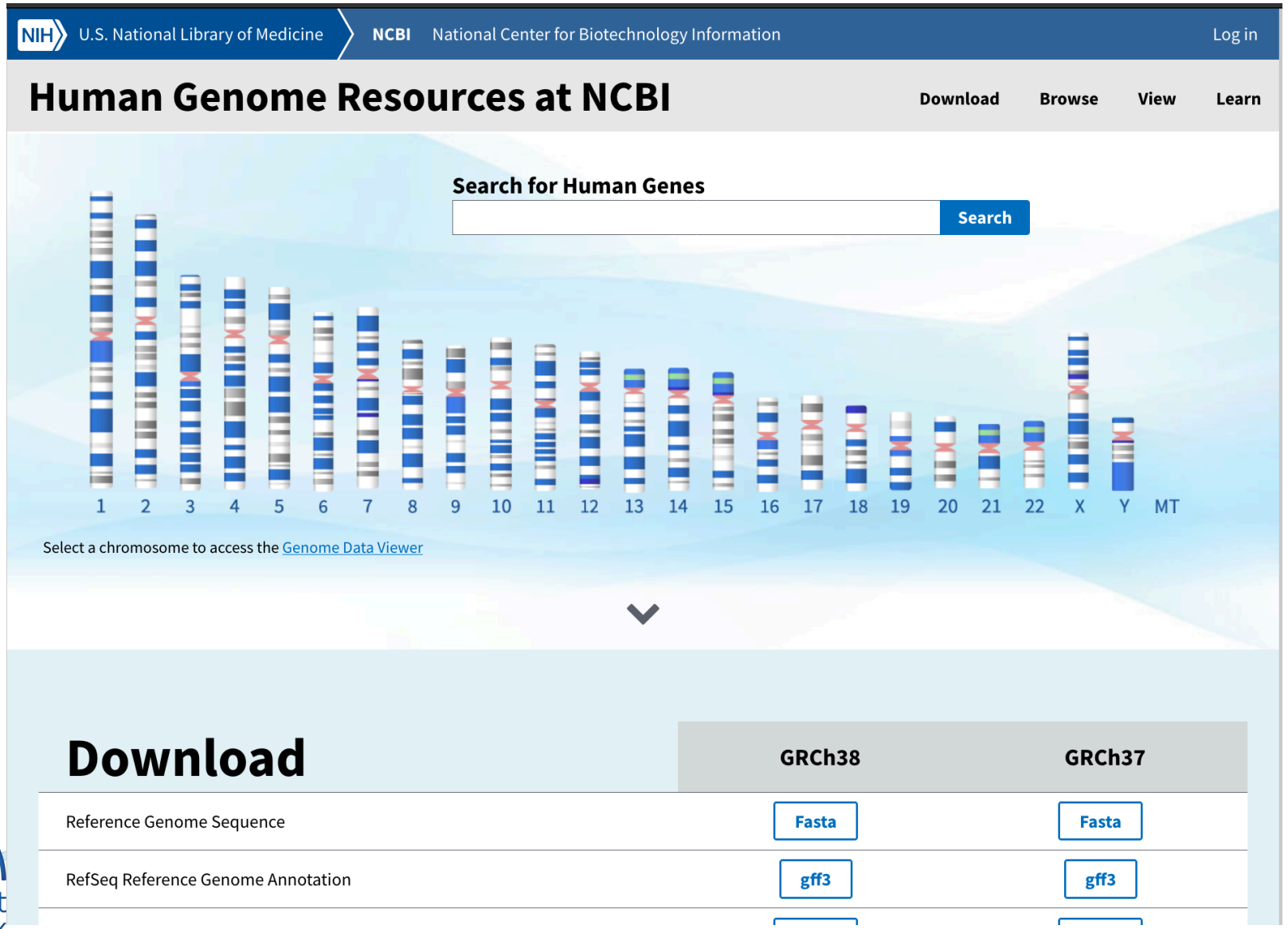
# 4. Les analyses génomiques

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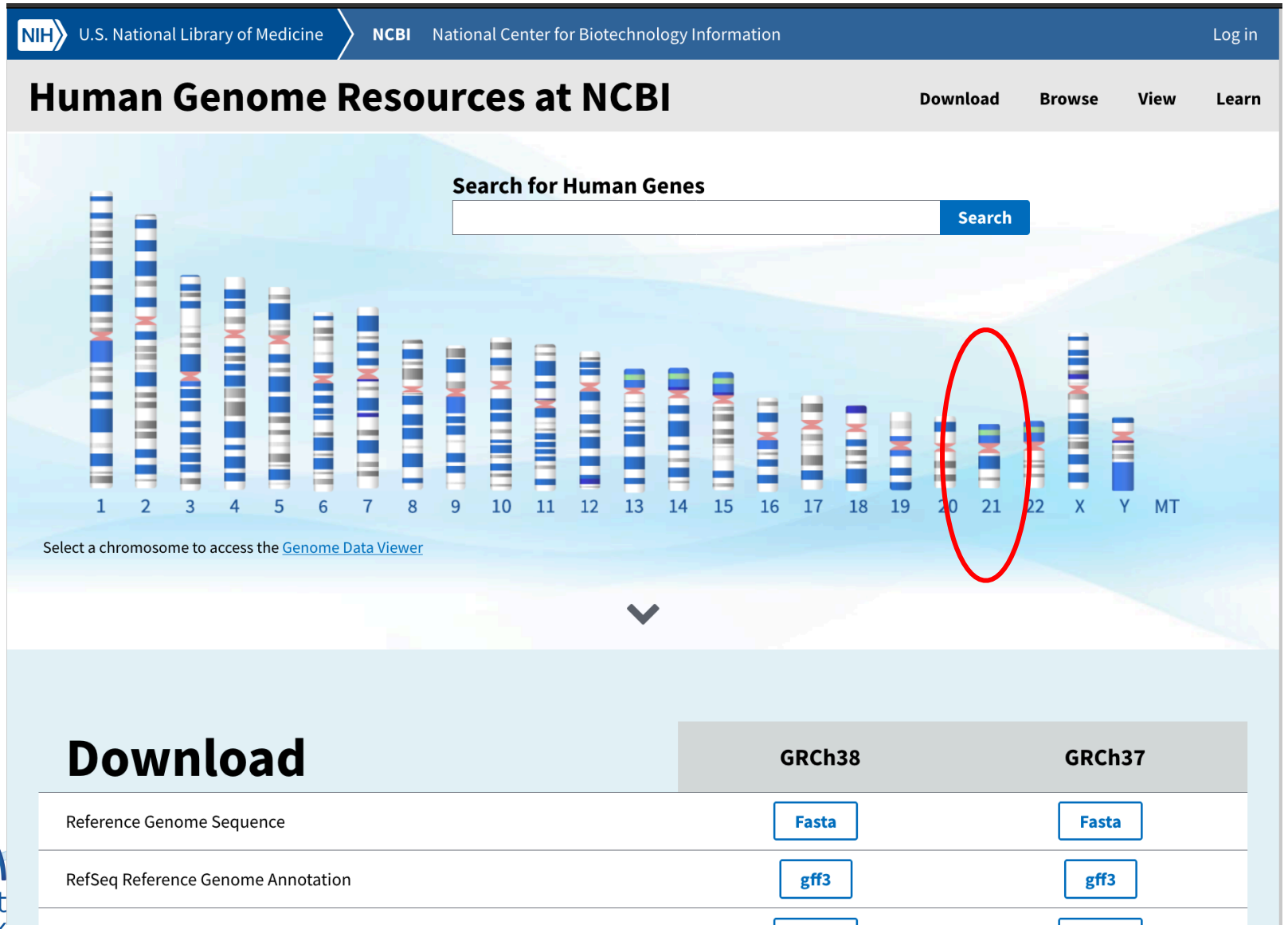
# 4. Les analyses génomiques

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# 4. Les analyses génomiques


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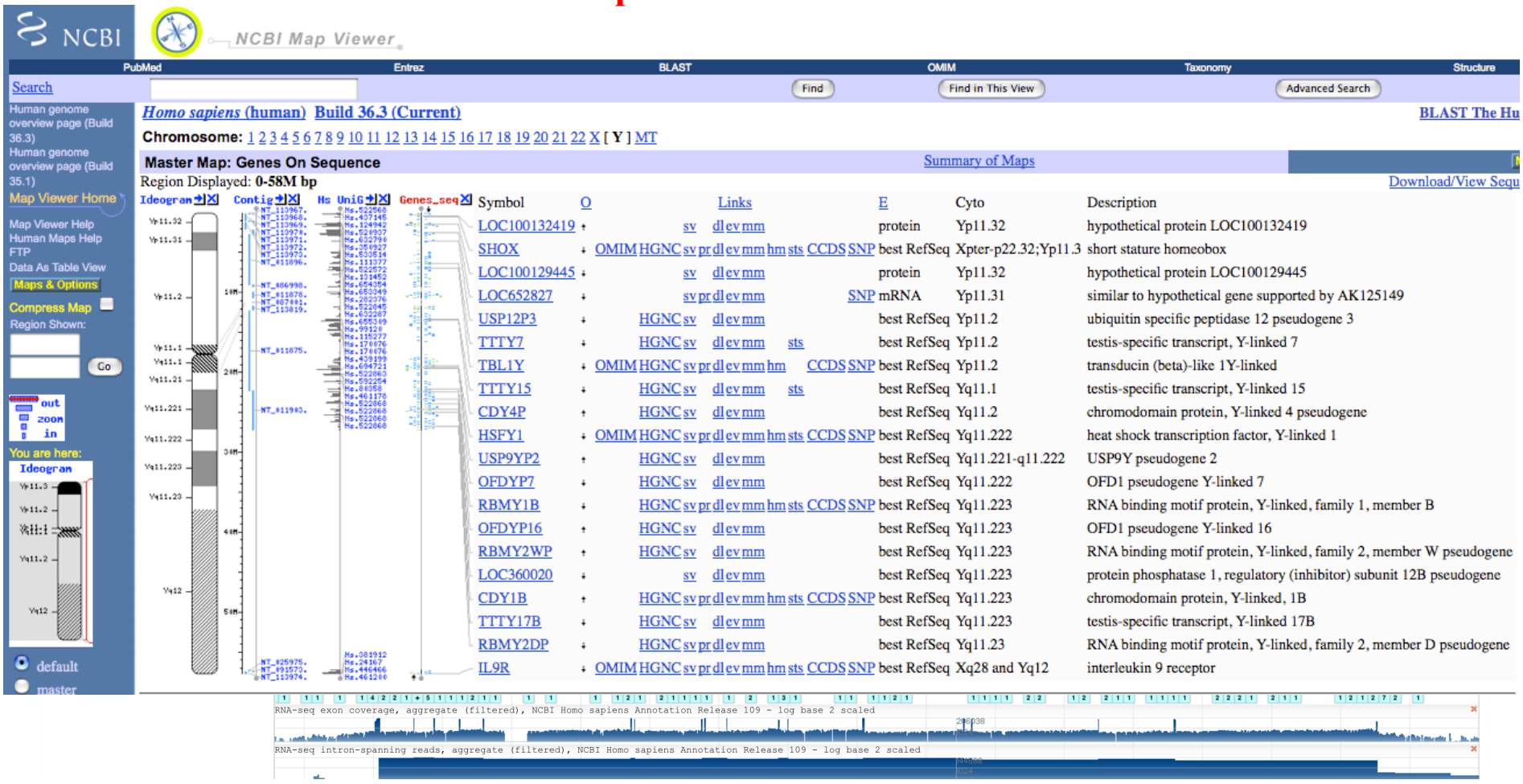
# 4. Les analyses génomiques

**Ici un Map Viewer sur le chromosome Y.**

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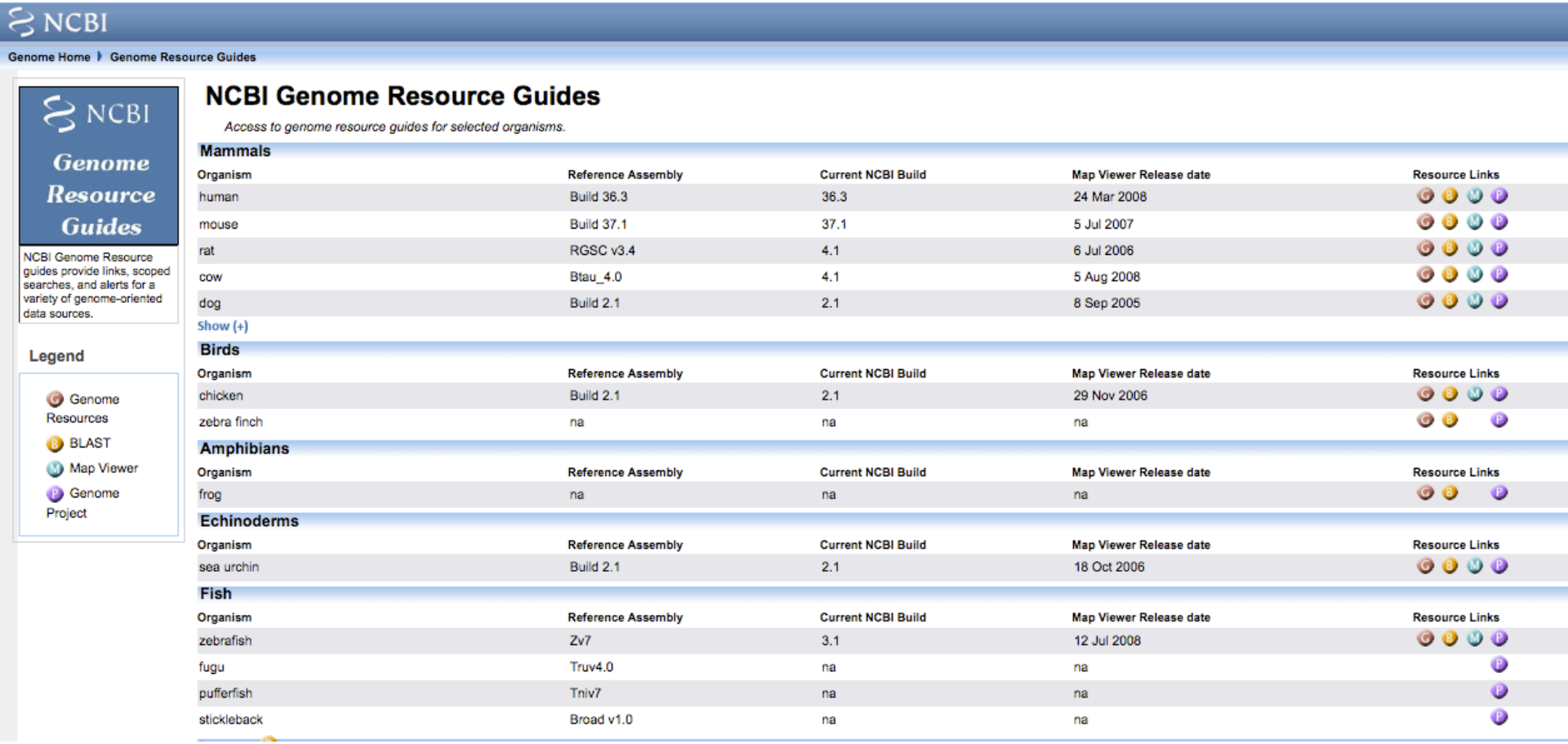
# 4. Les analyses génomiques



NCBI

Genome Home ▸ Genome Resource Guides

NCBI Genome Resource Guides

NCBI Genome Resource Guides

*Access to genome resource guides for selected organisms.*

NCBI Genome Resource guides provide links, scoped searches, and alerts for a variety of genome-oriented data sources.

Legend

- Genome Resources
- BLAST
- Map Viewer
- Genome Project

**Mammals**

| Organism | Reference Assembly | Current NCBI Build | Map Viewer Release date | Resource Links |
|---|---|---|---|---|
| human | Build 36.3 | 36.3 | 24 Mar 2008 | |
| mouse | Build 37.1 | 37.1 | 5 Jul 2007 | |
| rat | RGSC v3.4 | 4.1 | 6 Jul 2006 | |
| cow | Btau_4.0 | 4.1 | 5 Aug 2008 | |
| dog | Build 2.1 | 2.1 | 8 Sep 2005 | |

Show (+)

**Birds**

| Organism | Reference Assembly | Current NCBI Build | Map Viewer Release date | Resource Links |
|---|---|---|---|---|
| chicken | Build 2.1 | 2.1 | 29 Nov 2006 | |
| zebra finch | na | na | na | |

**Amphibians**

| Organism | Reference Assembly | Current NCBI Build | Map Viewer Release date | Resource Links |
|---|---|---|---|---|
| frog | na | na | na | |

**Echinoderms**

| Organism | Reference Assembly | Current NCBI Build | Map Viewer Release date | Resource Links |
|---|---|---|---|---|
| sea urchin | Build 2.1 | 2.1 | 18 Oct 2006 | |

**Fish**

| Organism | Reference Assembly | Current NCBI Build | Map Viewer Release date | Resource Links |
|---|---|---|---|---|
| zebrafish | Zv7 | 3.1 | 12 Jul 2008 | |
| fugu | Truv4.0 | na | na | |
| pufferfish | Tniv7 | na | na | |
| stickleback | Broad v1.0 | na | na | |

**Les autres espèces...**

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# 5. Les analyses protéiques

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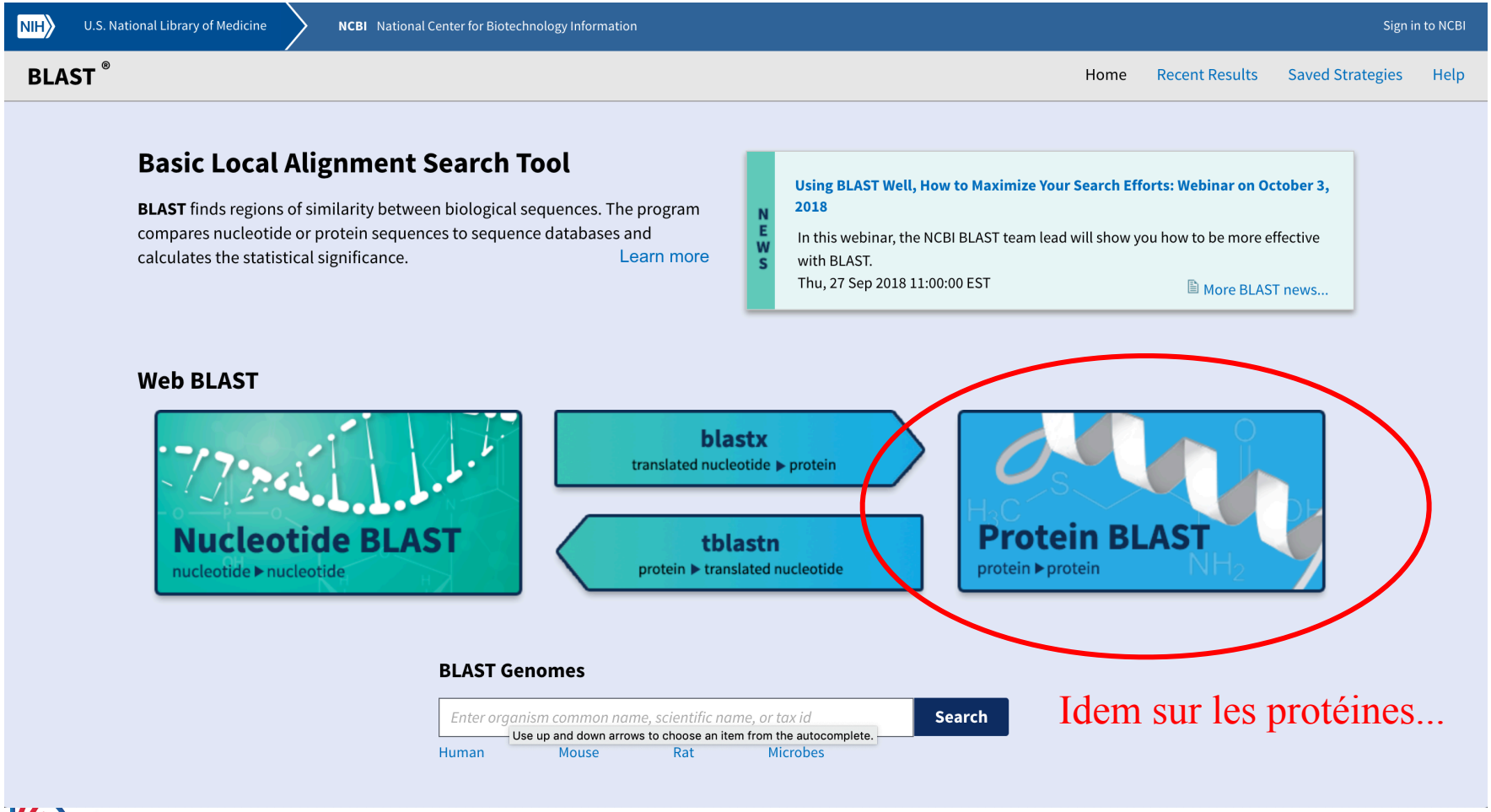
# 5. Les analyses protéiques




Idem sur les protéines...

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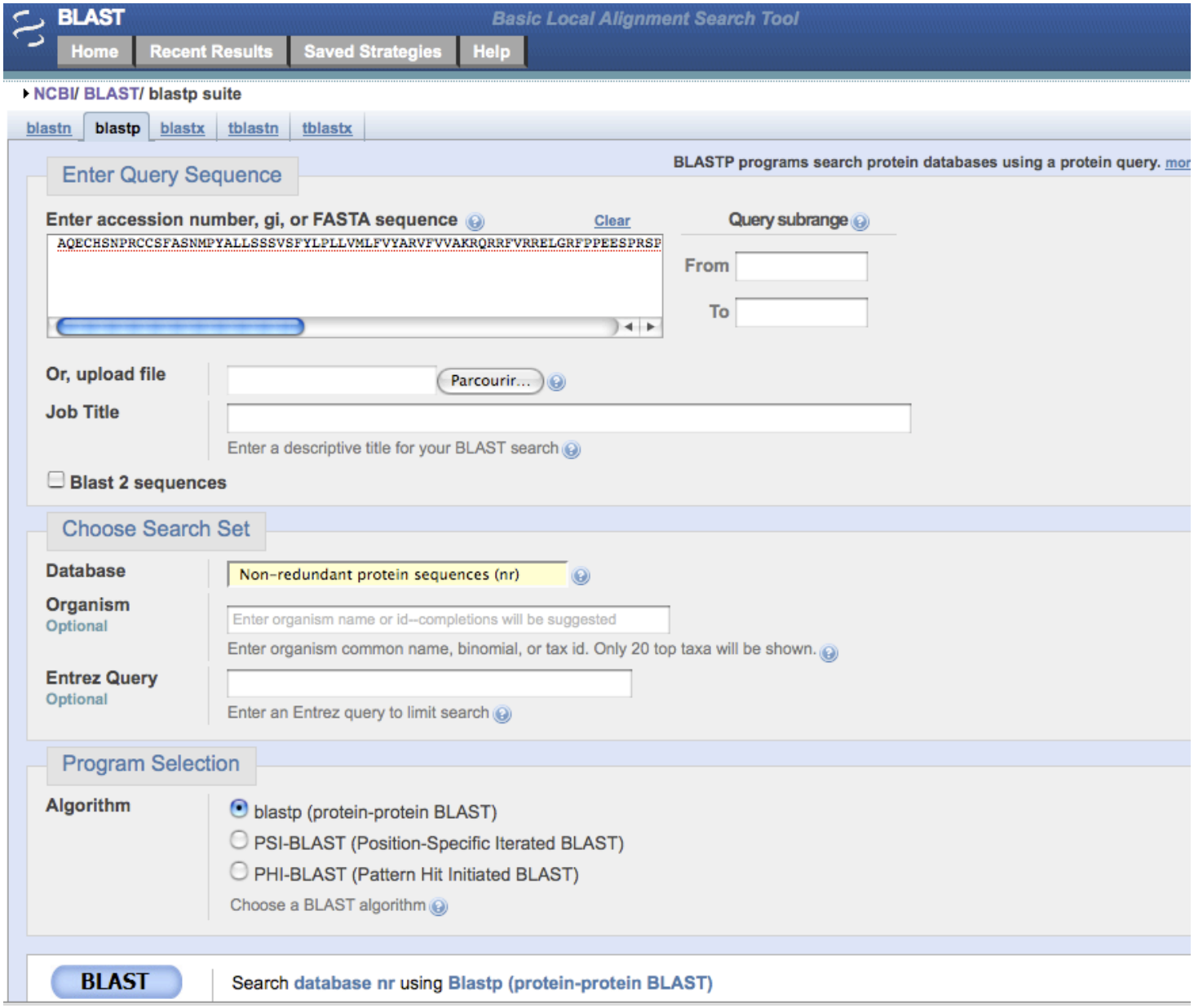
# 5. Les analyses protéiques

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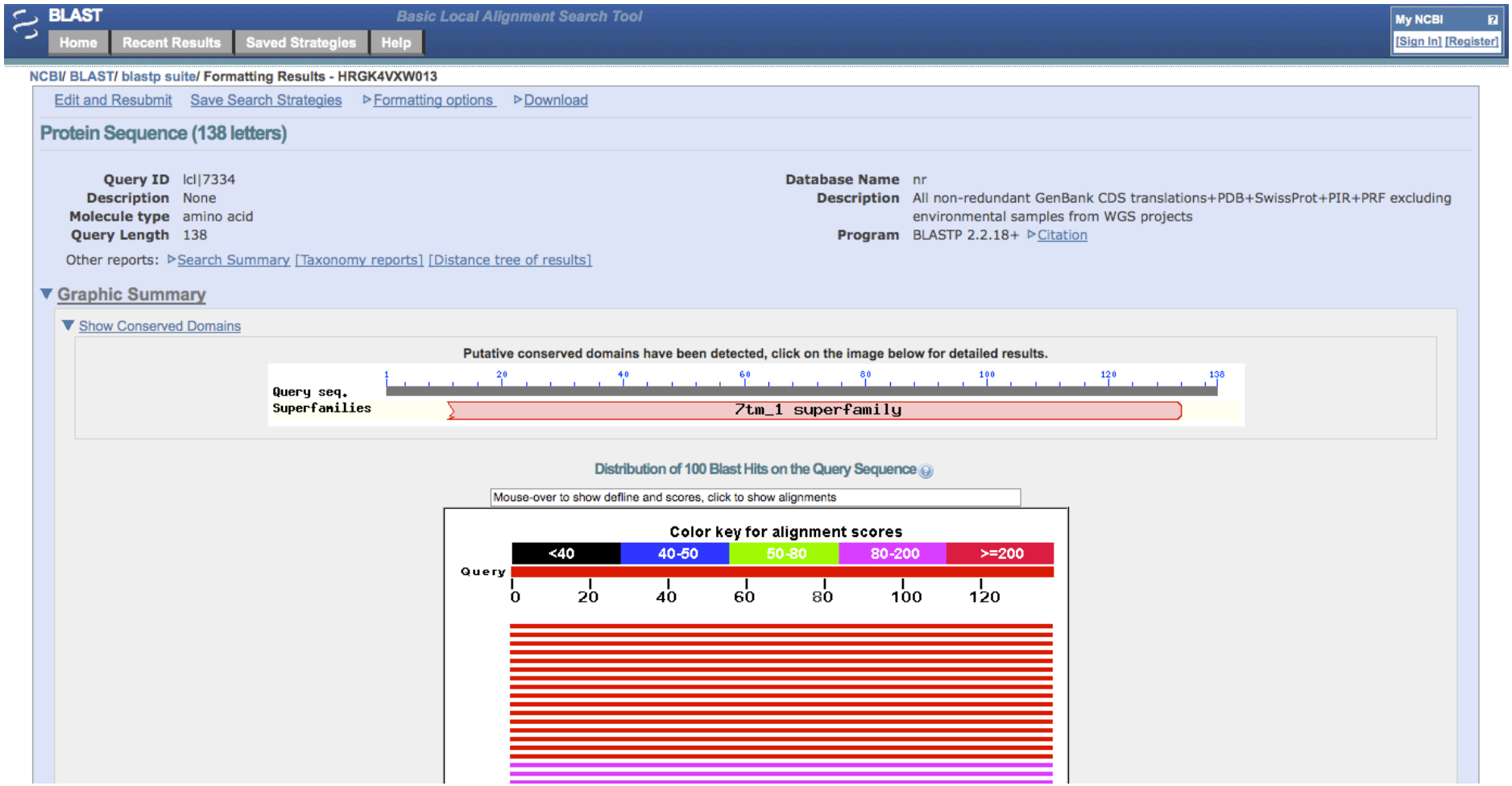
# 5. Les analyses protéiques

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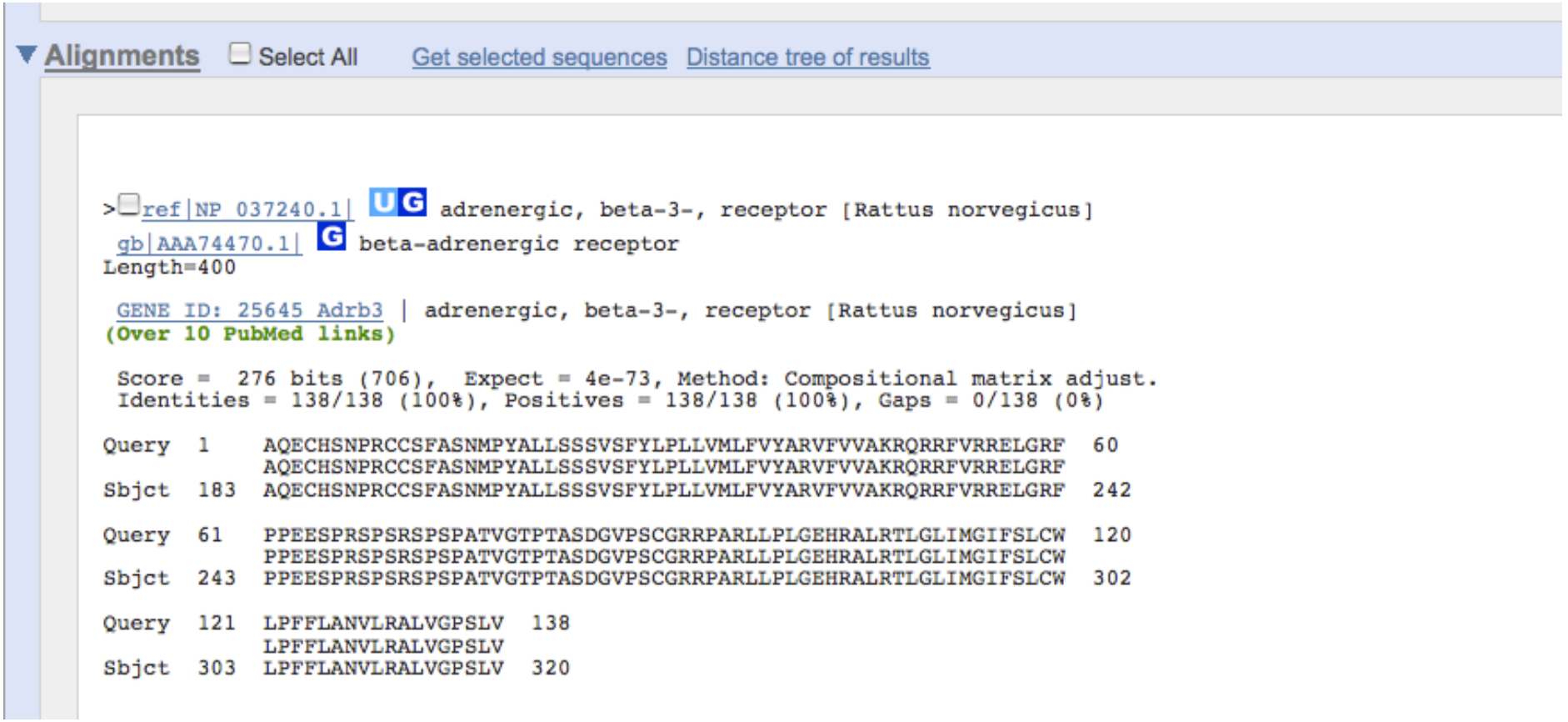
# 5. Les analyses protéiques



Alignments  Select All  Get selected sequences  Distance tree of results

>ref|NP_037240.1| adrenergic, beta-3-, receptor [Rattus norvegicus]
gb|AAA74470.1| beta-adrenergic receptor
Length=400

GENE ID: 25645 Adrb3 | adrenergic, beta-3-, receptor [Rattus norvegicus]
(Over 10 PubMed links)

Score = 276 bits (706), Expect = 4e-73, Method: Compositional matrix adjust.
Identities = 138/138 (100%), Positives = 138/138 (100%), Gaps = 0/138 (0%)

```
Query  1    AQECHSNPRCCSFASNMPYALLSSSVSFYLPLLVMLFVYARVFVVAKRQRRFVRRELGRF  60
            AQECHSNPRCCSFASNMPYALLSSSVSFYLPLLVMLFVYARVFVVAKRQRRFVRRELGRF
Sbjct  183  AQECHSNPRCCSFASNMPYALLSSSVSFYLPLLVMLFVYARVFVVAKRQRRFVRRELGRF  242

Query  61   PPEESPRSPSRSPSPATVGTPTASDGVPSCGRRPARLLPLGEHRALRTLGLIMGIFSLCW  120
            PPEESPRSPSRSPSPATVGTPTASDGVPSCGRRPARLLPLGEHRALRTLGLIMGIFSLCW
Sbjct  243  PPEESPRSPSRSPSPATVGTPTASDGVPSCGRRPARLLPLGEHRALRTLGLIMGIFSLCW  302

Query  121  LPFFLANVLRALVGPSLV  138
            LPFFLANVLRALVGPSLV
Sbjct  303  LPFFLANVLRALVGPSLV  320
```

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# 6. Exemple publication utilisant la bioinfo

Xu *et al. Orphanet Journal of Rare Diseases* (2023) 18:273
https://doi.org/10.1186/s13023-023-02885-1

Orphanet Journal of Rare Diseases

RESEARCH Open Access

## The metabolomic plasma profile of patients with Duchenne muscular dystrophy: providing new evidence for its pathogenesis

Huayan Xu[1†], Xiaotang Cai[2†], Ke Xu[1], Qihong Wu[1] and Bei Xu[3,4*]

# 6. Exemple publication utilisant la bioinfo

Huayan Xu[1†], Xiaotang Cai[2†], Ke Xu[1], Qihong Wu[1] and Bei Xu[3,4*]

**Abstract**

**Background** Duchenne muscular dystrophy (DMD) is a fatal genetic muscle-wasting disease that affects 1 in 5000 male births with no current cure. Despite great progress has been made in the research of DMD, its underlying pathological mechanism based on the metabolomics is still worthy of further study. Therefore, it is necessary to gain a deeper understanding of the mechanisms or pathogenesis underlying DMD, which may reveal potential therapeutic targets and/or biomarkers.

**Results** Plasma samples from 42 patients with DMD from a natural history study and 40 age-matched healthy volunteers were subjected to a liquid chromatography-mass spectrometry-based non-targeted metabolomics approach. Acquired metabolic data were evaluated by principal component analysis, partial least squares-discriminant analysis, and metabolic pathway analysis to explore distinctive metabolic patterns in patients with DMD. Differentially expressed metabolites were identified using publicly available and integrated databases. By comparing the DMD and healthy control groups, 25 differential metabolites were detected, including amino acids, unsaturated fatty acids, carnitine, lipids, and metabolites related to the gut microbiota. Correspondingly, linoleic acid metabolism, D-glutamine and D-glutamate metabolism, glycerophospholipid metabolism, and alanine, aspartate, and glutamate metabolism were significantly altered in patients with DMD, compared with those of healthy volunteers.

**Conclusions** Our study demonstrated the abnormal metabolism of amino acids, energy, and lipids in patients with DMD, consistent with pathological features, such as recurrent muscle necrosis and regeneration, interstitial fibrosis, and fat replacement. Additionally, we found that metabolites of intestinal flora were disordered in DMD patients, providing support for treatment of intestinal microbia disturbance in DMD diseases. Our study provides a new research strategy for understanding the pathogenesis of DMD.

**Keywords** Duchenne muscular dystrophy, Metabonomics, Mass spectrometry, Plasma

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# *6. Exemple publication utilisant la bioinfo*

**Physiologie « classique »**

**Fonction**

⇩

**Protéines**

⇩

**Gènes**

**Vision restreinte**

**Physiologie « inverse »**

**Gènes**

⇩

**Protéines**

⇩

**Fonction**

**Vision globale**

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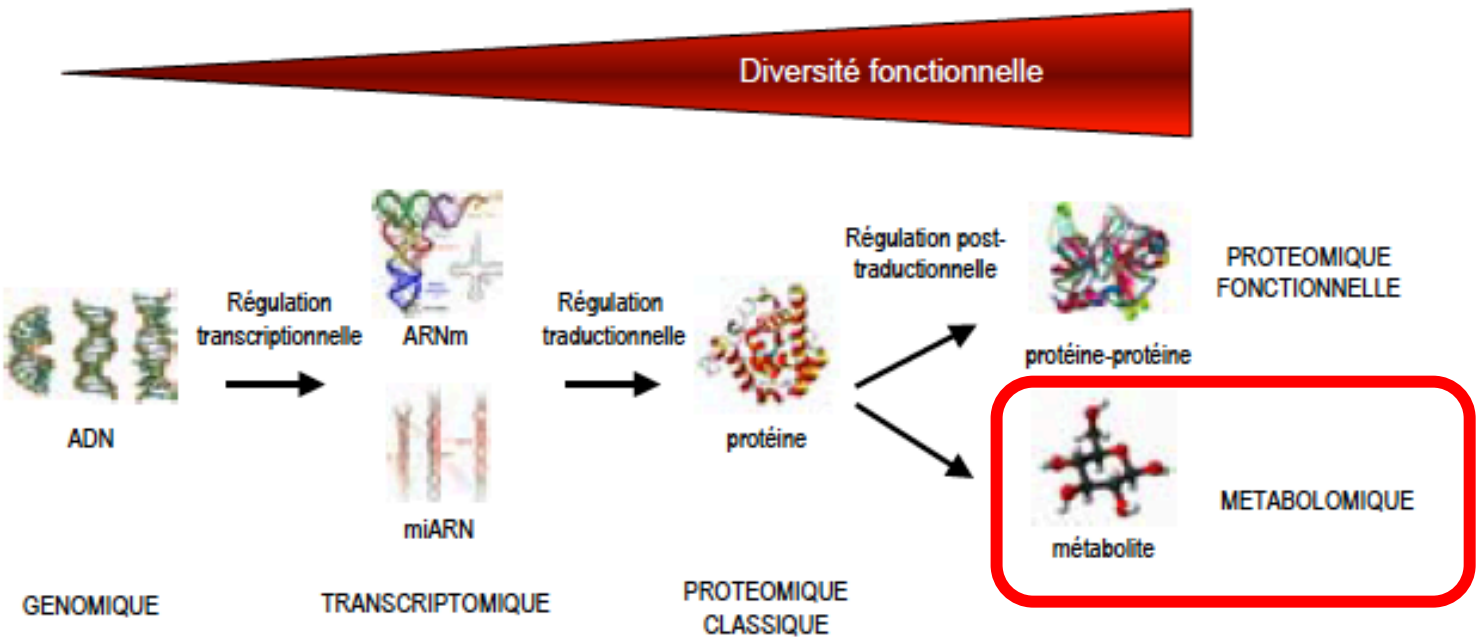
## Intérêt de la recherche « OMICS »

❑ Approche globale sans aucun *a priori*




❑ Protéomique

Caractérisation qualitative et quantitative de l'ensemble des protéines présentes dans un échantillon biologique obtenu dans des conditions définies

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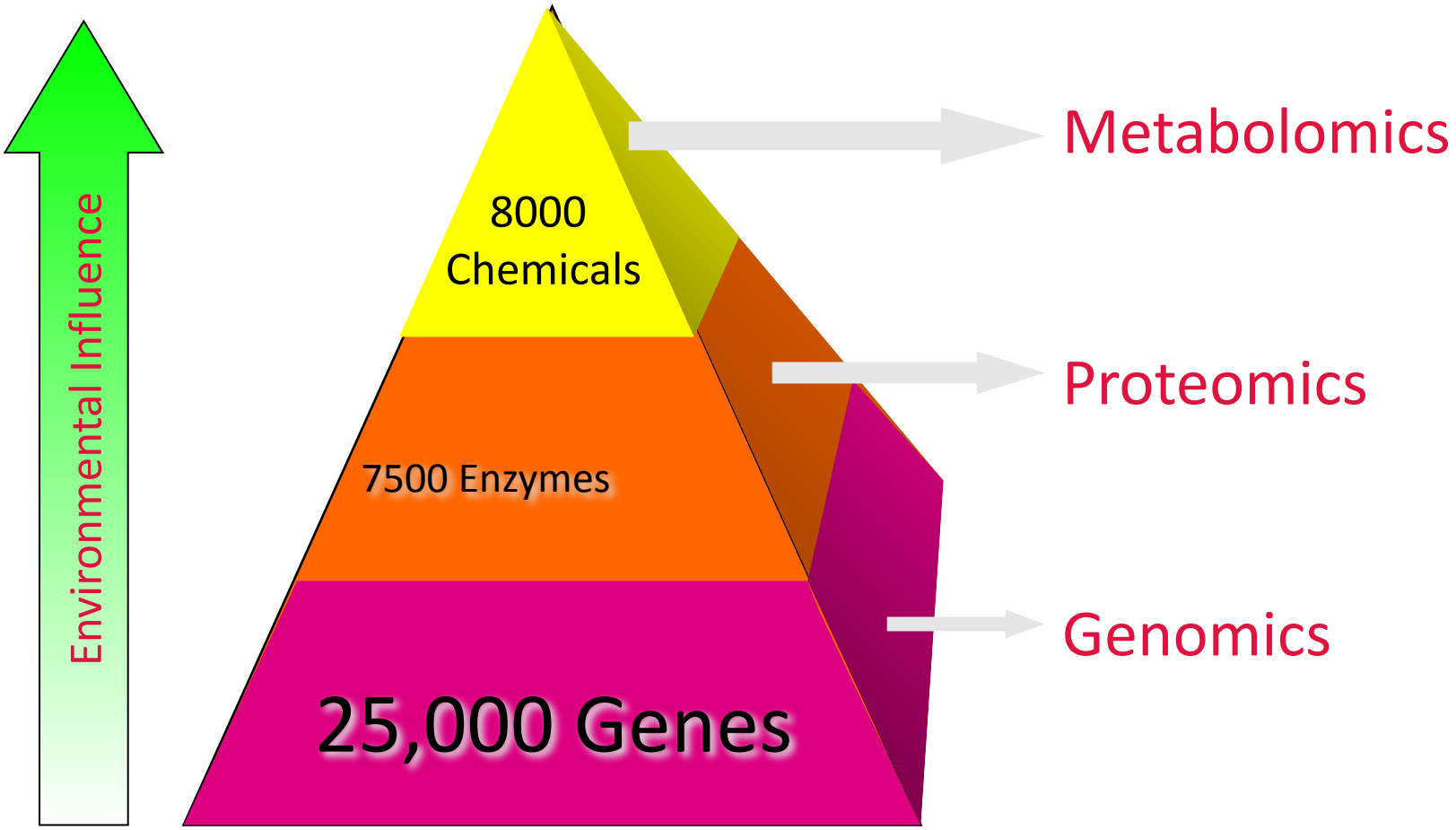


The Pyramid of Life

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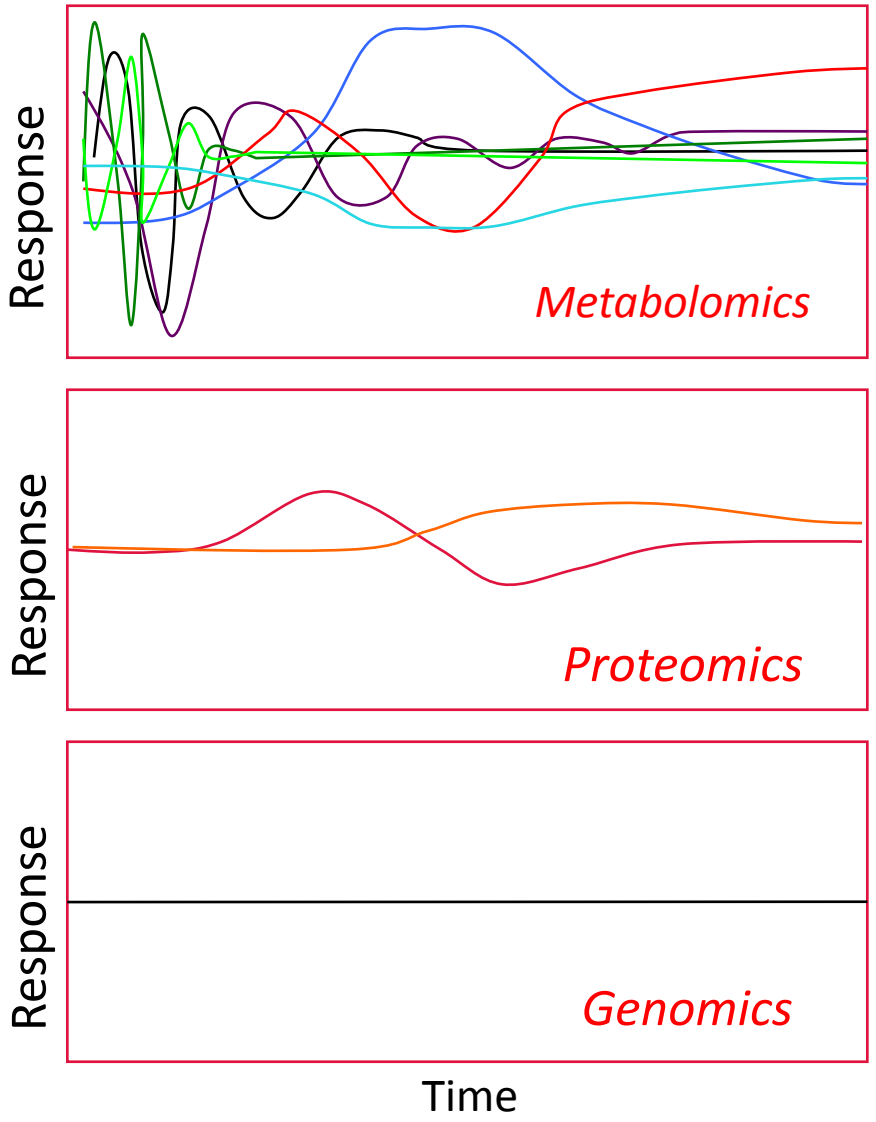


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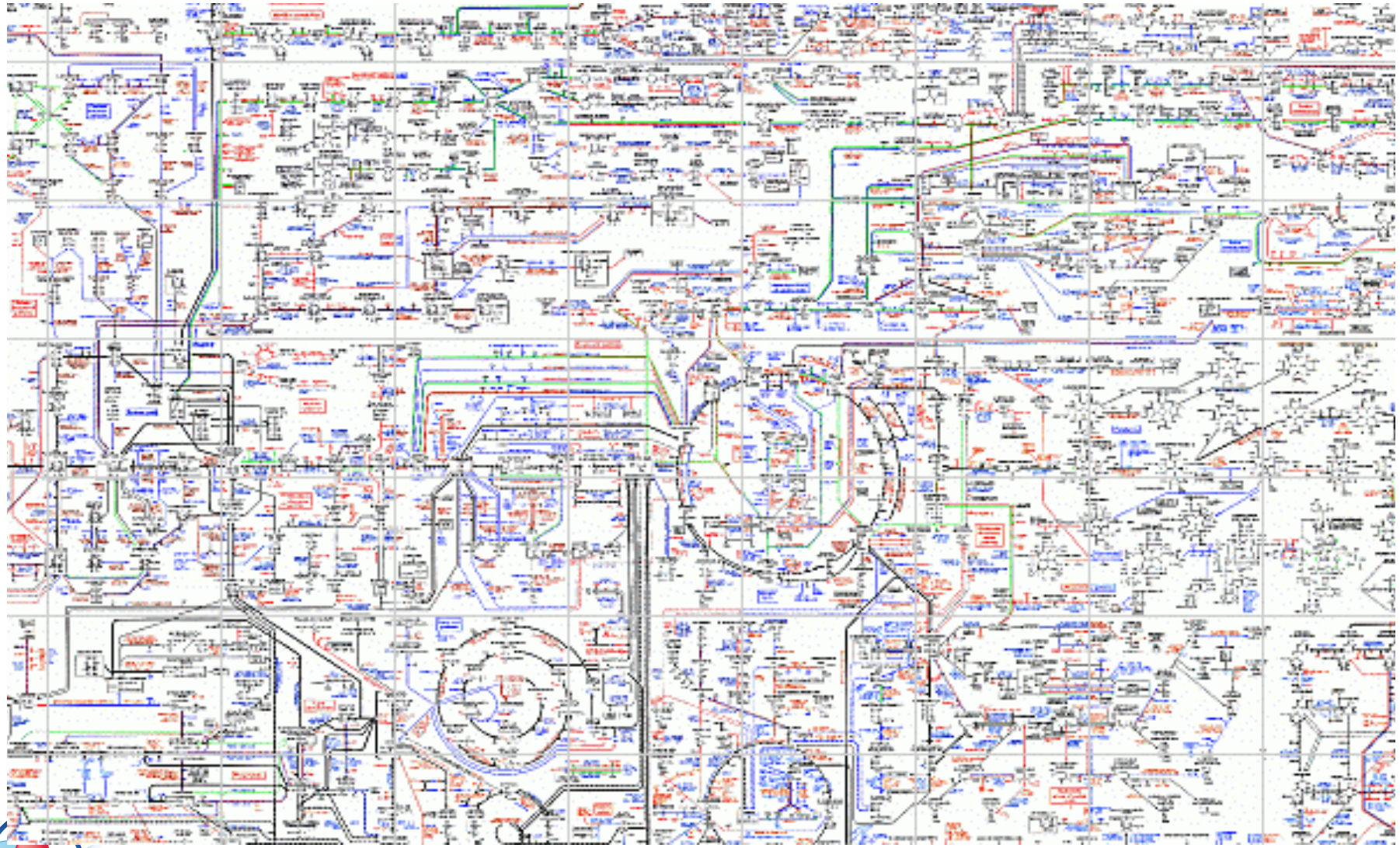

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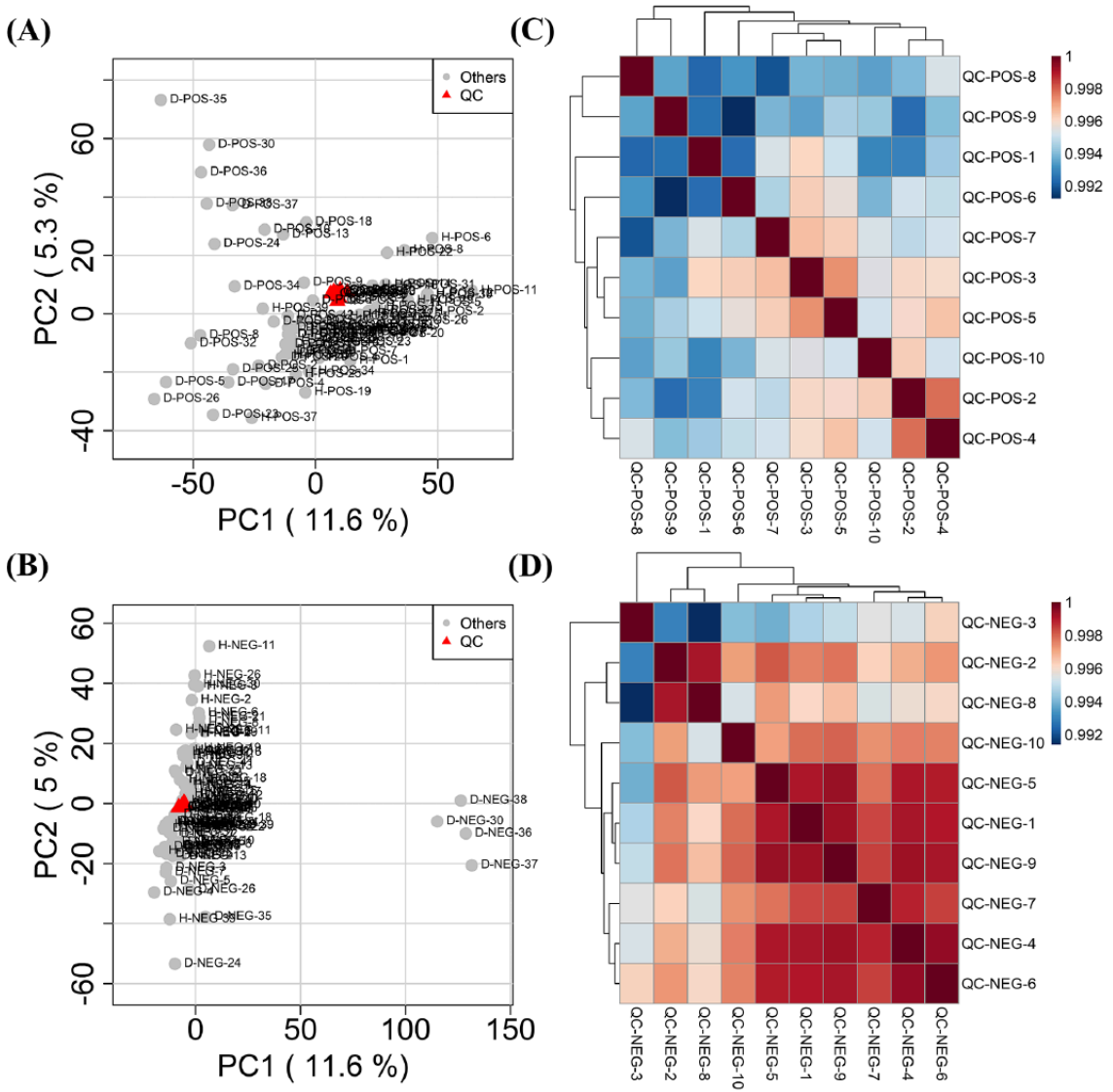


**Fig. 1** PCA score plots and correlation analysis of QC samples in ESI+ (**A, C**) and ESI– (**B, D**) scan modes

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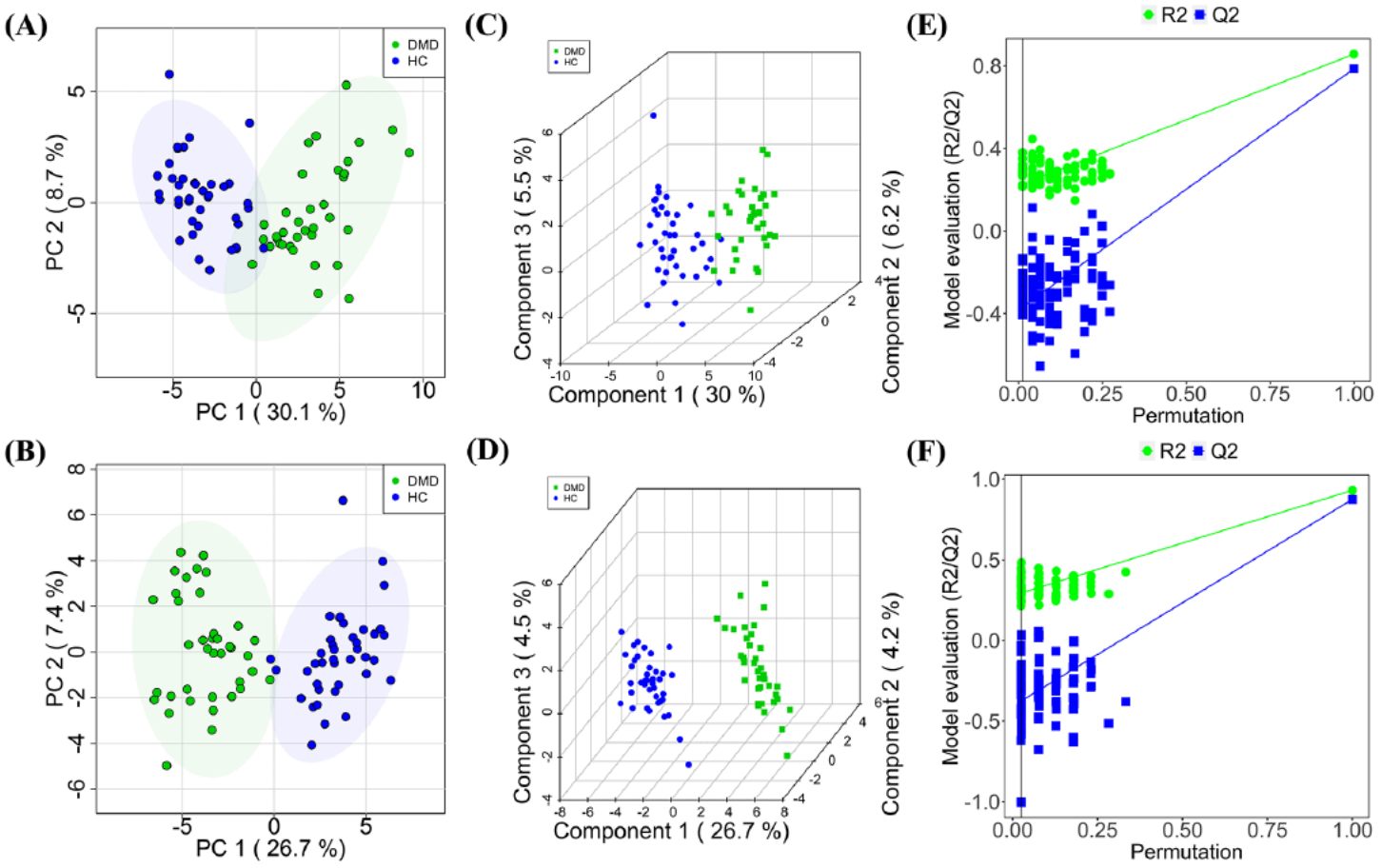


**Fig. 2** Plots of PCA (**A, B**) and PLS-DA scores (**C, D**) with permutation testing (**E, F**) for healthy controls and DMD patients comparison in the ESI+and ESI−scan modes

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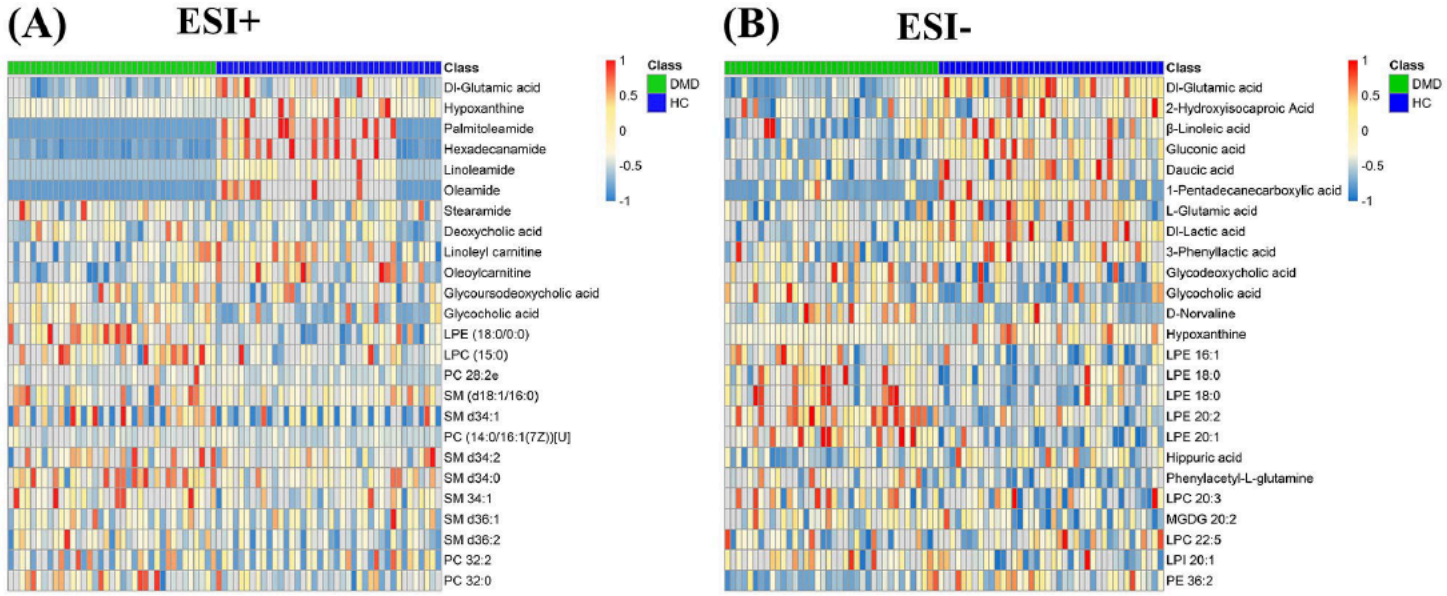


**Fig. 3** Differential metabolite heat maps in ESI+ (**A**) and ESI− (**B**) scan modes. The columns represent samples, the rows represent metabolites, and the relative content of the metabolites is displayed by color

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**Metabolite detection**

An ultra-performance liquid chromatography (UPLC) system (Agilent1290 Infinity II; Agilent Technologies Inc., CA, USA) connected to a high-resolution tandem mass spectrometer (TripleTOF 5600 Plus; AB SCIEX, Framingham, MA, USA) was used to conduct the metabolomic analysis. Reversed-phase separation was performed on an ACQUITY HSS T3 column (100×2.1 mm, i.d. 1.8 µm; Waters, Milford, USA). The mobile phase composition was determined using a gradient elution of solvent A (0.1% formic acid in water) and solvent B (0.1% formic acid in acetonitrile), as previously described [19]. The flow rate was constant at 0.30 mL/min, and the column temperature was set at 30 °C.

- La spectrométrie de masse (mass spectrometry ou MS) est une technique physique d'analyse permettant de détecter et d'identifier des molécules d'intérêt par mesure de leur masse mono-isotopique.

- De plus, la spectrométrie de masse permet de caractériser la structure chimique des molécules en les fragmentant.

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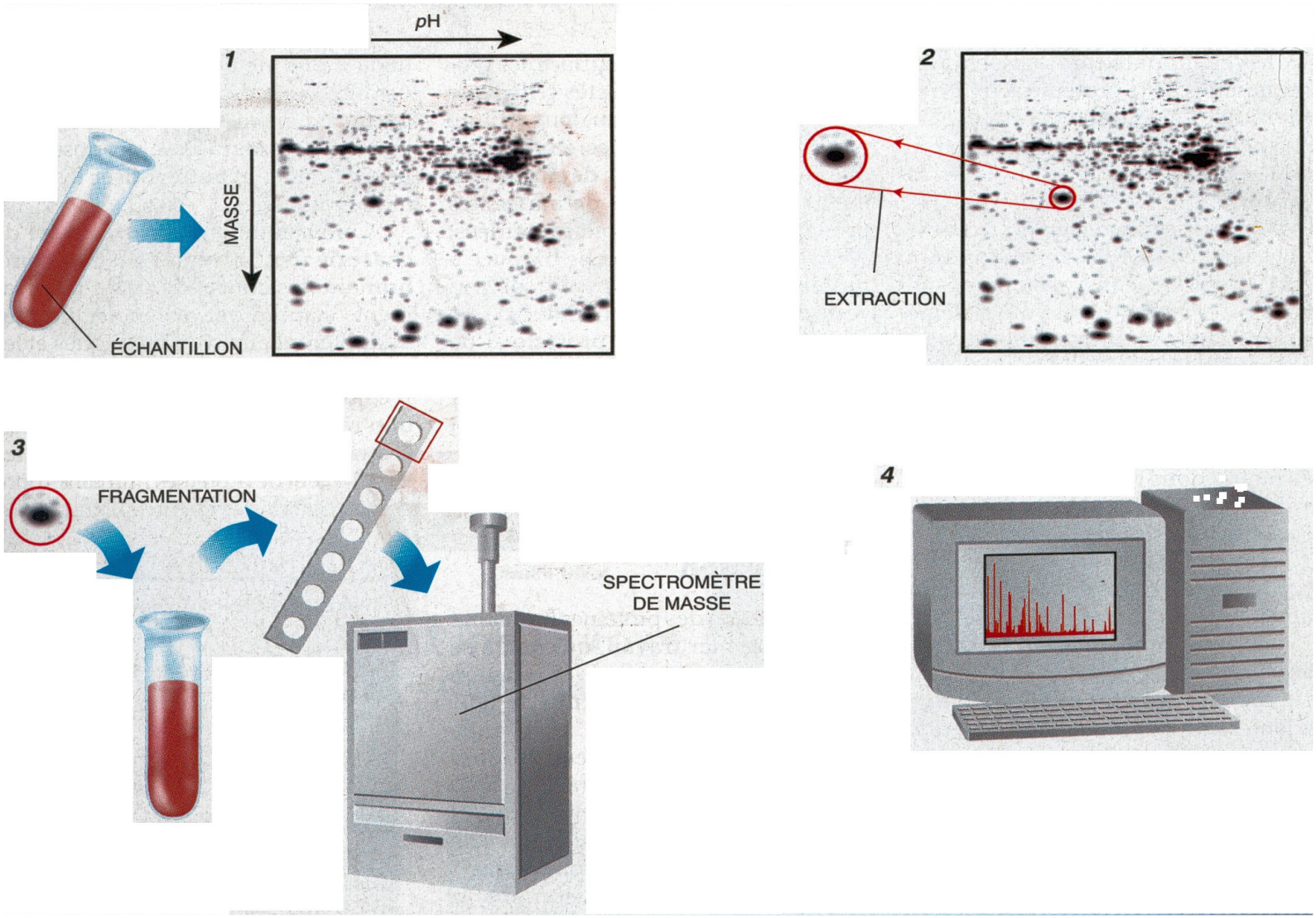


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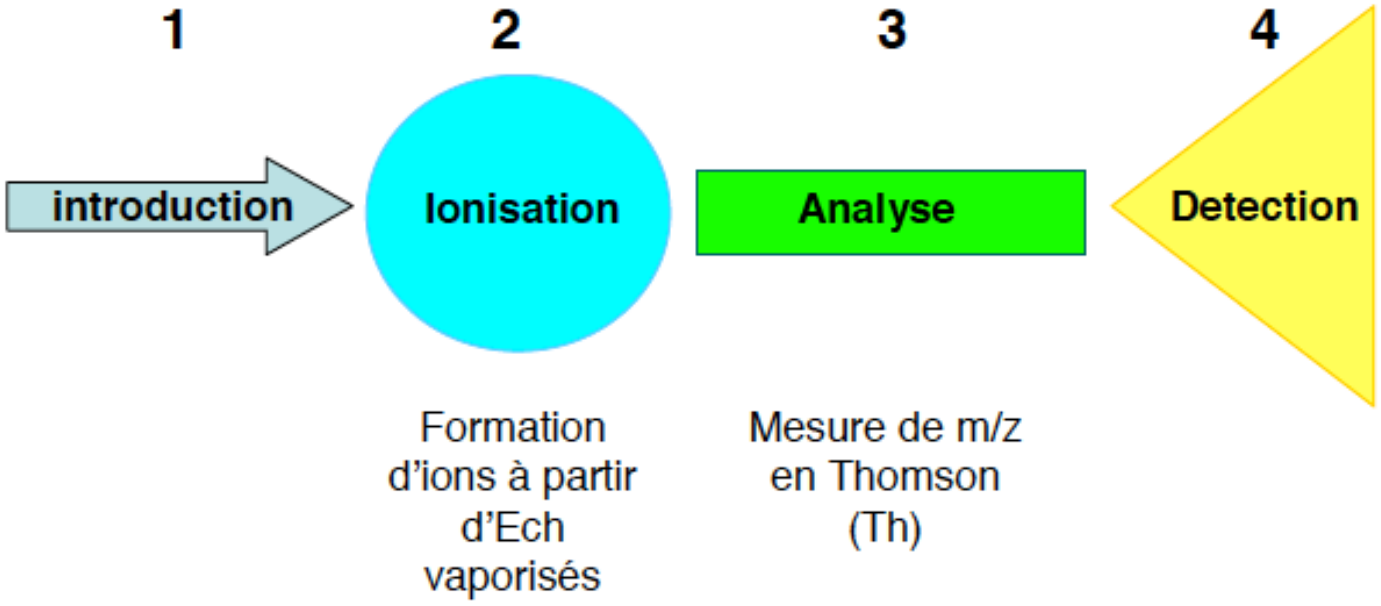
Le spectromètre de masse se compose donc de quatre parties :

1- Le système d'introduction de l'échantillon

2- La source d'ionisation: elle consiste à vaporiser les molécules et à les ioniser.

3- L'analyseur

4- Le détecteur et système de traitement

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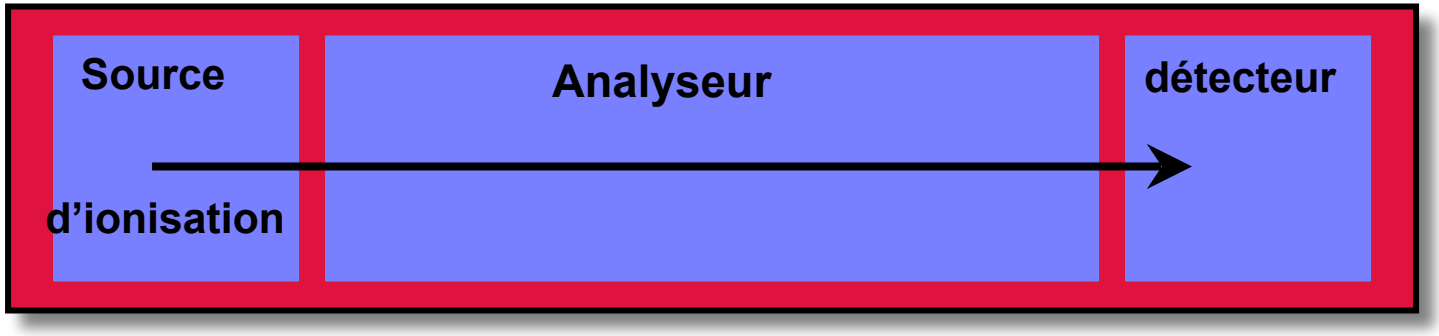
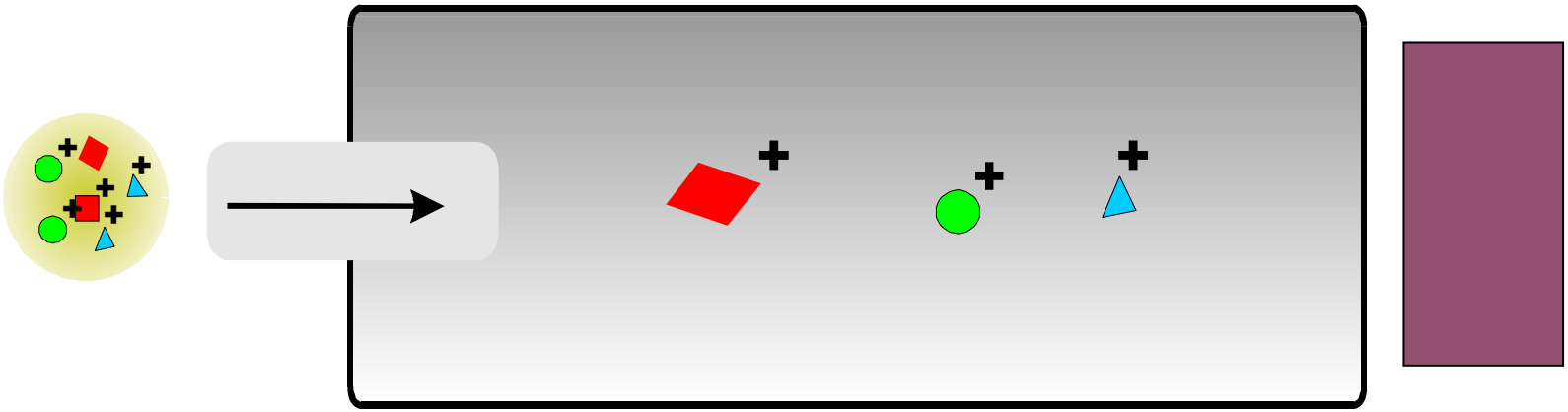



L'analyseur de masse

Détecteur



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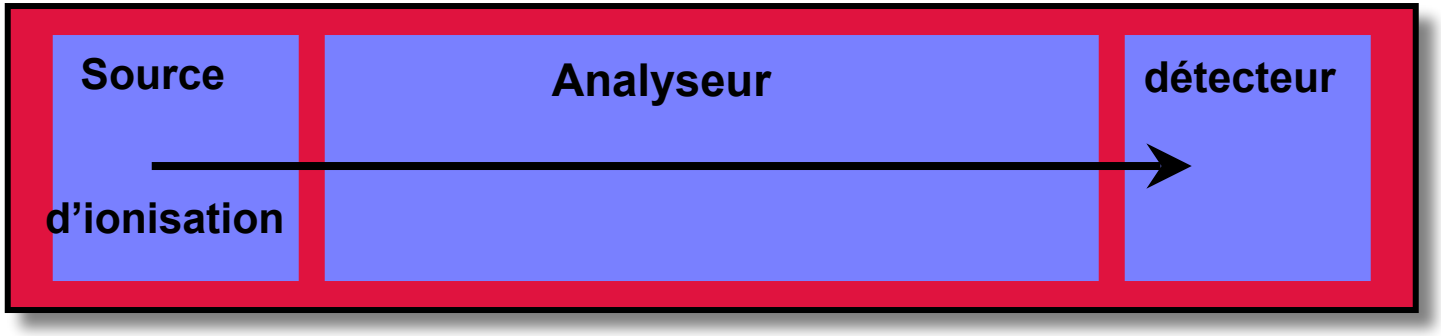
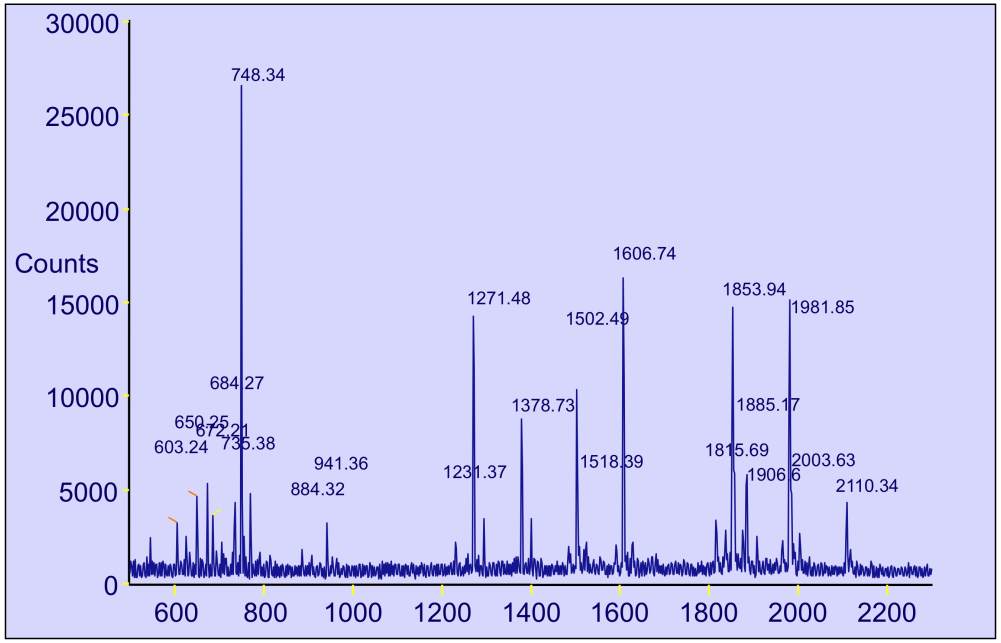



## Détecteur

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# *6. Exemple publication utilisant la bioinfo*

Cartographie massique par SM

4148.1061
3221.5113
3392.5756
2993.3522
2468.2415
2325.0207
2144.9770
1948.9585
2005.9800
1906.8817
1883.0497
1721.7765
1618.7577
1732.8006
1508.7889
1288.7259
1134.6742
1008.5360
1008.5295
1065.5509
950.4499
1007.4714
880.4159
832.3658
792.3709

La carte massique obtenue est **l'empreinte massique** de la protéine. Elle est très spécifique.

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# 6. Exemple publication utilisant la bioinfo

**Liste de masses expérimentale**

| |
|---|
| 4148.1061 |
| 3221.5113 |
| 3392.5756 |
| 2993.3522 |
| 2468.2415 |
| 2325.0207 |
| 2144.9770 |
| 1948.9585 |
| 2005.9800 |
| 1906.8817 |
| 1883.0497 |
| 1721.7765 |
| 1618.7577 |
| 1732.8006 |
| 1508.7889 |
| 1288.7259 |
| 1134.6742 |
| 1008.5360 |
| 1008.5295 |
| 1065.5509 |
| 950.4499 |
| 1007.4714 |
| 880.4159 |
| 832.3658 |
| 792.3709 |

## Interrogation des banques de données

**Comparaison avec tous les profils théoriques des séquences de protéines connues présentes dans les banques**

**Sélection de la protéine la plus probable.**

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# 6. Exemple publication utilisant la bioinfo

**Table 2** List of statistically significant metabolites in DMD vs. HC comparisons

| Metabolites | | Scan mode | Rt (s) | m/z | Adducts | DMD vs. HC | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | | | Log2(FC) | *P* (T test) | VIP | Trends |
| Amino acids | Glutamic acid | ESI- | 73.431 | 128.036 | M-$H_2O$-H | -1.181 | < 0.001 | 1.955 | ↓ |
| | Glutamine | ESI+ | 47.218 | 146.080 | M + H | -1.072 | < 0.001 | 1.857 | ↓ |
| | Hippuric acid | ESI- | 300.935 | 178.051 | M-H | -0.802 | 0.021 | 1.009 | ↓ |
| | Phenylacetyl-glutamine | ESI- | 348.896 | 527.213 | 2 M-H | 1.143 | < 0.001 | 2.008 | ↑ |
| | Valine | ESI- | 420.136 | 293.176 | 2 M + Hac-H | 1.072 | 0.005 | 1.263 | ↑ |
| Unsaturated fatty acids | β-Linolenic acid | ESI- | 419.308 | 279.232 | M-H | -0.766 | 0.0001 | 1.582 | ↓ |
| Carnitine | Linoleyl carnitine | ESI+ | 435.747 | 424.342 | M + H | -0.784 | < 0.001 | 1.536 | ↓ |
| | Oleoylcarnitine | ESI+ | 461.927 | 426.358 | M + H | -0.766 | < 0.001 | 1.635 | ↓ |
| Bile acids | Glycocholic acid | ESI- | 372.288 | 464.302 | M-H | 1.121 | 0.005 | 1.122 | ↑ |
| | Glycodeoxycholic acid | ESI- | 406.477 | 448.307 | M-H | 0.950 | 0.0004 | 1.460 | ↑ |
| | Glycoursodeoxycholic acid | ESI+ | 406.026 | 450.322 | M + H | 1.031 | < 0.001 | 1.543 | ↑ |
| | Deoxycholic acid | ESI+ | 462.698 | 357.279 | M + H-2$H_2O$ | 1.174 | 0.002 | 1.323 | ↑ |
| Lipids | PC 32:0 | ESI+ | 1117.300 | 756.555 | M + Na | 0.712 | 0.006 | 1.058 | ↑ |
| | PC 32:2 | ESI+ | 730.026 | 730.539 | M + H | 0.872 | 0.029 | 1.018 | ↑ |
| | LPE 18:0 | ESI- | 552.975 | 480.310 | M-H | 0.655 | < 0.001 | 2.289 | ↑ |
| | LPE 20:1 | ESI- | 590.366 | 506.326 | M-H | 0.748 | < 0.001 | 1.656 | ↑ |
| | LPE 20:2 | ESI- | 526.317 | 504.311 | M-H | 0.856 | < 0.001 | 2.269 | ↑ |
| | LPE (18:0/0:0) | ESI+ | 574.100 | 482.324 | M + H | 0.785 | < 0.001 | 2.489 | ↑ |
| | LPI 20:1 | ESI- | 386.676 | 625.361 | M-H | 0.799 | < 0.001 | 1.997 | ↑ |
| | LPE 16:1 | ESI- | 444.569 | 450.263 | M-H | 0.803 | < 0.001 | 1.733 | ↑ |
| | LPC 20:3 | ESI- | 405.790 | 590.235 | M + FA-H | 0.976 | < 0.001 | 1.525 | ↑ |
| | LPC 15:0 | ESI+ | 487.913 | 504.309 | M + Na | 0.634 | < 0.001 | 1.675 | ↑ |
| | SM d34:0 | ESI+ | 1118.730 | 705.591 | M + H | 0.851 | < 0.001 | 1.360 | ↑ |
| | SM d36:2 | ESI+ | 812.360 | 729.590 | M + H | 0.983 | 0.002 | 1.203 | ↑ |
| | SM 34:1 | ESI+ | 729.672 | 725.557 | M + Na | 1.034 | < 0.001 | 1.383 | ↑ |

"↑": Compared with HC group, the differential metabolites were significantly increased in DMD group

"↓": Compared with HC group, the differential metabolites were significantly decreased in DMD group

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# 6. Exemple publication utilisant la bioinfo

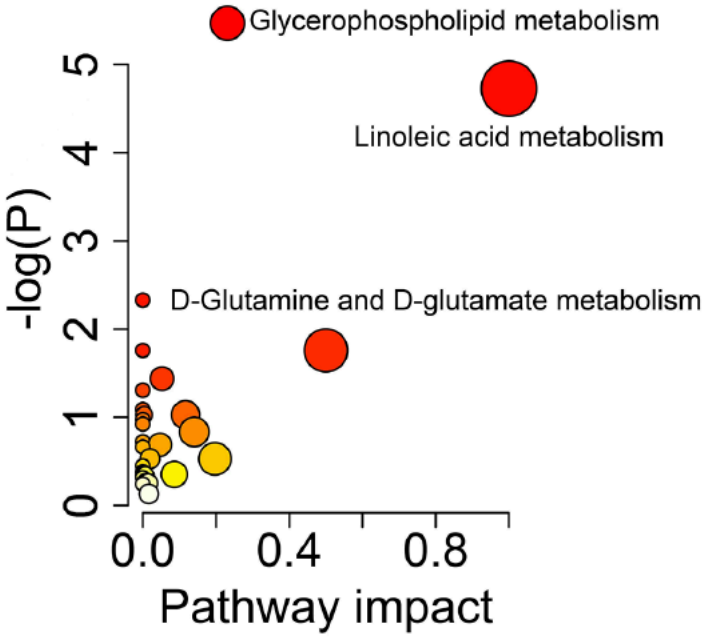


**Fig. 5** Bubble diagram of metabolic pathways between DMD and HC groups

**Table 3** Significantly altered metabolic pathways between DMD and HC groups

| Pathway name | KEGG.id | -log(P) | Impact | Hits |
|---|---|---|---|---|
| Linoleic acid metabolism | Hsa00591 | 4.73 | 1 | 2 |
| D-Glutamine and D-glutamate metabolism | Has00471 | 1.76 | 0.5 | 1 |
| Glycerophospholipid metabolism | Hsa00564 | 5.47 | 0.23 | 5 |
| Alanine, aspartate and glutamate metabolism | Hsa00250 | 0.53 | 0.20 | 1 |

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## Conclusions

Overall, our study demonstrated the abnormal metabolism of amino acids, energy, and lipids in patients with DMD, consistent with pathological features, such as recurrent muscle necrosis and regeneration, interstitial fibrosis, and fat replacement. In addition, we also identified a number of differential metabolites associated with gut microbiota, which may be related to nutritional disorders and intestinal muscle dysfunction in DMD patients. Although our study provides a new research strategy for the pathogenesis of DMD, there are some limitations. First, the sample size was small, so we hope to conduct a multi-center study with a large sample size in a later stage to reduce sampling error. Second, due to the different types, treatment courses, and doses of corticosteroids used by DMD group in this article, we were unable to completely distinguish the corticosteroid-treated group from the untreated group using PCA. Therefore, we could not obtain differences in disease metabolism at corticosteroid treated or nontreated conditions. Although we cannot separate DMD patients into treated and untreated group, this article can still be considered as the first exploratory study on metabolic changes in clinical patients with DMD (regardless of medication use) in natural research history. In the future, we will conduct a prospective study with larger samples to focus on drug treatments (such as glucocorticoids, calcium channel blockers and vitamin D) and explore their impacts on the metabolic spectrum of DMD patients. Furthermore, target validation should be applied in an in-depth study to validate our selected metabolic indicators.

**List of abbreviations**

| | |
|---|---|
| DMD | Duchenne muscular dystrophy |
| HC | healthy control |
| UPLC-MS/MS | ultra-high performance liquid chromatography-tandem mass spectrometry |
| IRB | Institutional Review Board |
| QC | quality control |
| UPLC | ultra-high performance liquid chromatography |
| IDA | independent data acquisition |
| KEGG | Kyoto Encyclopedia of Genes and Genomes |
| HMDB | Human Metabolome Database |
| PCA | principal component analysis |
| PLS-DA | partial least-squares discriminant analysis |
| VIP | variable importance in projection |
| ANOVA | analysis of variance |
| LDS | least significant difference |
| PC | phosphatidylcholines |
| LPE | lysophosphatidylethanolamines |
| SM | sphingomyelin |
| FDR | false discovery rate |
| GLS | glutaminases |
| LPC | lysophosphatidylcholine |
| PA | phosphatidic acid |
| PS | phosphatidylserine |
| PAGln | phenylacetylglutamine |
| FXR | farnesoid X receptor |
| GPBAR-1 | G-protein-coupled bile acid receptor-1 |
| GUDCA | glycoursodeoxycholic acid |
| FGF | fibroblast growth factor |

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# MERCI à tous!

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