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, 17 Octobre 2024

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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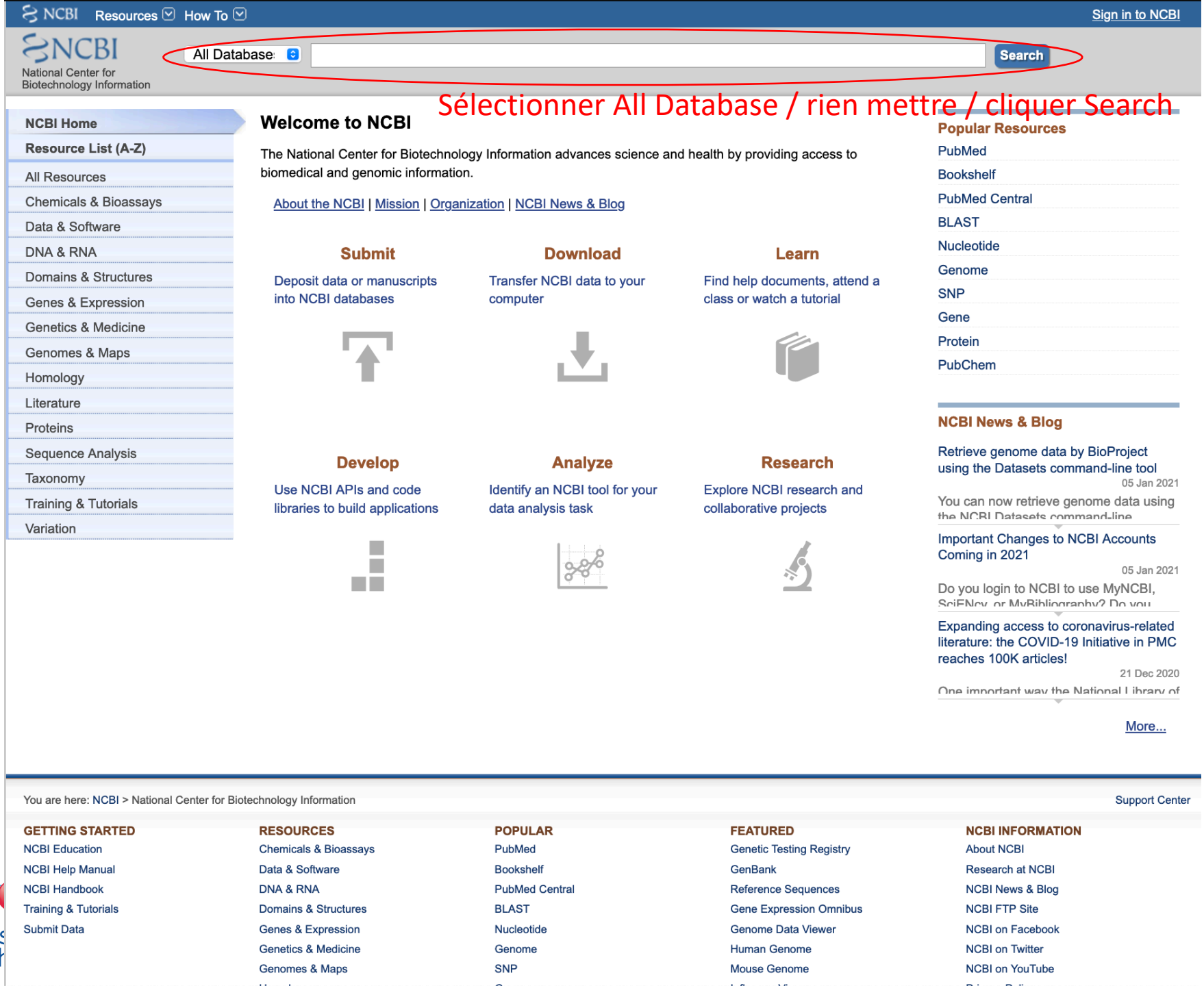
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NCBI databases

NCBI Virus
The most up-to-date set of SARS-CoV-2 nucleotide and protein sequences

LitCovid
A curated literature hub for the latest scientific information on COVID-19

BLAST
Use our new Betacoronavirus database for SARS-CoV-2 genome sequence analysis

Literature
The World's largest repository of medical and scientific abstracts, full-text articles, books and reports

- **Bookshelf** — Books and reports
- **MeSH** — Ontology used for PubMed indexing
- **NLM Catalog** — Books, journals and more in the NLM Collections
- **PubMed** — Scientific and medical abstracts/citations
- **PubMed Central** — Full-text journal articles

Genes
Gene sequences and annotations used as references for the study of orthologs structure, expression, and evolution

- **Gene** — Collected information about gene loci
- **GEO DataSets** — Functional genomics studies
- **GEO Profiles** — Gene expression and molecular abundance profiles
- **HomoloGene** — Homologous genes sets for selected organisms
- **PopSet** — Sequence sets from phylogenetic and population studies

Proteins
Protein sequences, 3-D structures, and tools for the study of functional protein domains and active sites

- **Conserved Domains** — Conserved protein domains
- **Identical Protein Groups** — Protein sequences grouped by identity
- **Protein** — Protein sequences
- **Protein Clusters** — Sequence similarity-based protein clusters
- **Protein Family Models** — Models representing homologous proteins with a common function
- **Structure** — Experimentally-determined biomolecular structures

Genomes
Genome sequence assemblies, large-scale functional genomics data, and source biological samples

- **Assembly** — Genome assembly information
- **BioCollections** — Museum, herbaria, and other biorepository collections
- **BioProject** — Biological projects providing data to NCBI
- **BioSample** — Descriptions of biological source materials
- **Genome** — Genome sequencing projects by organism
- **Nucleotide** — DNA and RNA sequences
- **SRA** — High-throughput sequence reads
- **Taxonomy** — Taxonomic classification and nomenclature

BLAST
A tool to find regions of similarity between biological sequences

- **blastn** — Search nucleotide sequence databases
- **blastp** — Search protein seqeuence databases
- **blastx** — Search protein databases using a translated nucleotide query
- **tblastn** — Search translated nucleotide databases using a protein query
- **Primer-BLAST** — Find primers specific to your PCR template

Clinical
Heritable DNA variations, associations with human pathologies, and clinical diagnostics and treatments

- **ClinicalTrials.gov** — Privately and publicly funded clinical studies conducted around the world
- **ClinVar** — Human variations of clinical significance
- **dbGaP** — Genotype/phenotype interaction studies
- **dbSNP** — Short genetic variations
- **dbVar** — Genome structural variation studies
- **GTR** — Genetic testing registry
- **MedGen** — Medical genetics literature and links
- **OMIM** — Online mendelian inheritance in man

PubChem
Repository of chemical information, molecular pathways, and tools for bioactivity screening

- **BioAssays** — Bioactivity screening studies
- **Compounds** — Chemical information with structures, information and links
- **Pathways** — Molecular pathways with links to genes, proteins and chemicals
- **Substances** — Deposited substance and chemical information

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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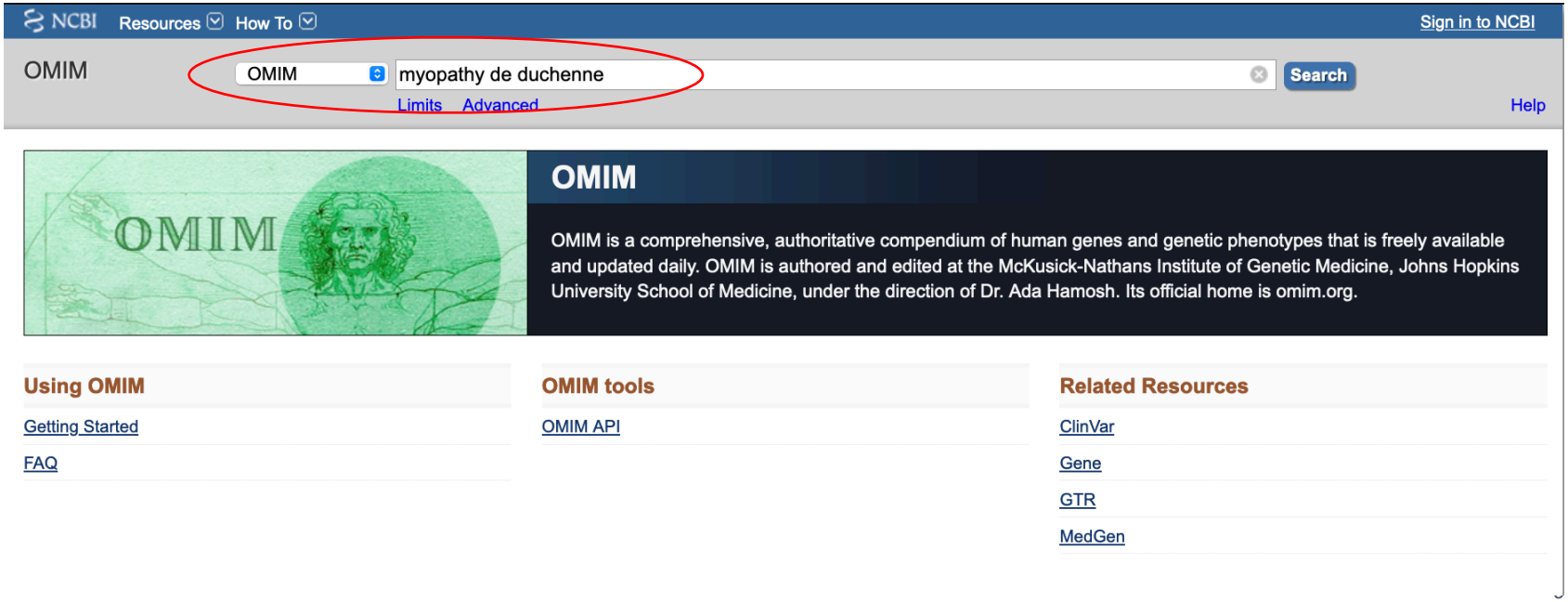
OMIM : Le projet Héritage mendélien chez l'humain (en anglais : Mendelian Inheritance in Man) est une base de données originellement compilée par Victor A. McKusick et qui dresse un catalogue de toutes les maladies connues qui relèvent de l'un ou l'autre composant génétique et — si possible — les relie 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
   OMIM: 253700
   Gene summaries Genetic tests Medical literature

2. #608099 - MUSCULAR DYSTROPHY, LIMB-GIRDLE, AUTOSOMAL RECESSIVE 3; LGMDR3
   Cytogenetic locations: 17q21.33
   OMIM: 608099
   Gene summaries Genetic tests Medical literature

3. #310200 - MUSCULAR DYSTROPHY, **DUCHENNE** TYPE; DMD
   Cytogenetic locations: Xp21.2-p21.1
   OMIM: 310200
   Gene summaries Genetic tests Medical literature

4. #158810 - BETHLEM **MYOPATHY** 1; BTHLM1
   Cytogenetic locations: 21q22.3, 1p36, 21q22.3
   OMIM: 158810
   Gene summaries Genetic tests Medical literature

5. #310400 - **MYOPATHY**, CENTRONUCLEAR, X-LINKED; CNMX
   Cytogenetic locations: Xq28
   OMIM: 310400
   Gene summaries Genetic tests Medical literature

6. #254130 - MIYOSHI MUSCULAR DYSTROPHY 1; MMD1
   Cytogenetic locations: 2p13.2
   OMIM: 254130
   Gene summaries Genetic tests Medical literature

7. #310440 - **MYOPATHY**, X-LINKED, WITH EXCESSIVE AUTOPHAGY; MEAX
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   OMIM: 310440
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8. #300257 - DANON DISEASE
   Cytogenetic locations: Xq24
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ICD+

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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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- Clinical Resources
  - Clinical Trials
  - EuroGentest
  - Gene Reviews
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  - Genetics Home
  - Reference
  - GTR
  - GARD
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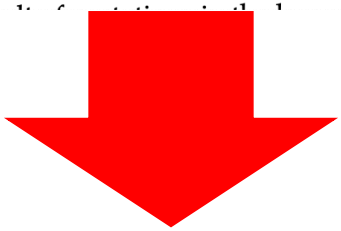

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Table of Contents

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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  - Gene Reviews
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  - GTR
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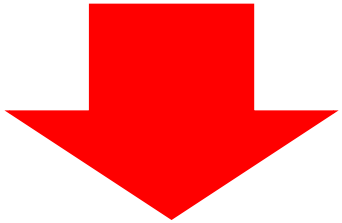

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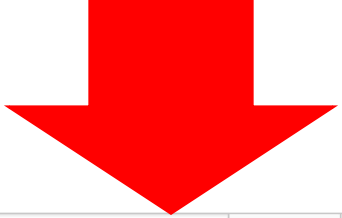

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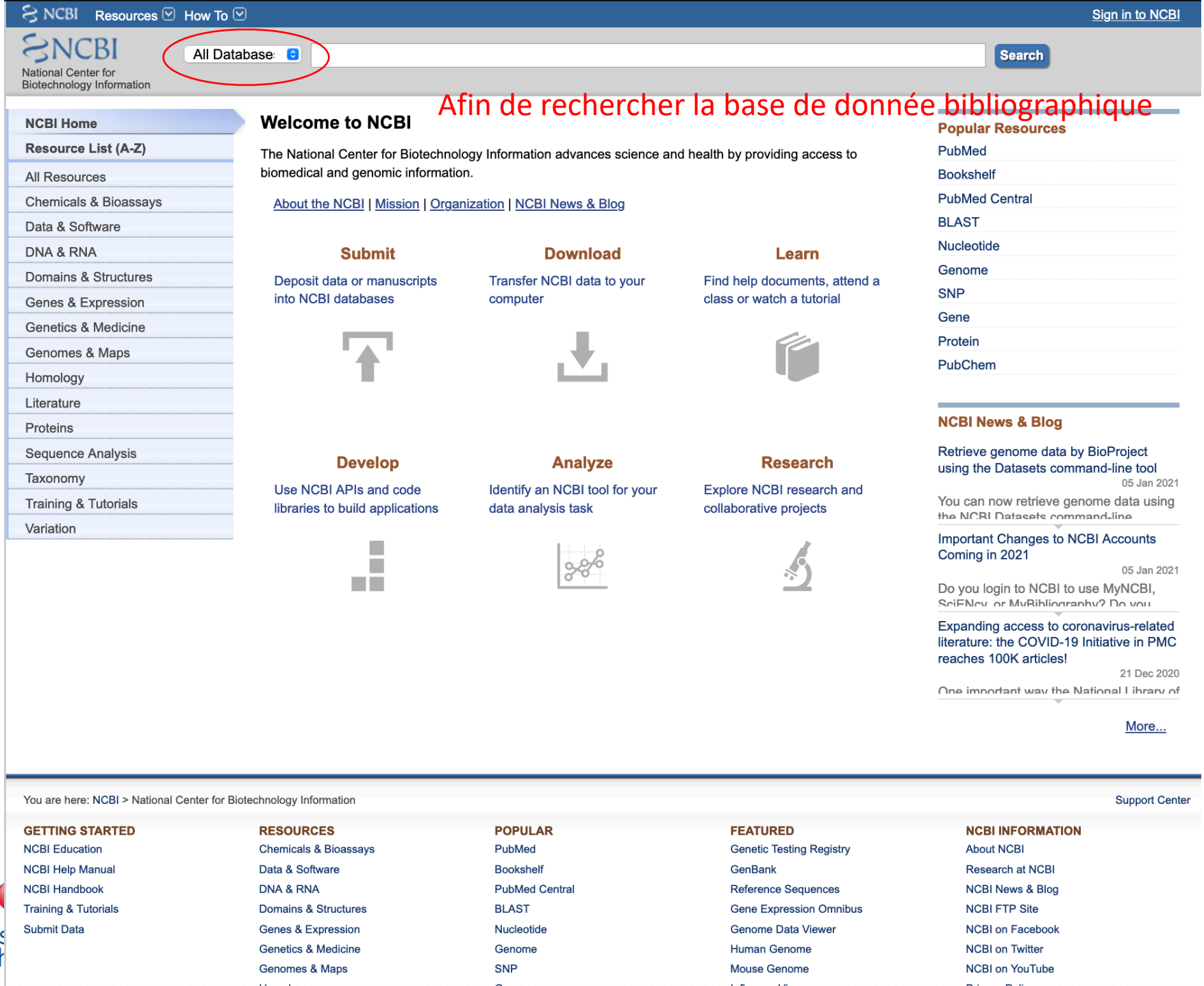
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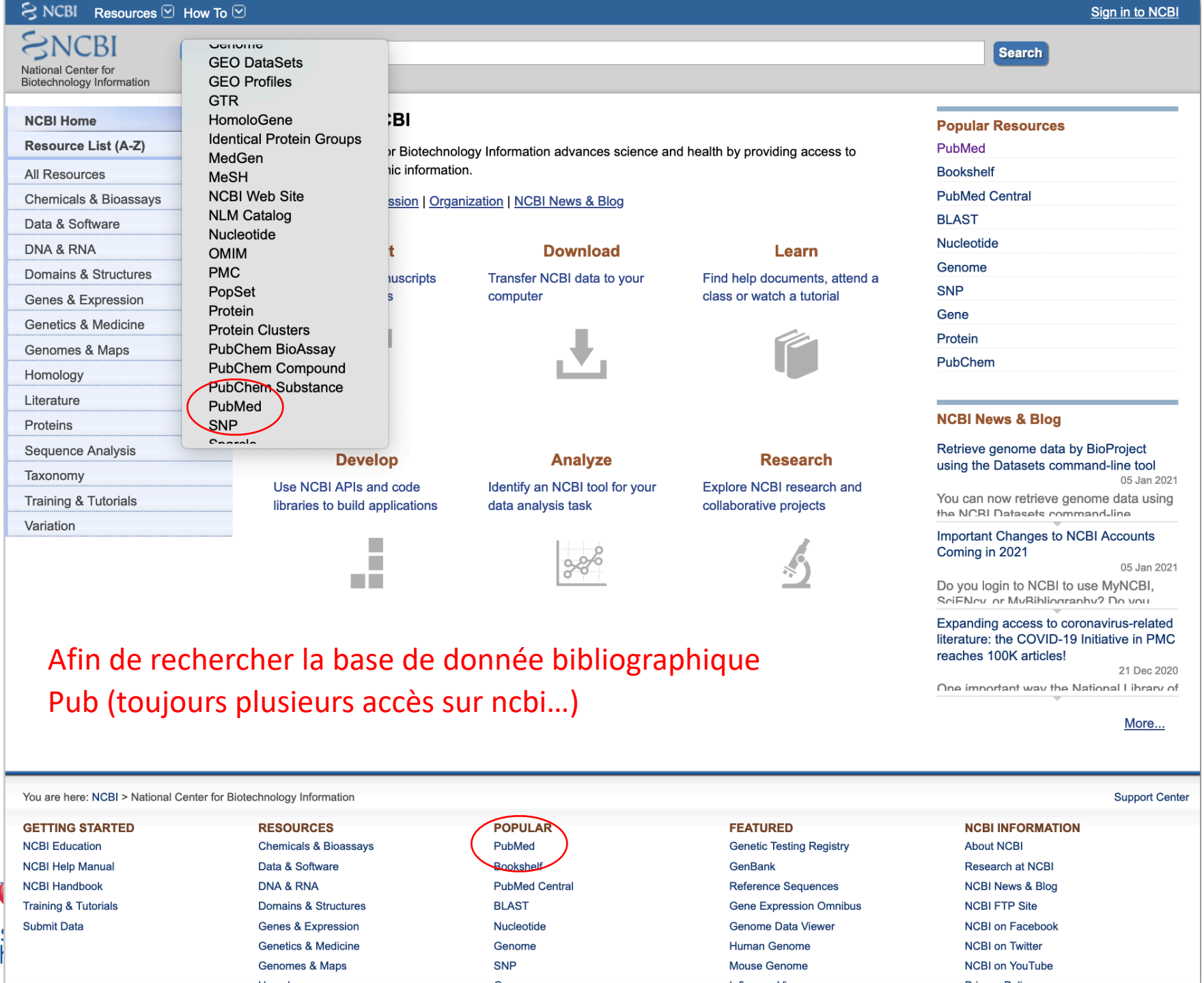

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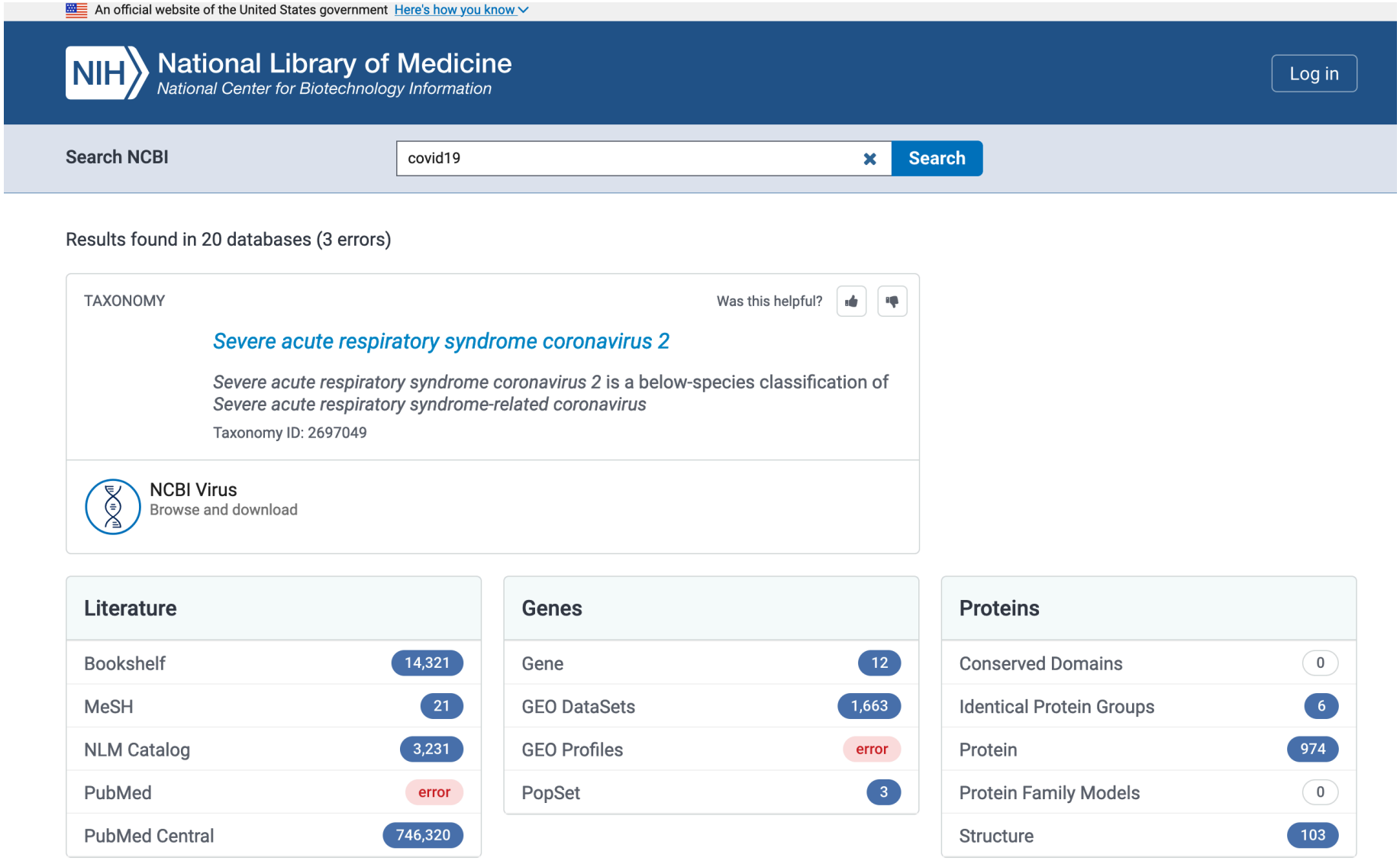

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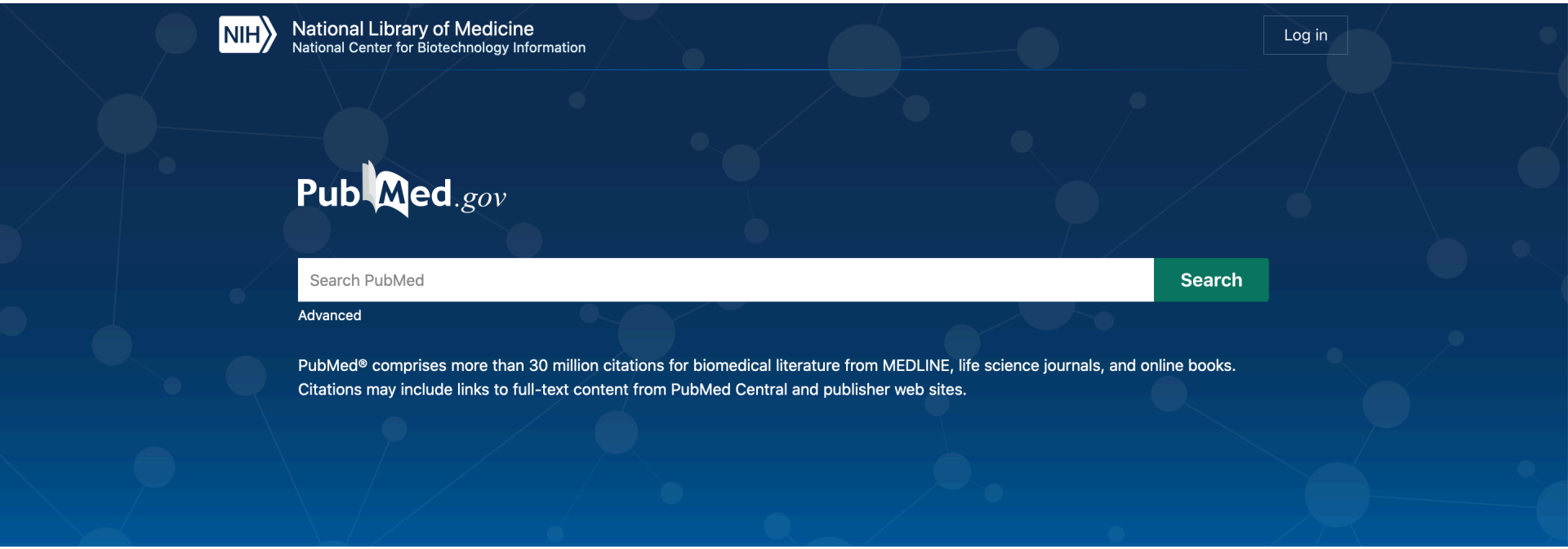

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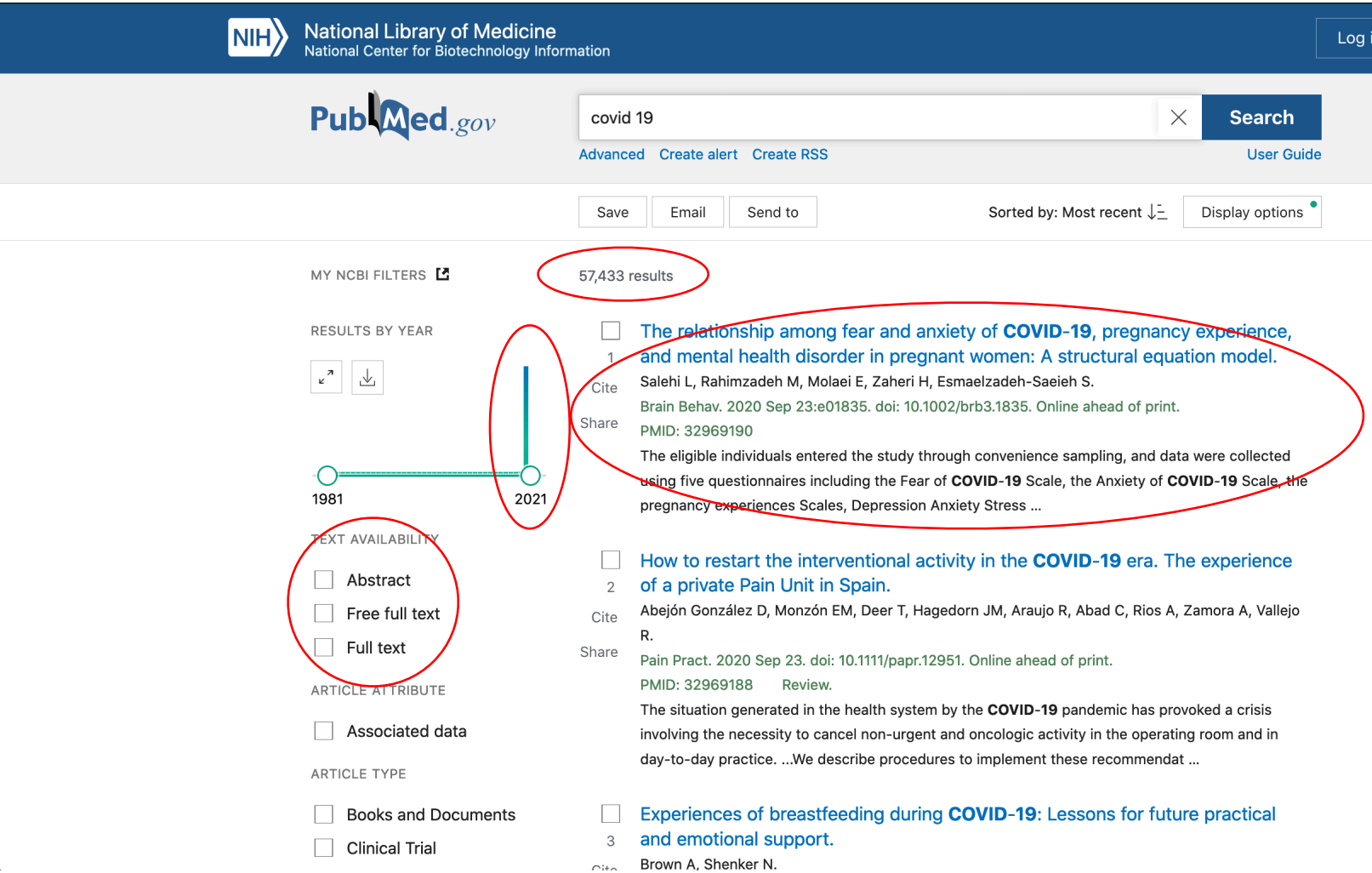

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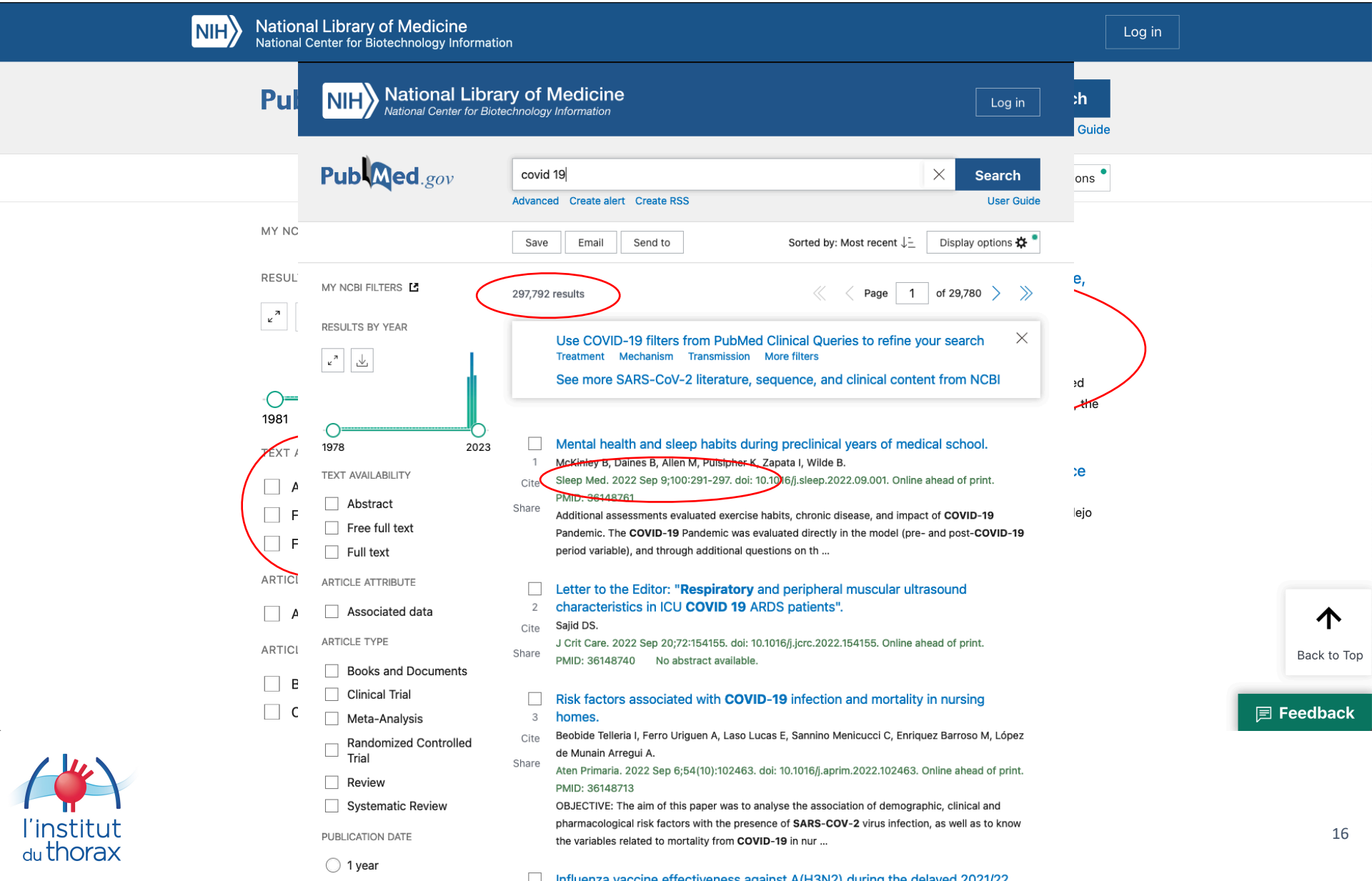

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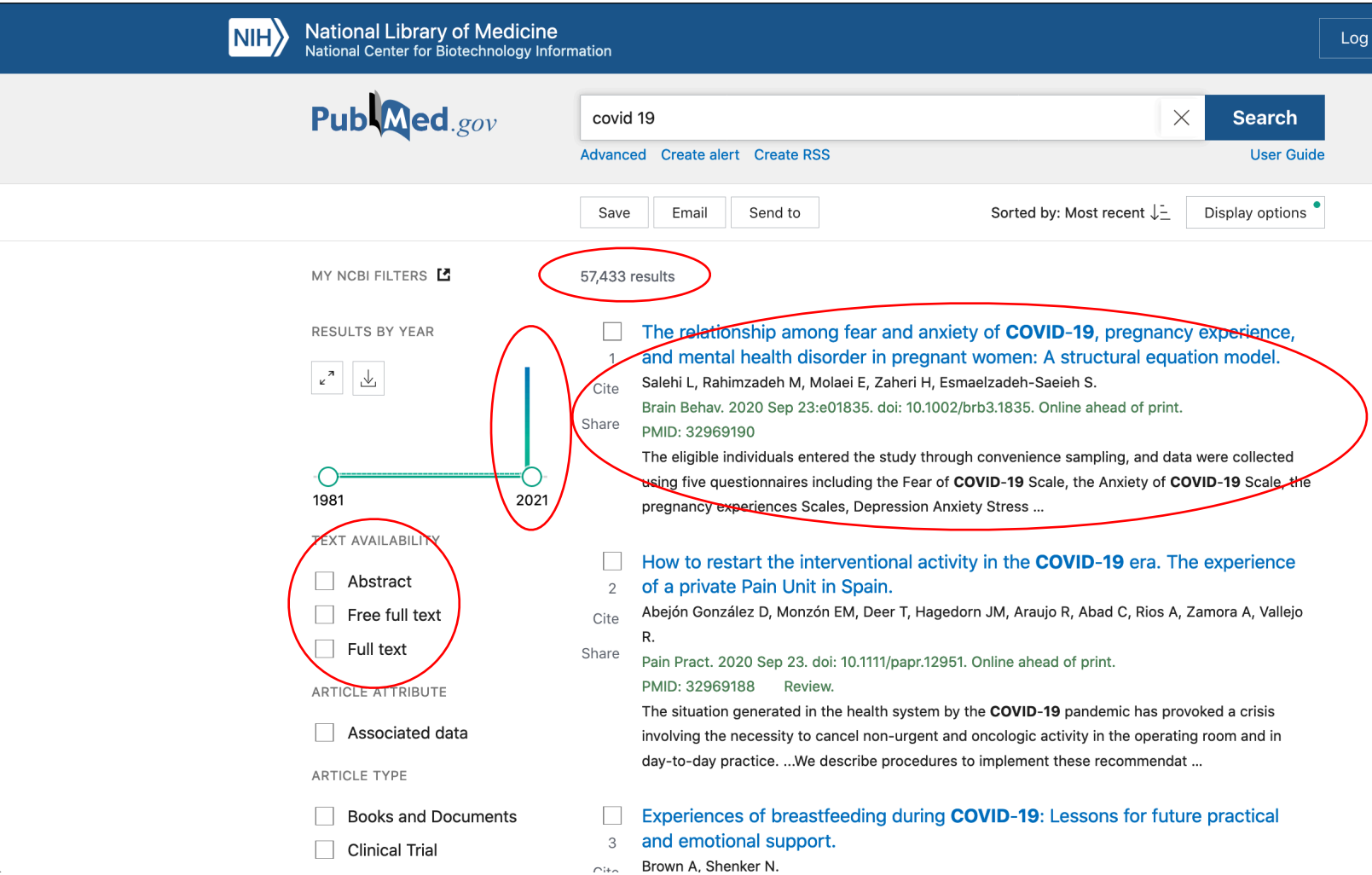

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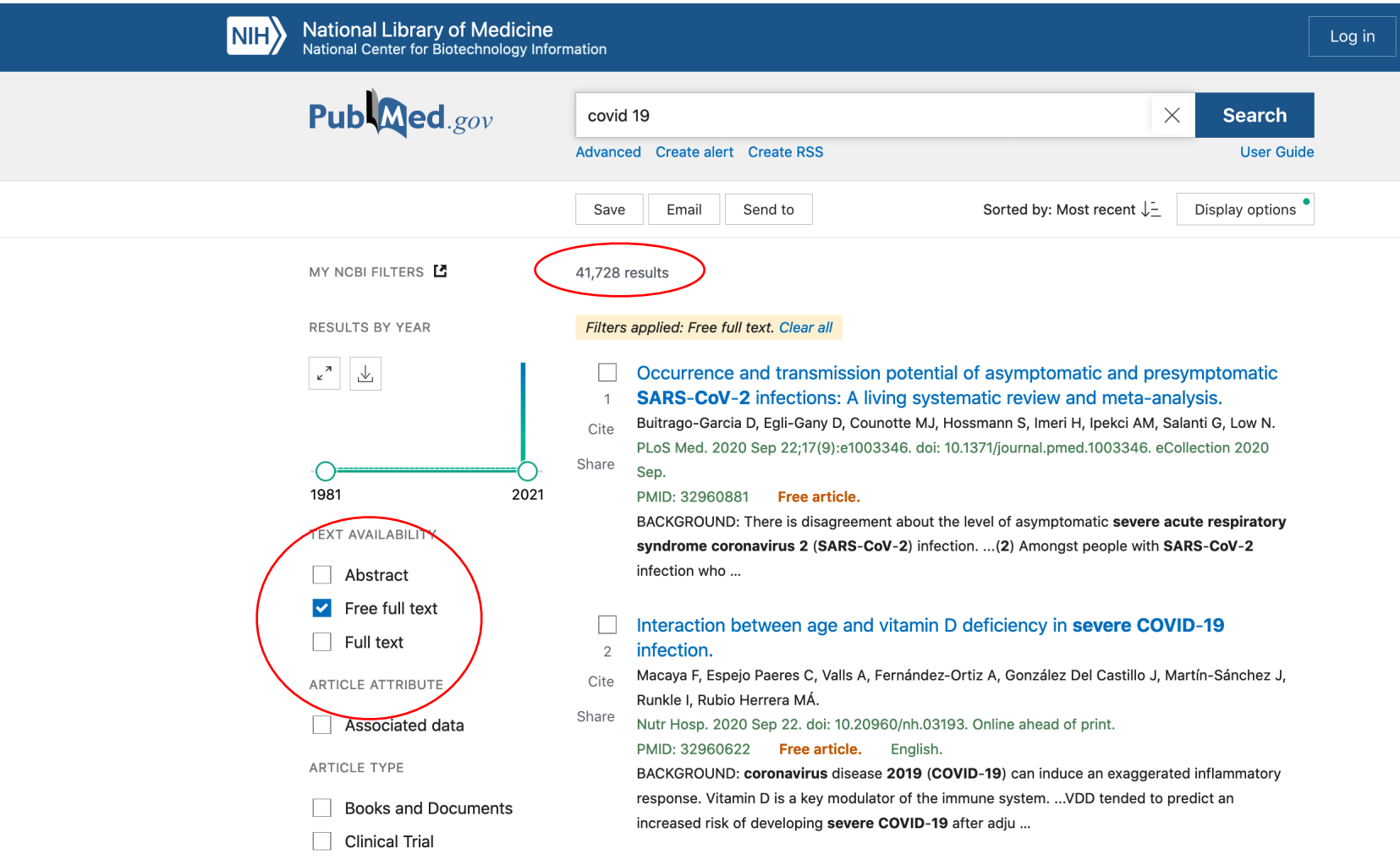

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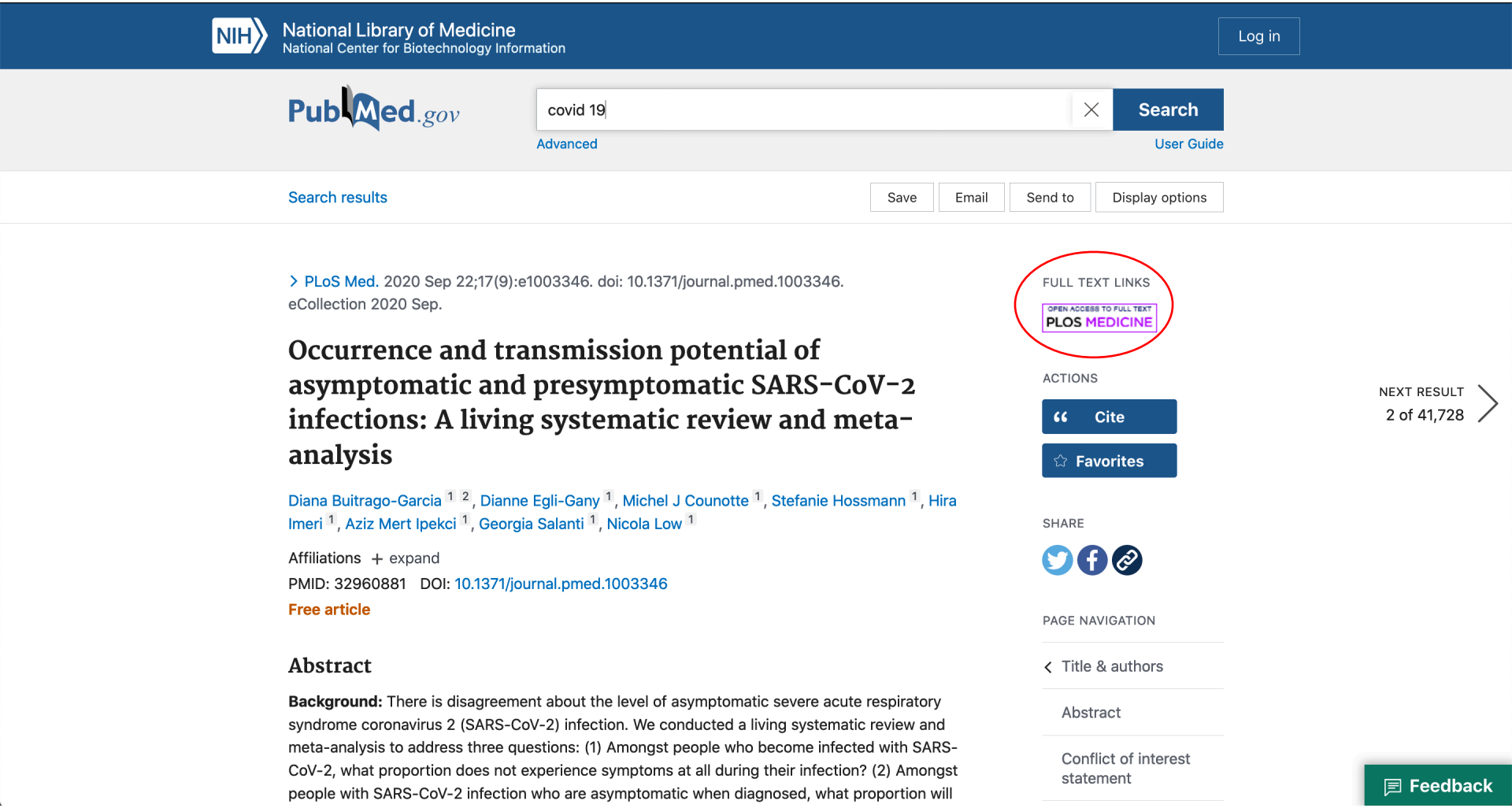

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Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis

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]

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PMID: 32960881 DOI: 10.1371/journal.pmed.1003346

Free article

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

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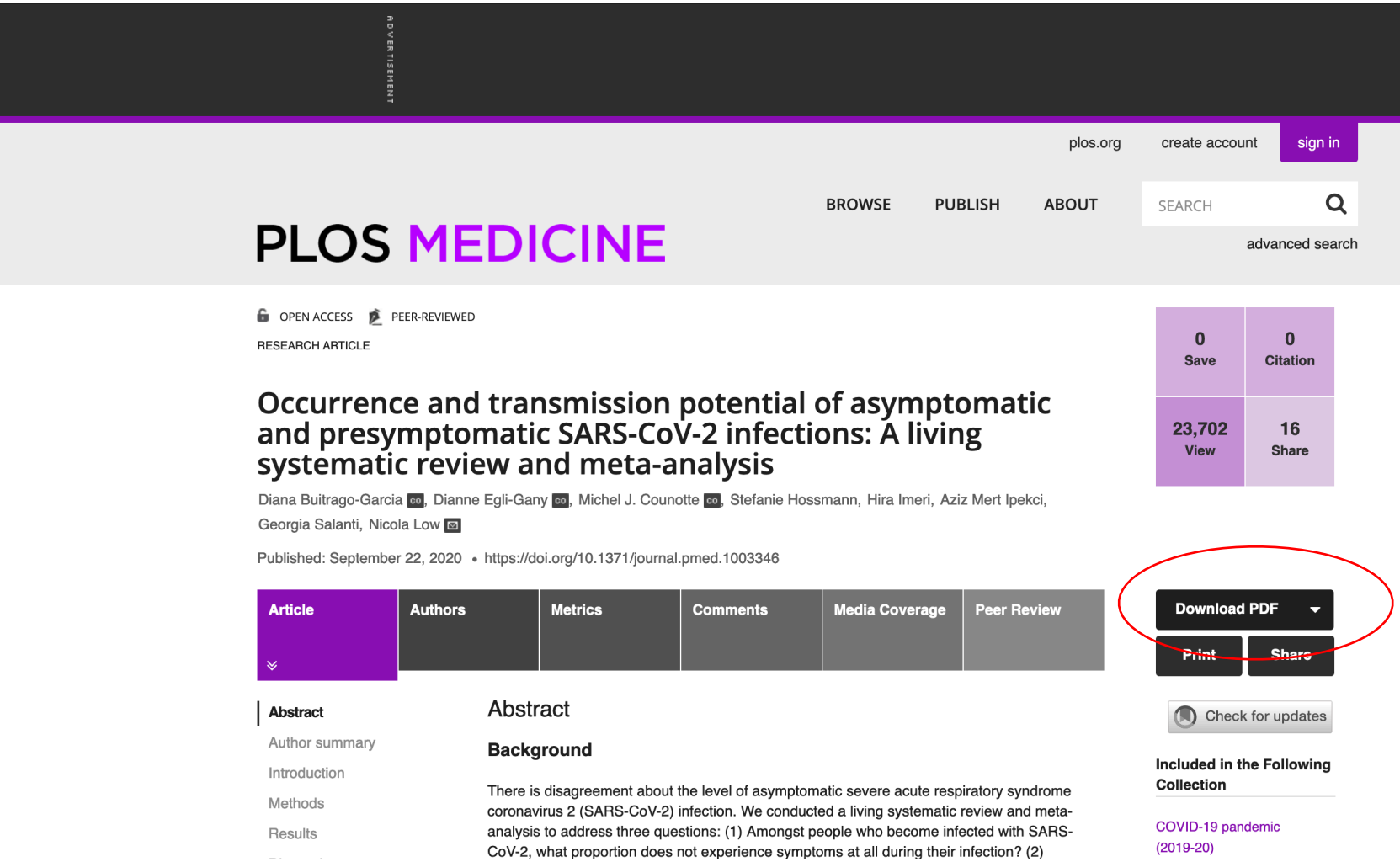

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Occurrence and transmission potential of asymptomatic and presymptomatic SARS-CoV-2 infections: A living systematic review and meta-analysis

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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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*)

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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.

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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

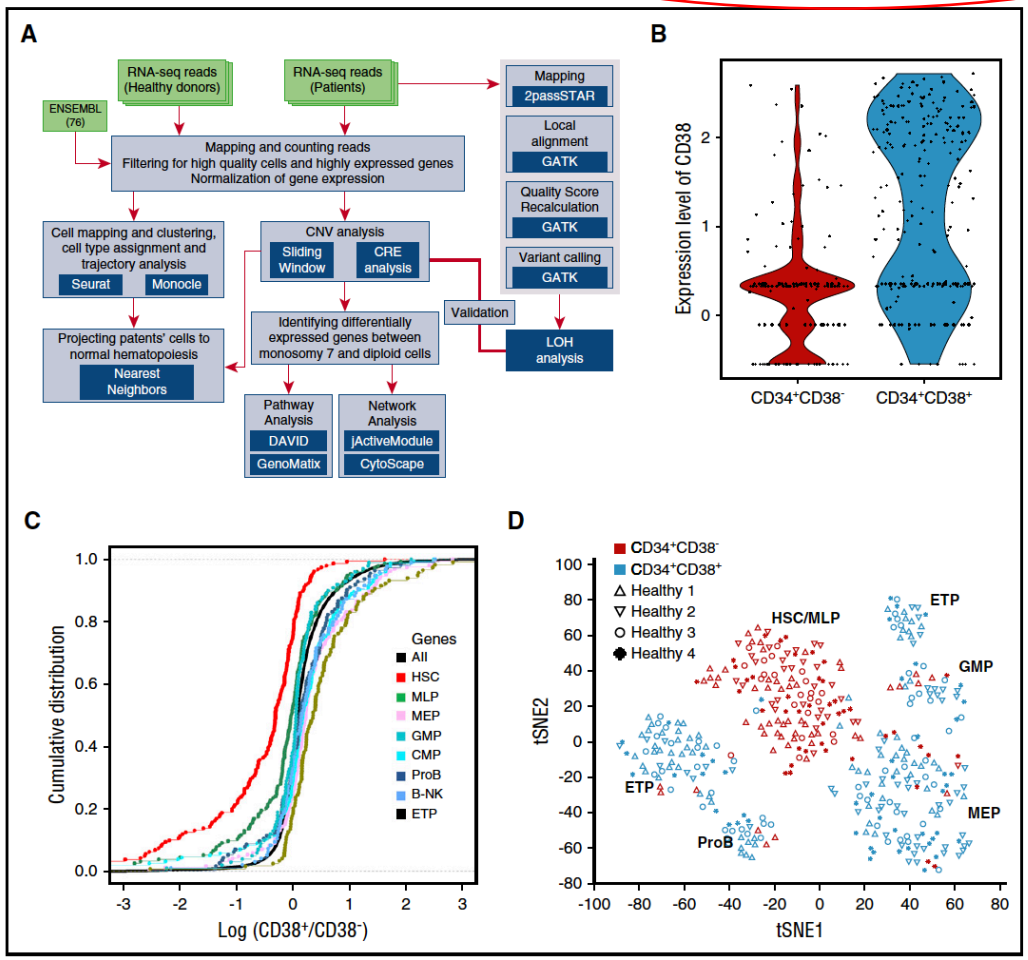

Figure 1. Hematopoietic heterogeneity in healthy donors quantified by scRNA-seq. $CD34^+CD38^-$ and $CD34^+CD38^+$ cells from 4 healthy donors (healthy 1-4) were sorted by surface-membrane markers and subjected to analyses. (A) The schematic pipeline consisting of 3 major analytic components: differentiation 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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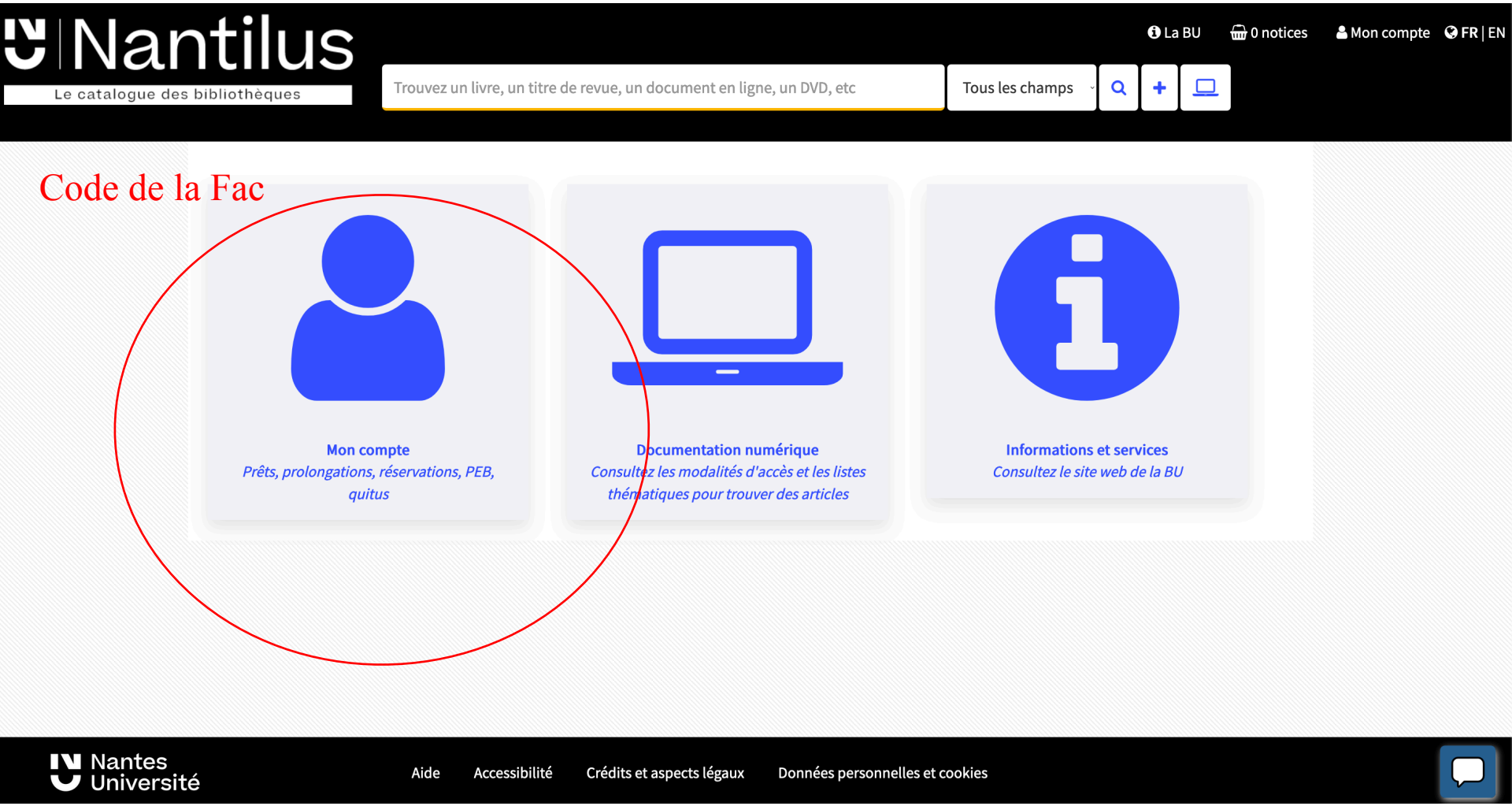
Un exemple de recherche: Covid19 ?



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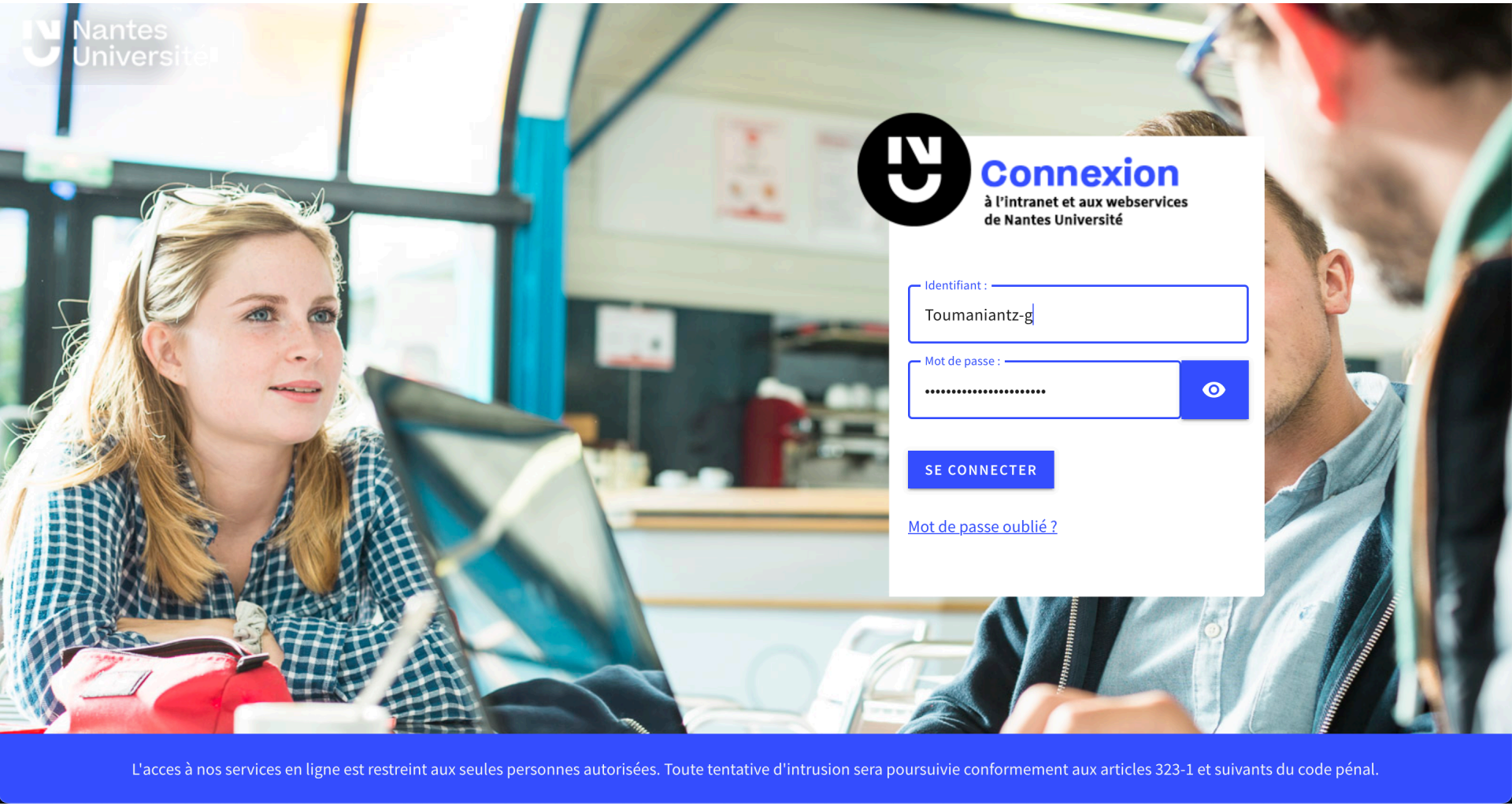

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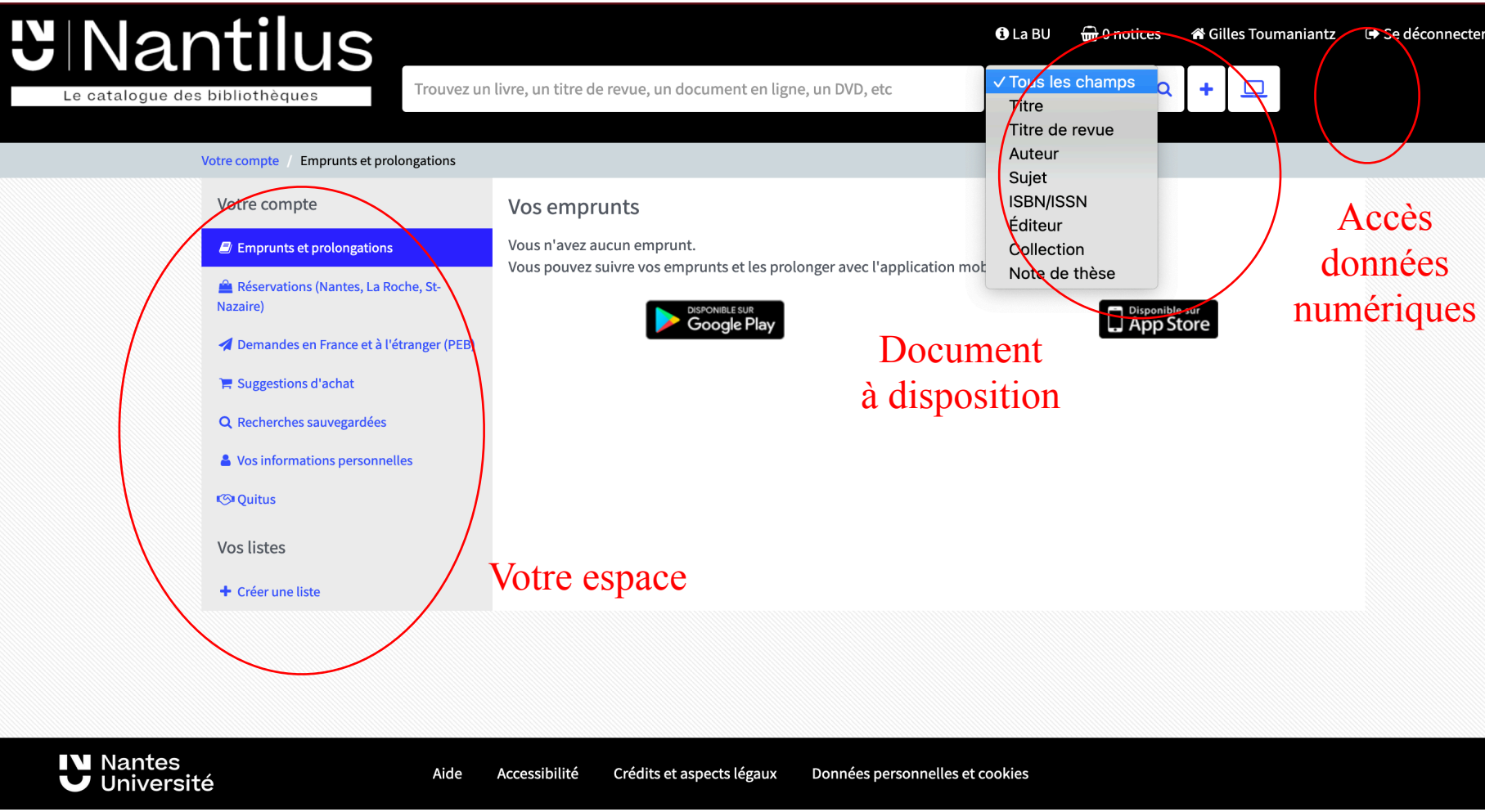

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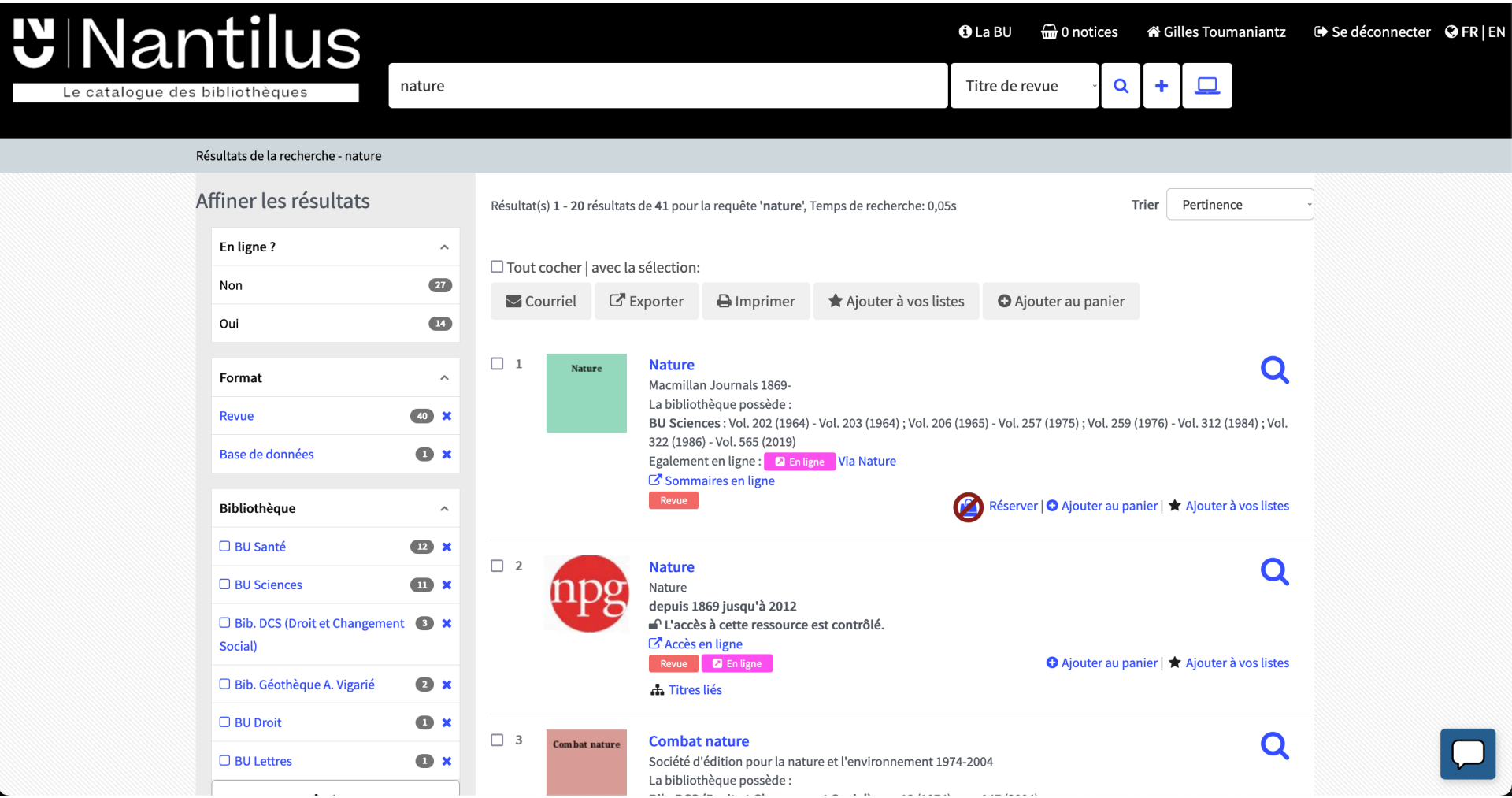

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Question à étudier:

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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.

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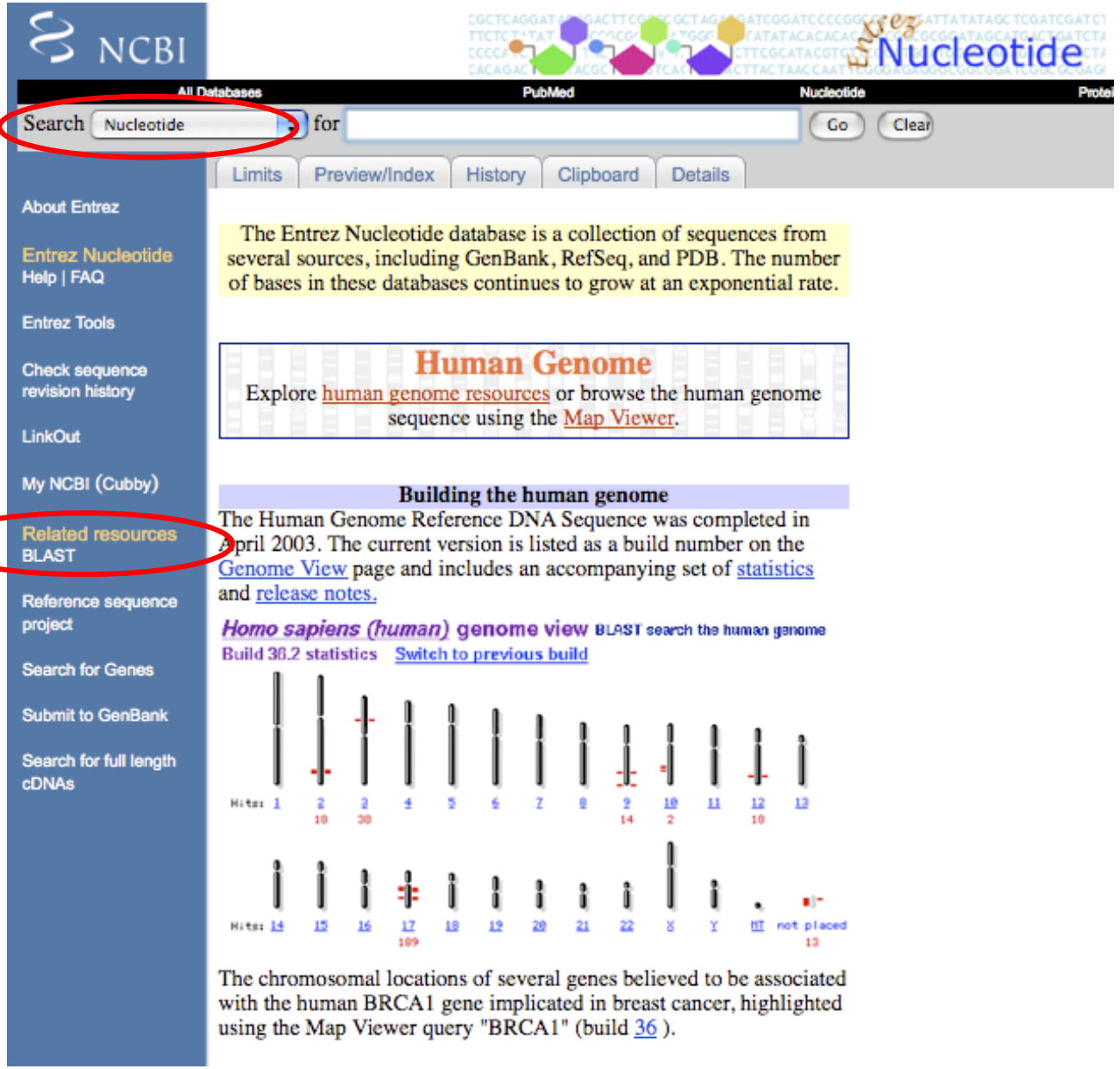

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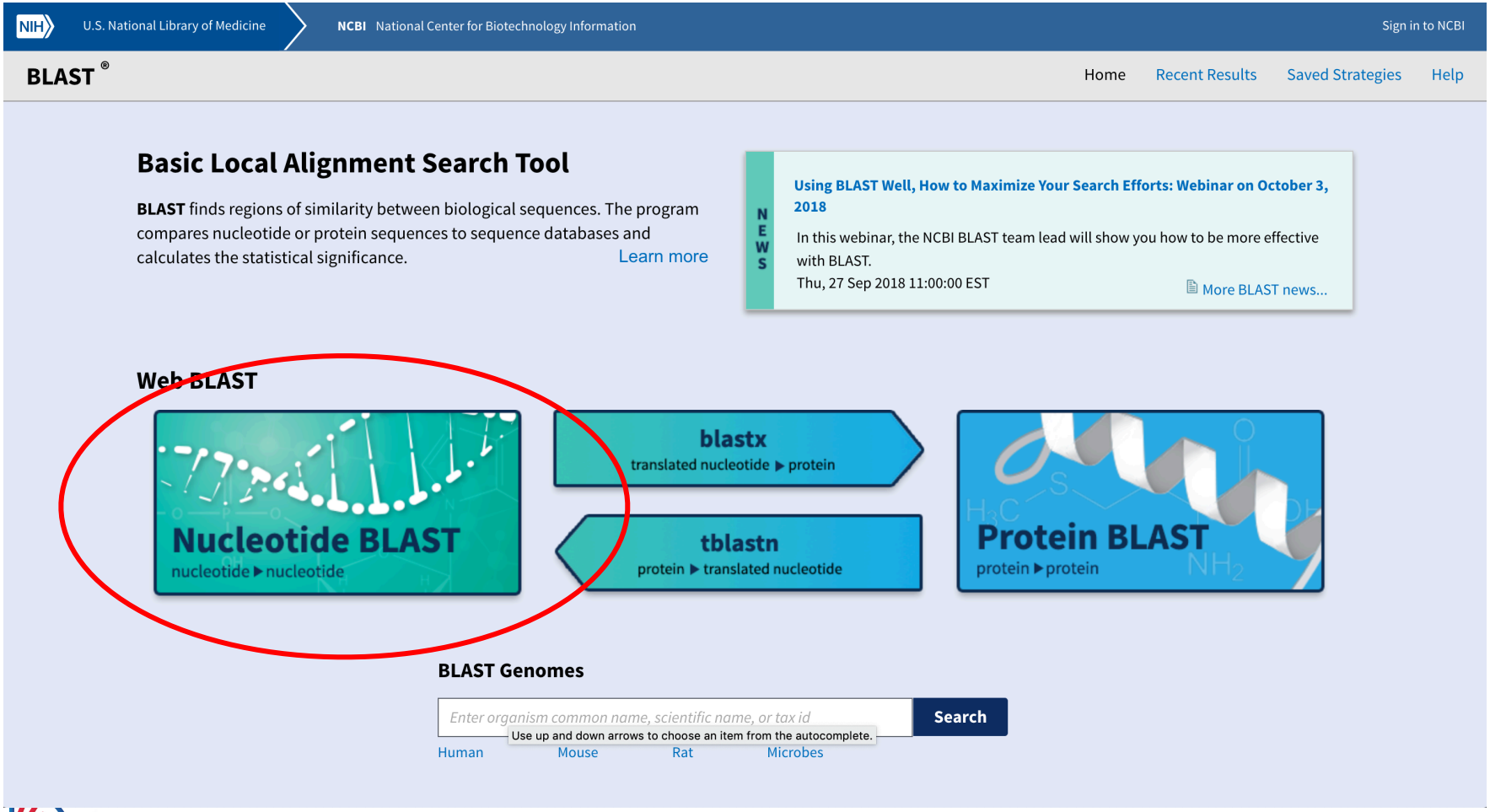

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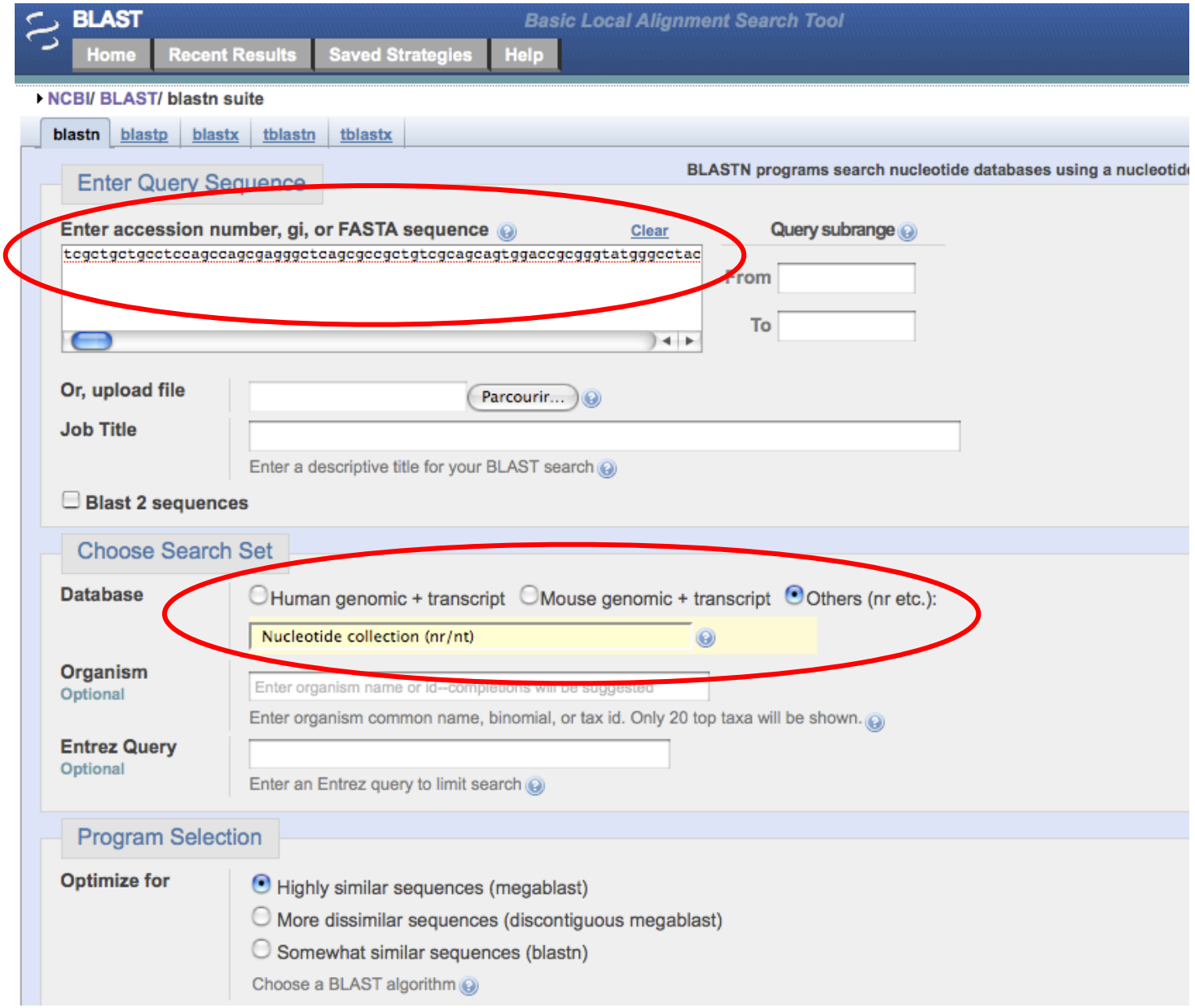

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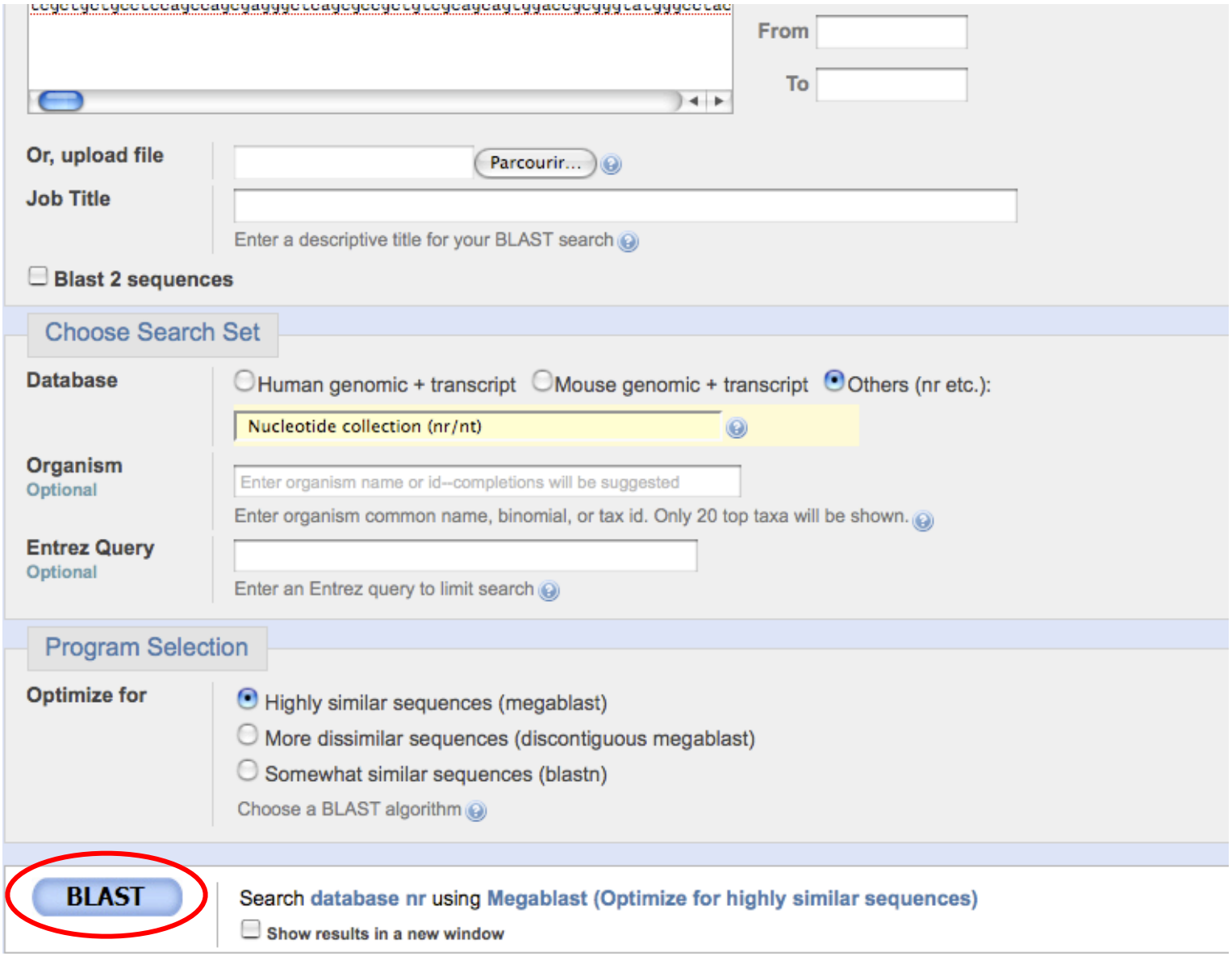

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BLAST Basic Local Alignment Search Tool

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

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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]

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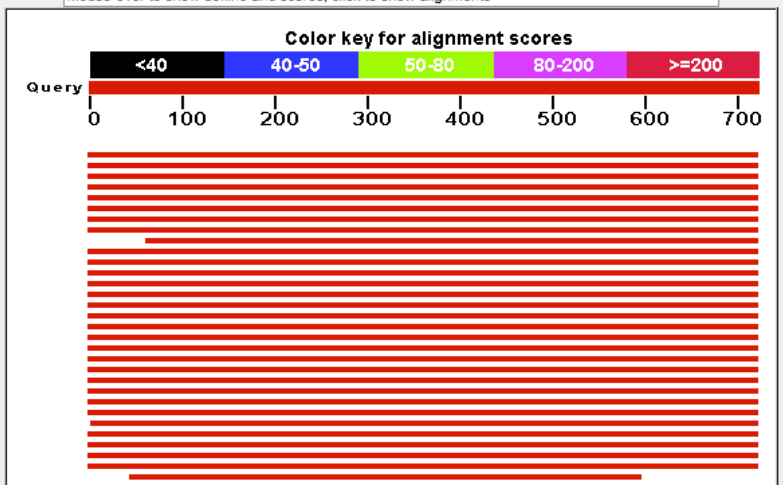
Distribution of 45 Blast Hits on the Query Sequence

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



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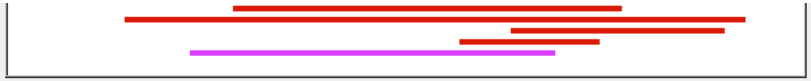

Descriptions

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
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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
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NM_001008713.1	Canis lupus familiaris adrenergic, beta-1-, receptor (ADRB1), mRNA	979	979	100%	0.0	91%	U G
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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

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▼ 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)

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Position 470/début séquence référencée

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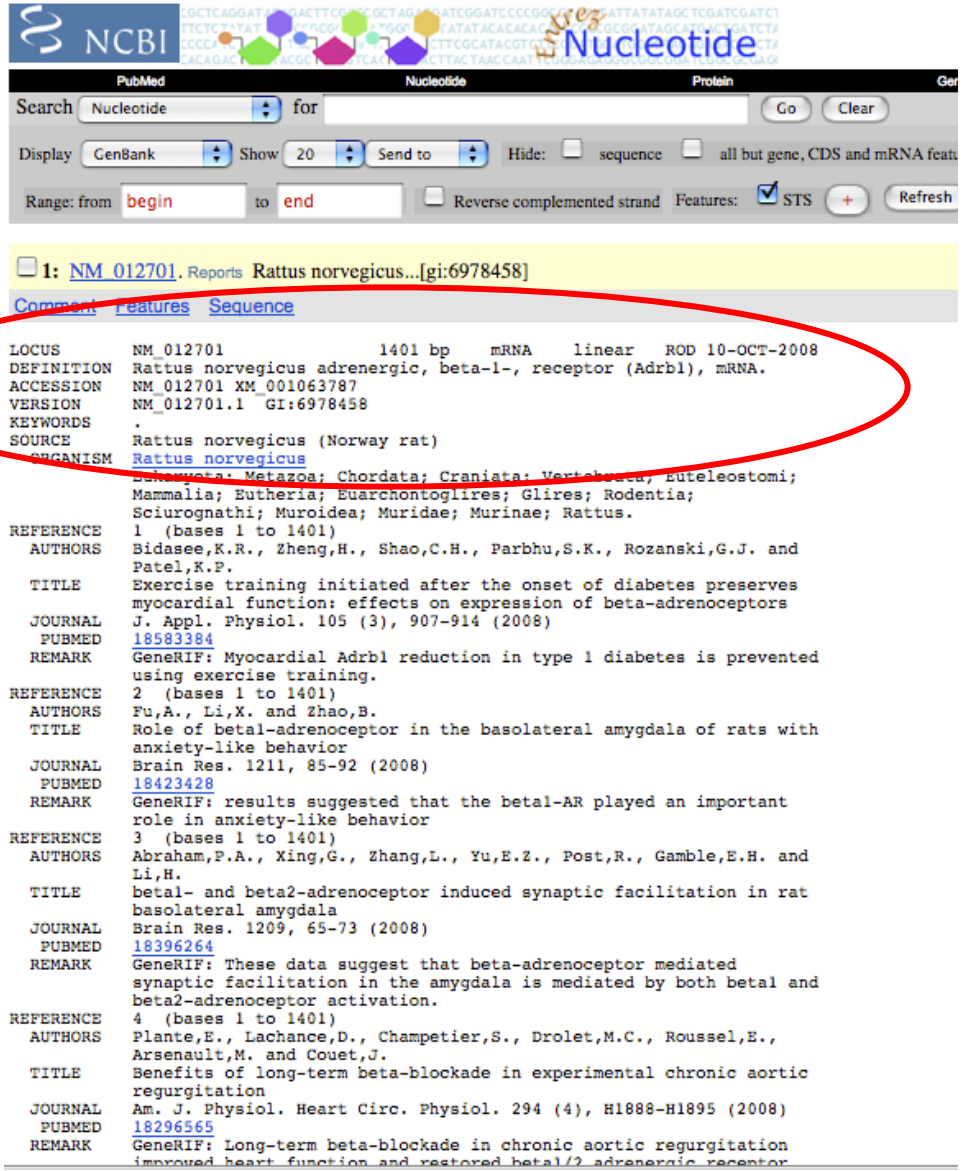
2. Les analyses nucléotidiques



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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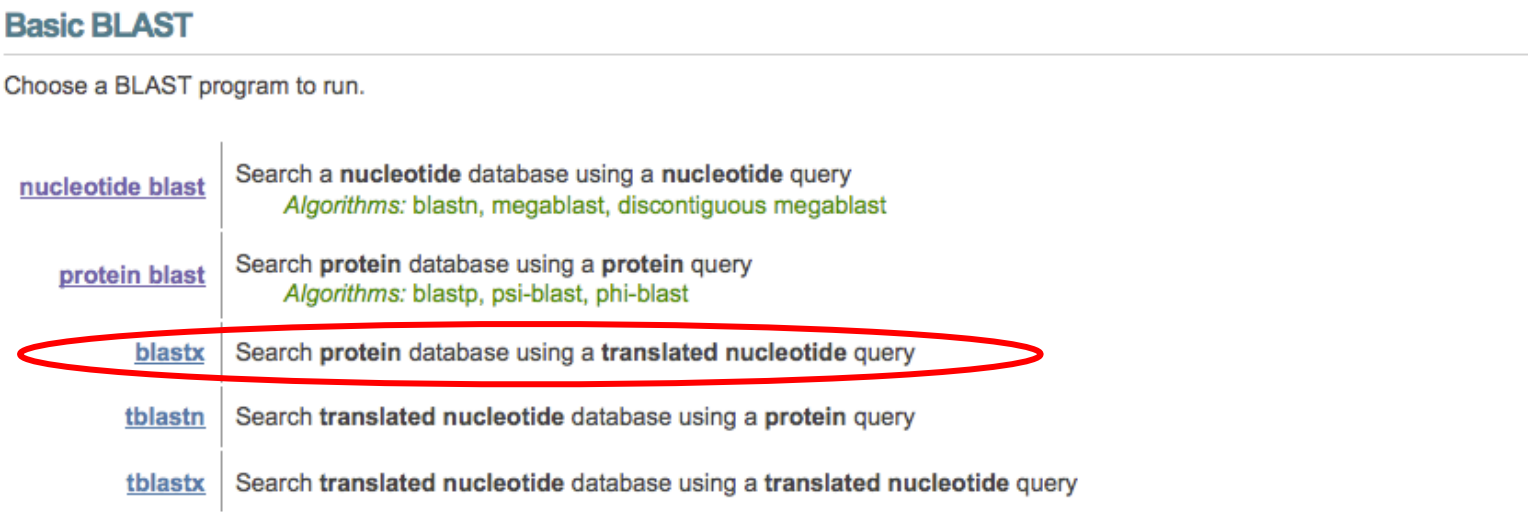
2. Les analyses nucléotidiques

Question à étudier:

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



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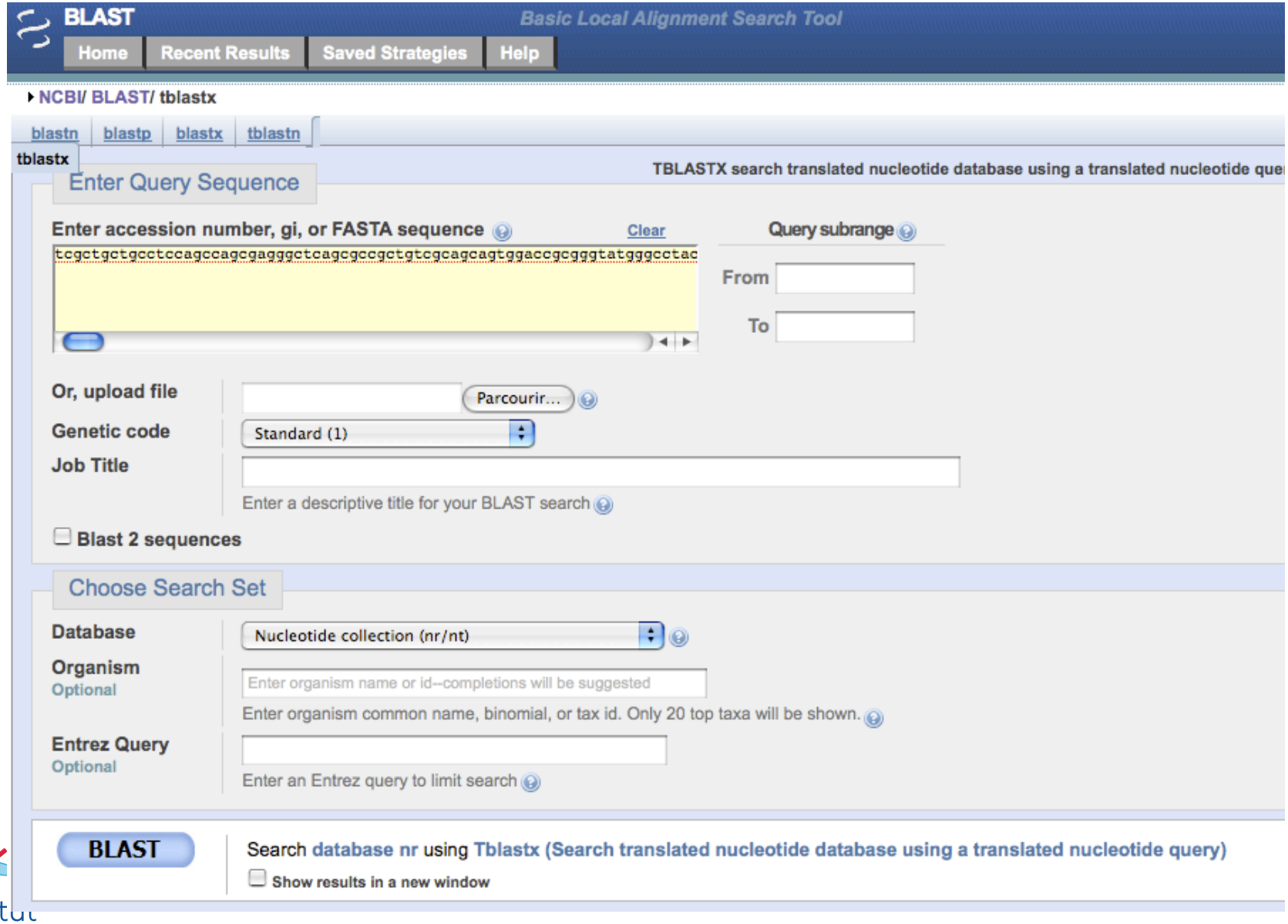
2. Les analyses nucléotidiques



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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

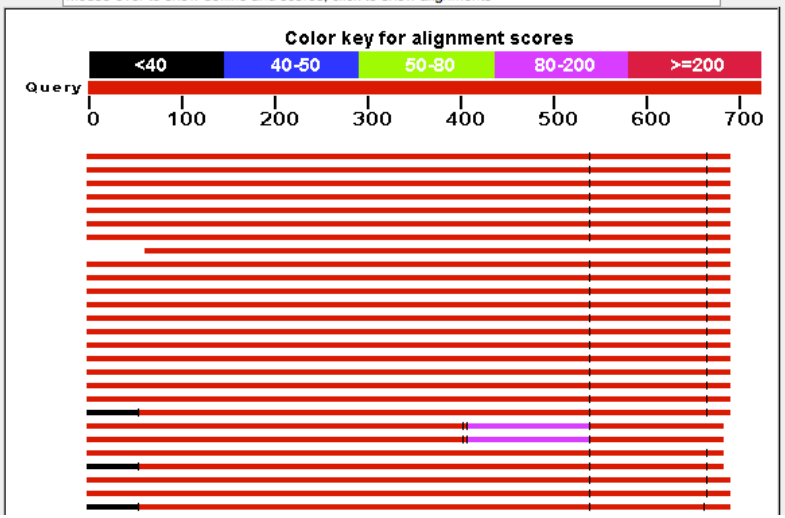
Database Name nr
Description All GenBank+EMBL+DDBJ+PDB sequences (but no EST, STS, GSS,environmental samples or phase 0, 1 or 2 HTGS sequences)
Program TBLASTX 2.2.18+ ▷Citation

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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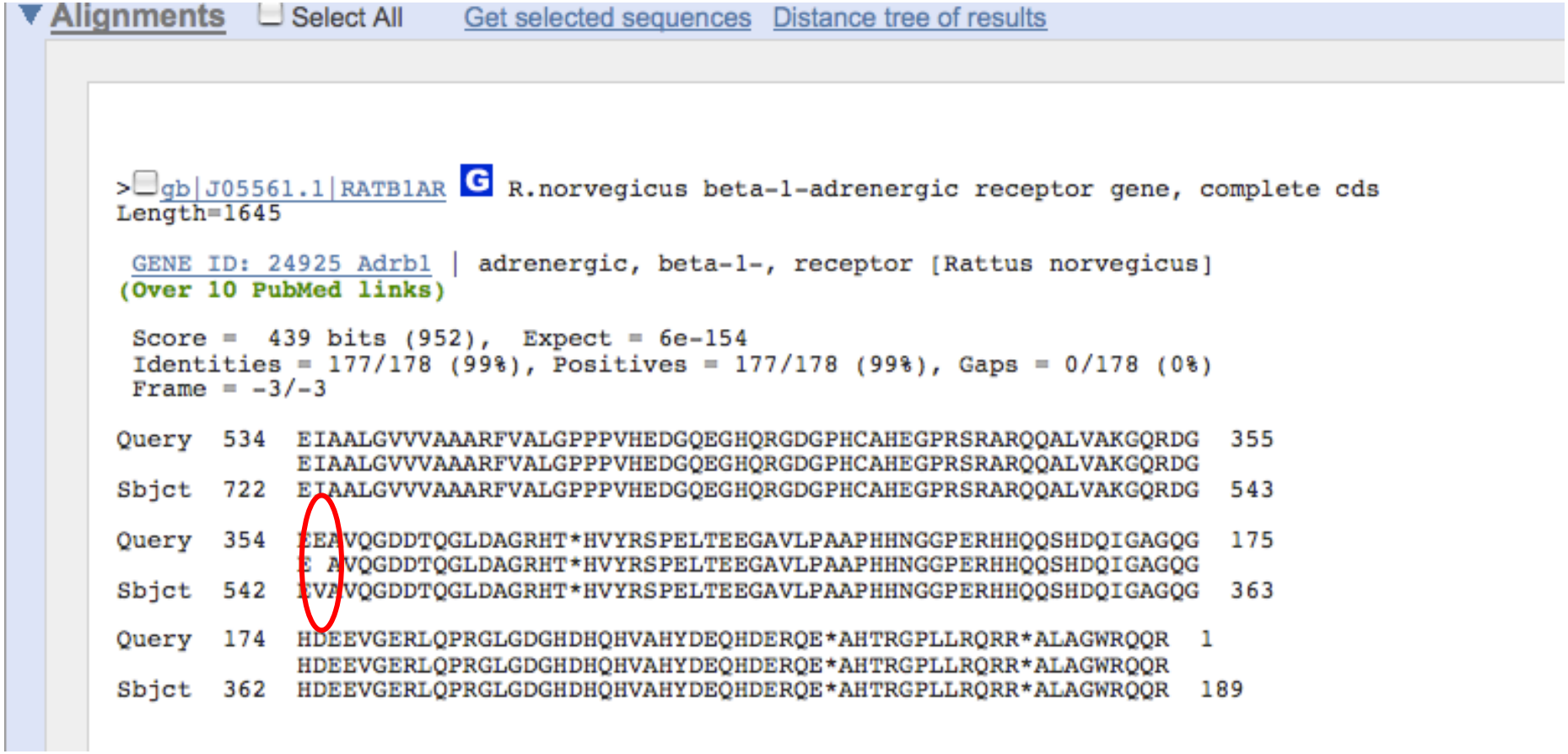
2. Les analyses nucléotidiques



Alignments Select All Get selected sequences Distance tree of results

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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*]

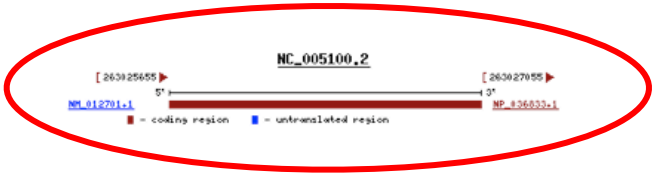
GeneID: 24925 updated 15-Oct-2008

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

Table Of Contents
- Summary
- Genomic regions, transcripts...
- Genomic context
- Bibliography
- Interactions
- General gene information
- General protein information
- Reference Sequences
- Related Sequences
- Additional Links

Links
- Conserved Domains
- Genome
- GEO Profiles
- HomoloGene
- Map Viewer
- Nucleotide
- PubChem Compound
- PubChem Substance
- Full text in PMC
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- PubMed (GeneRIF)
- Taxonomy
- UniSTS
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- RATMAP
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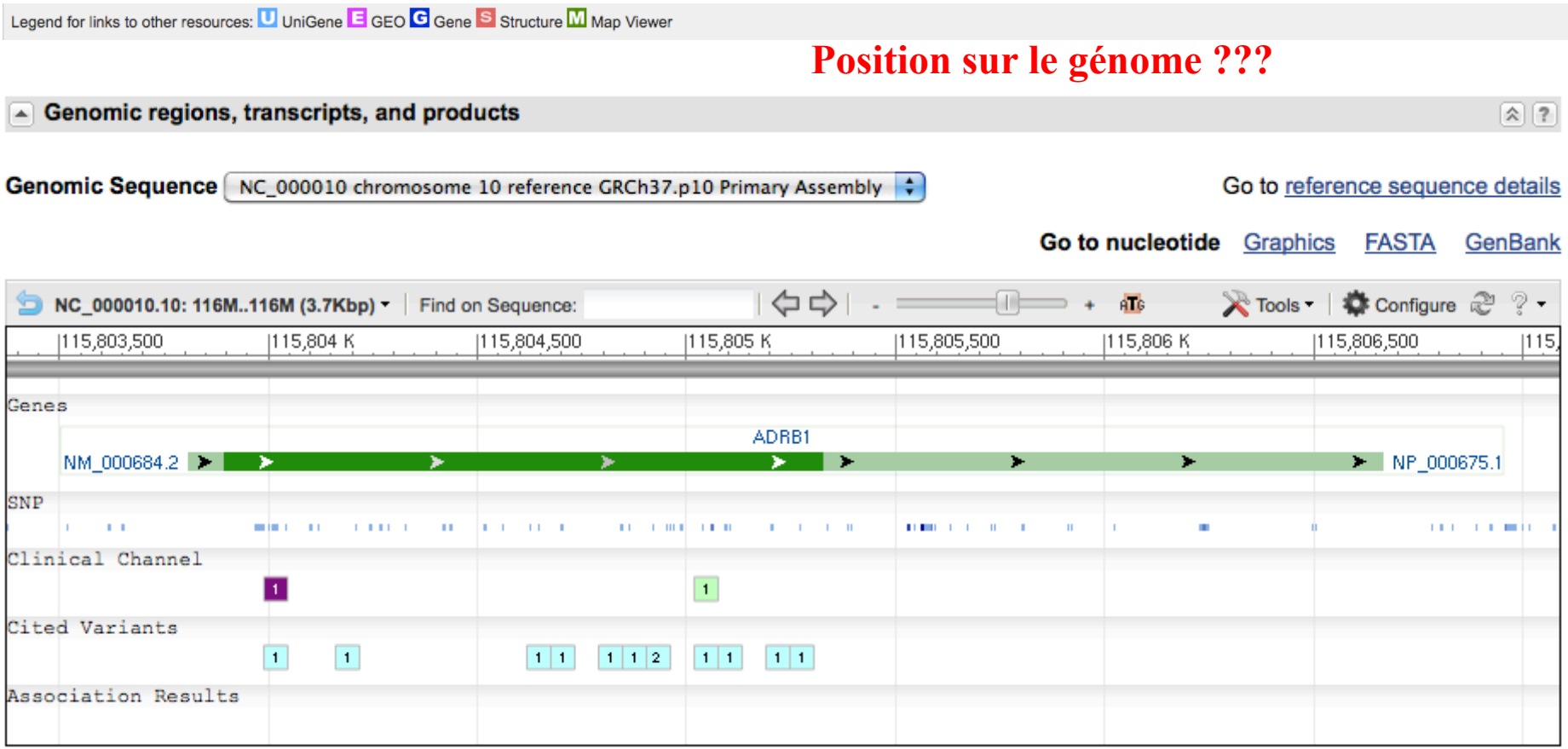
Entrez Gene Info

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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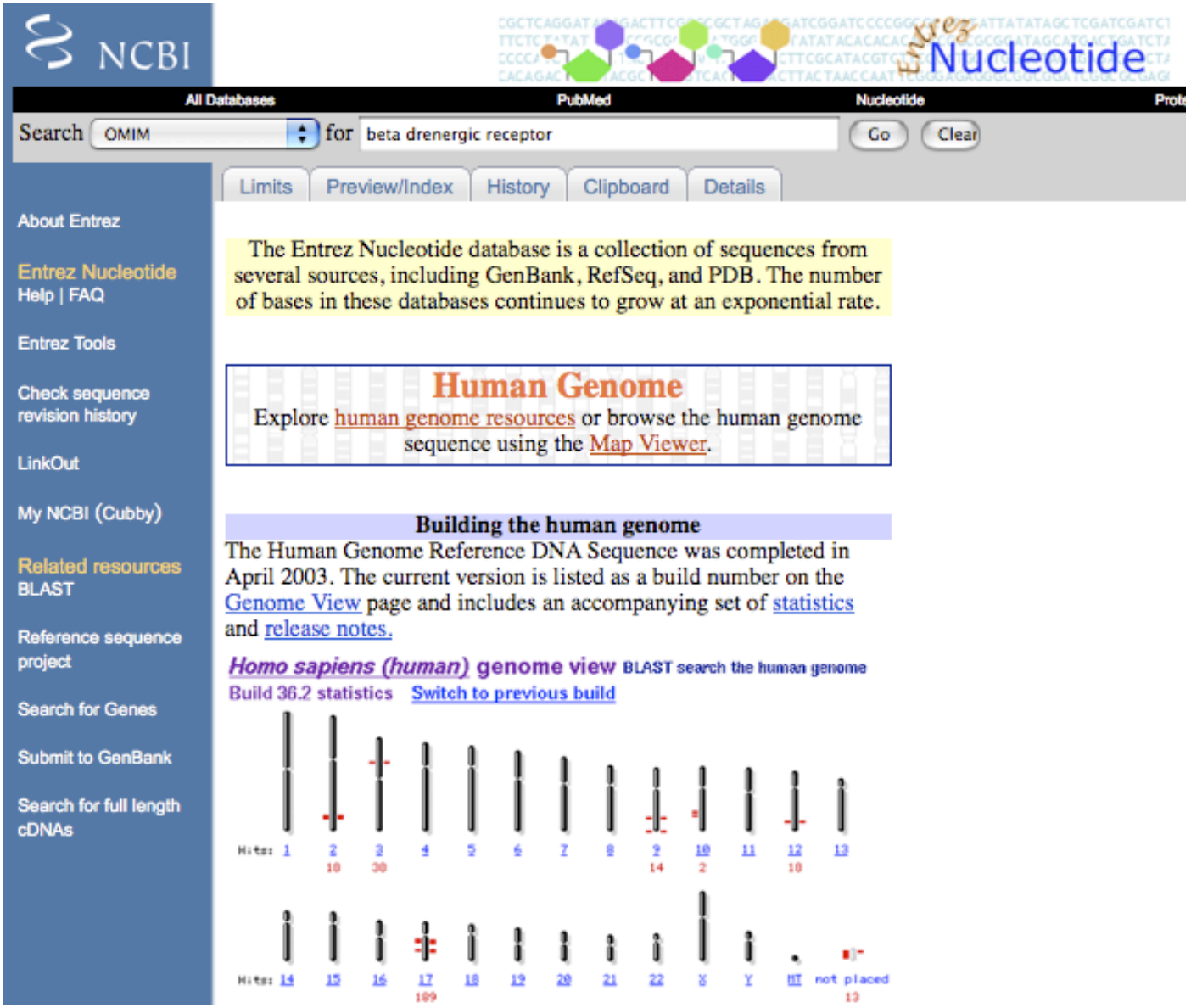
3. Les pathologies héréditaires



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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

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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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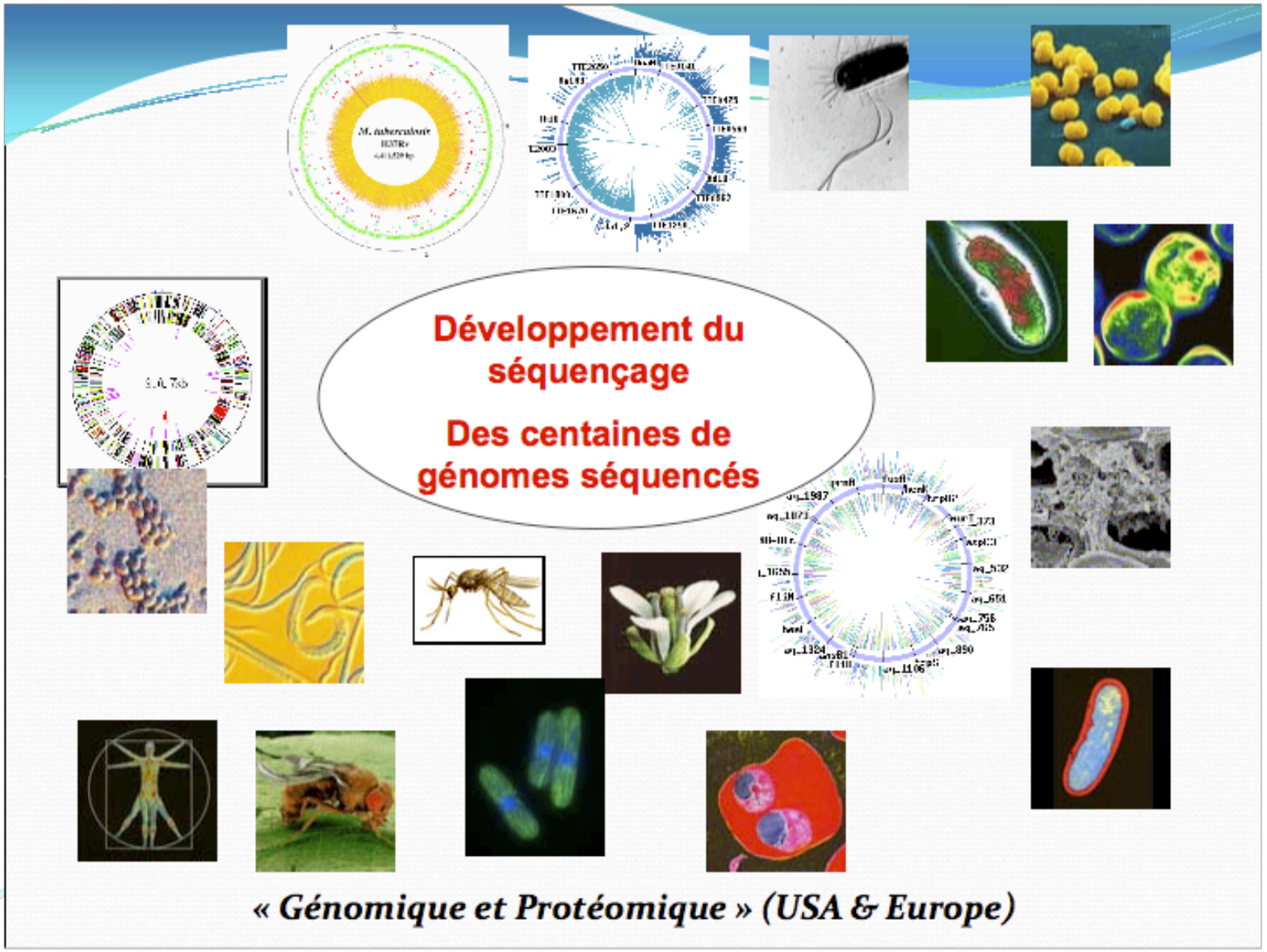
4. Les analyses génomiques



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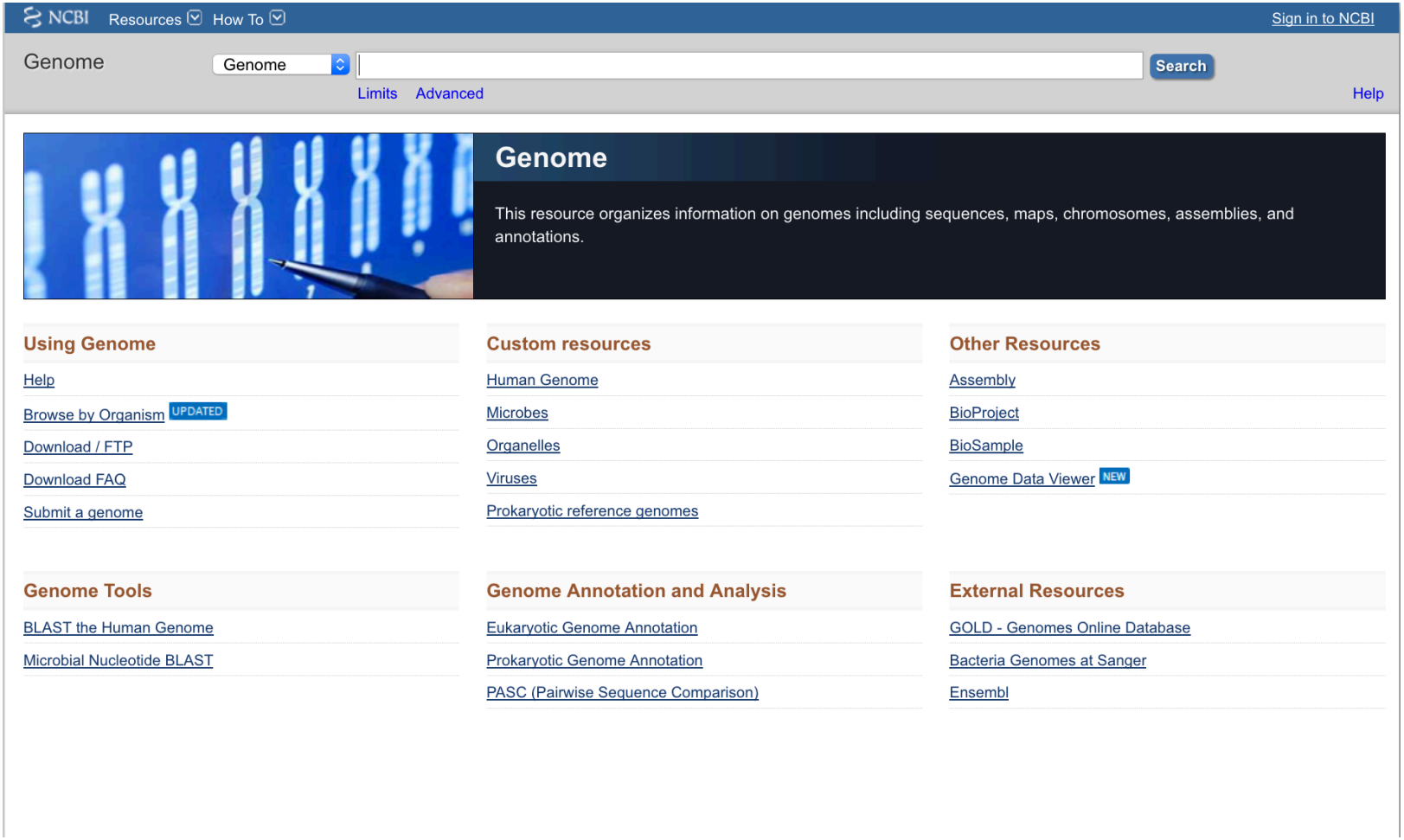
4. Les analyses génomiques



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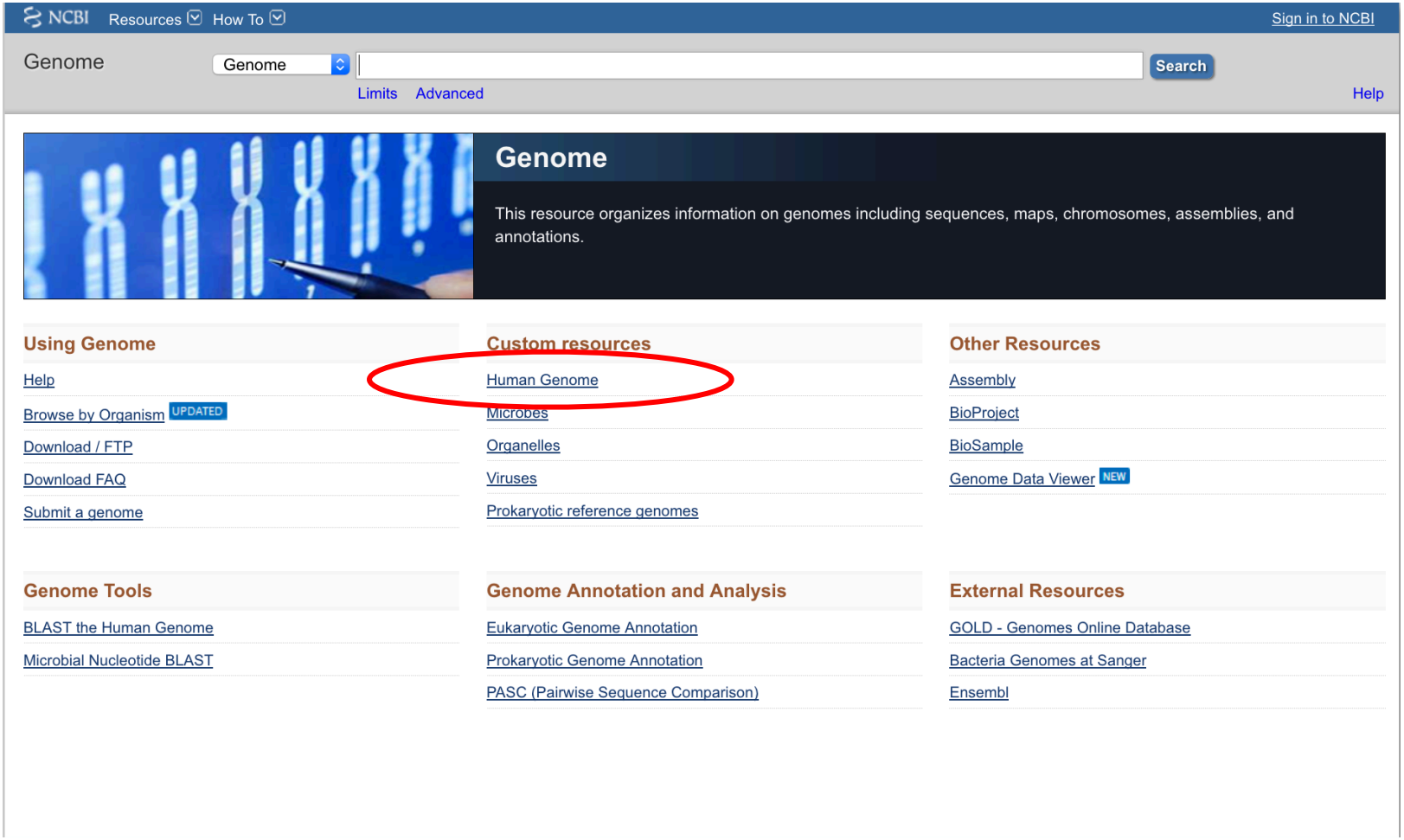
4. Les analyses génomiques



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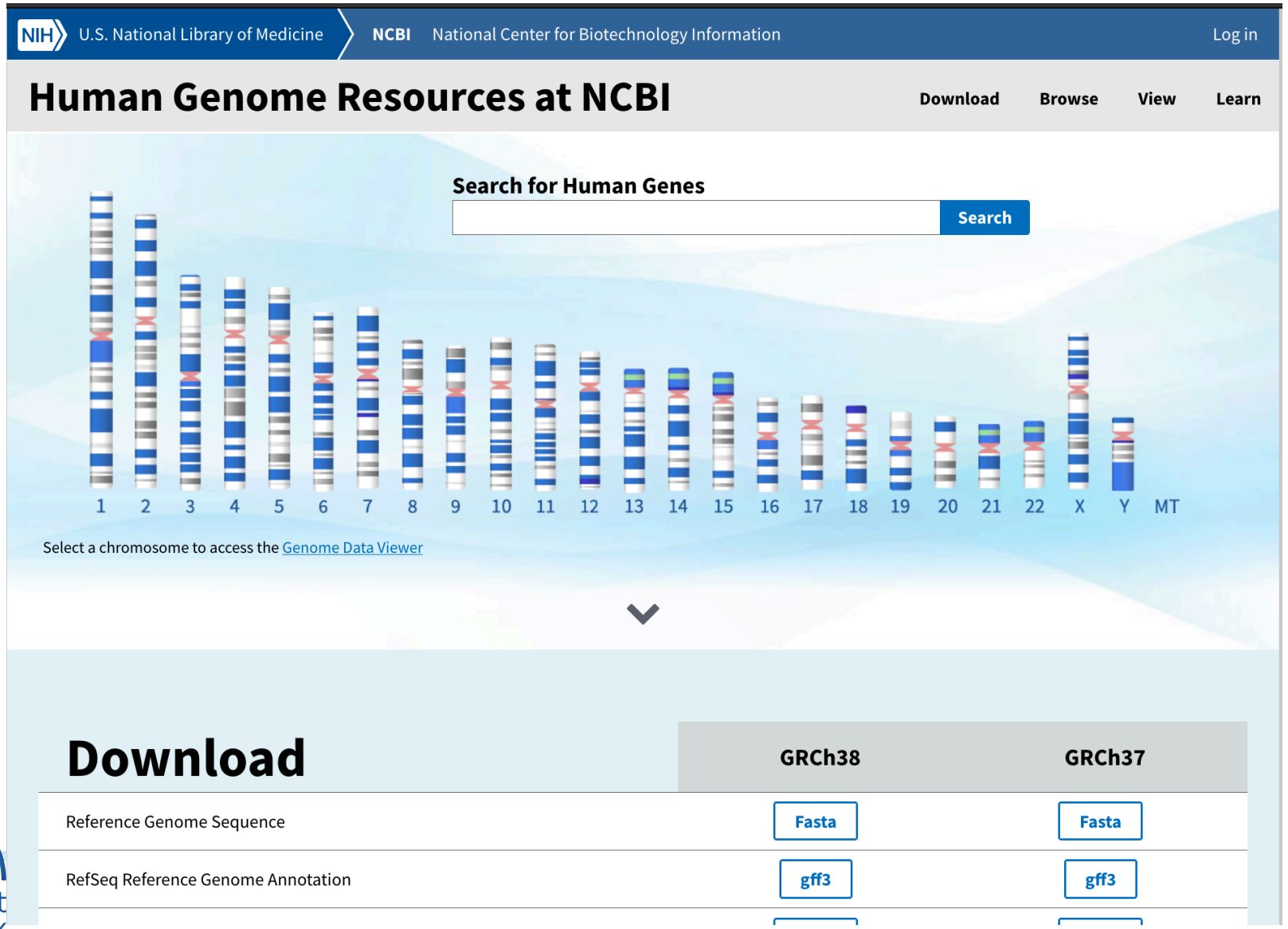
4. Les analyses génomiques



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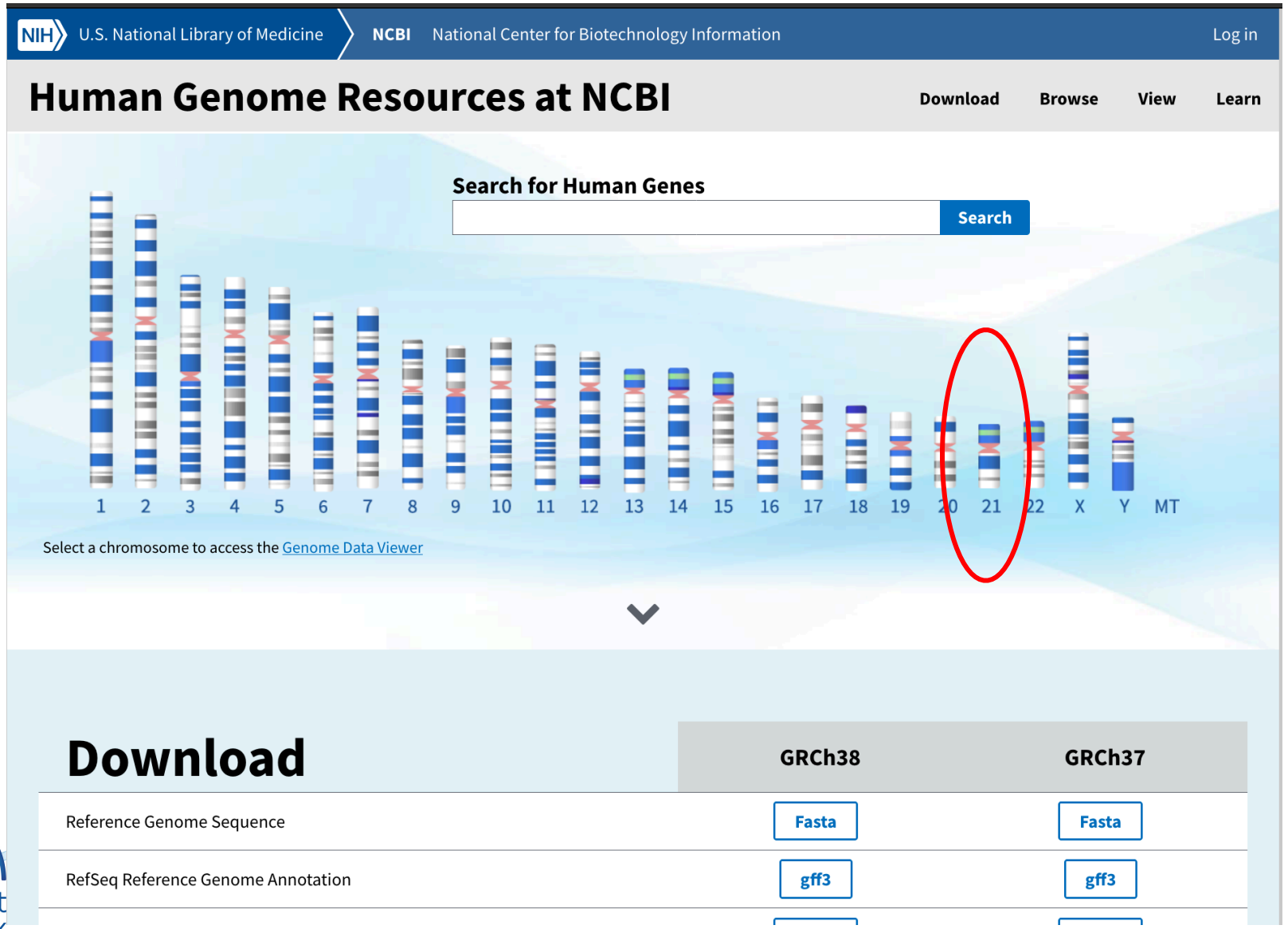
4. Les analyses génomiques



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4. Les analyses génomiques

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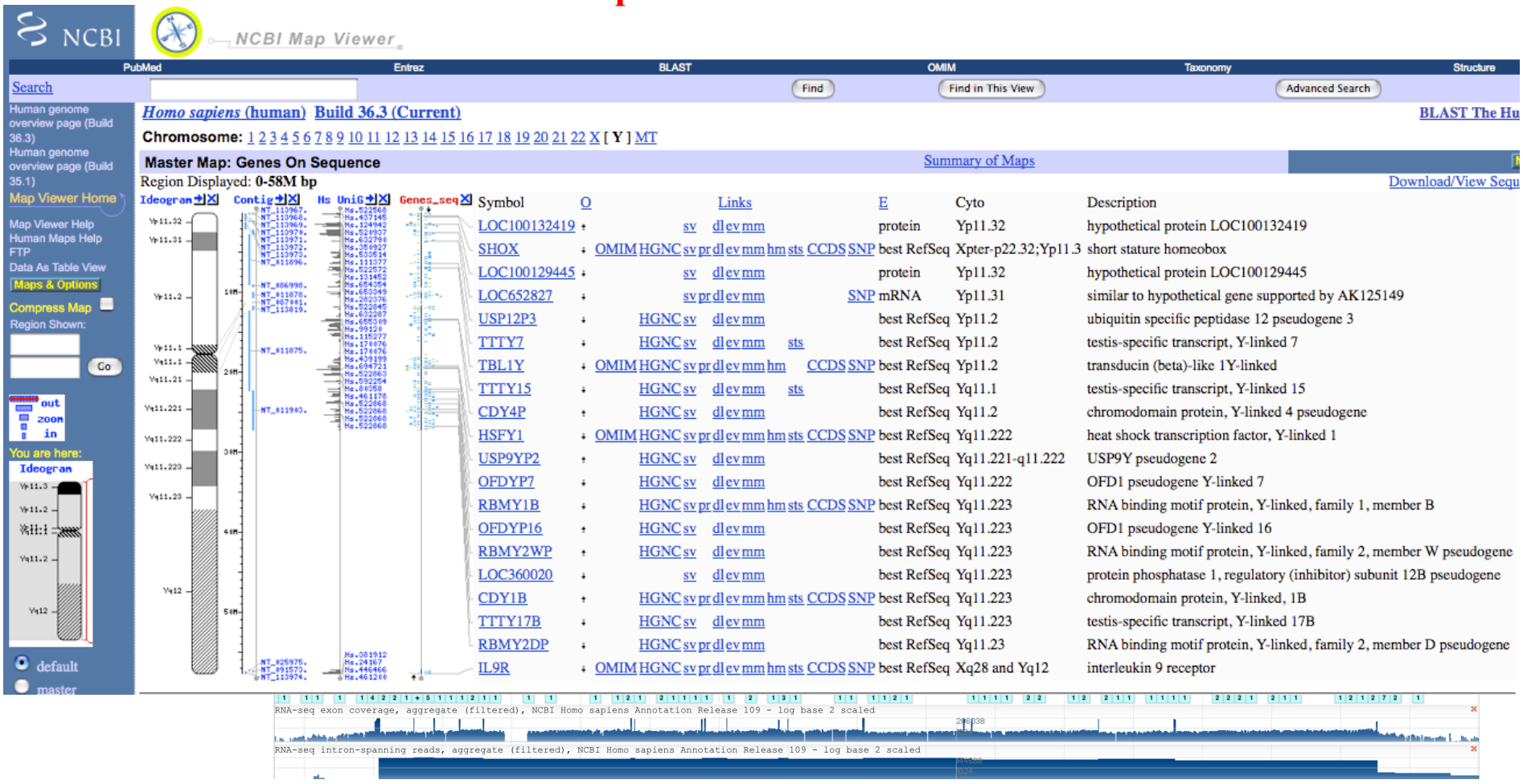
4. Les analyses génomiques

Ici un Map Viewer sur le chromosome Y.



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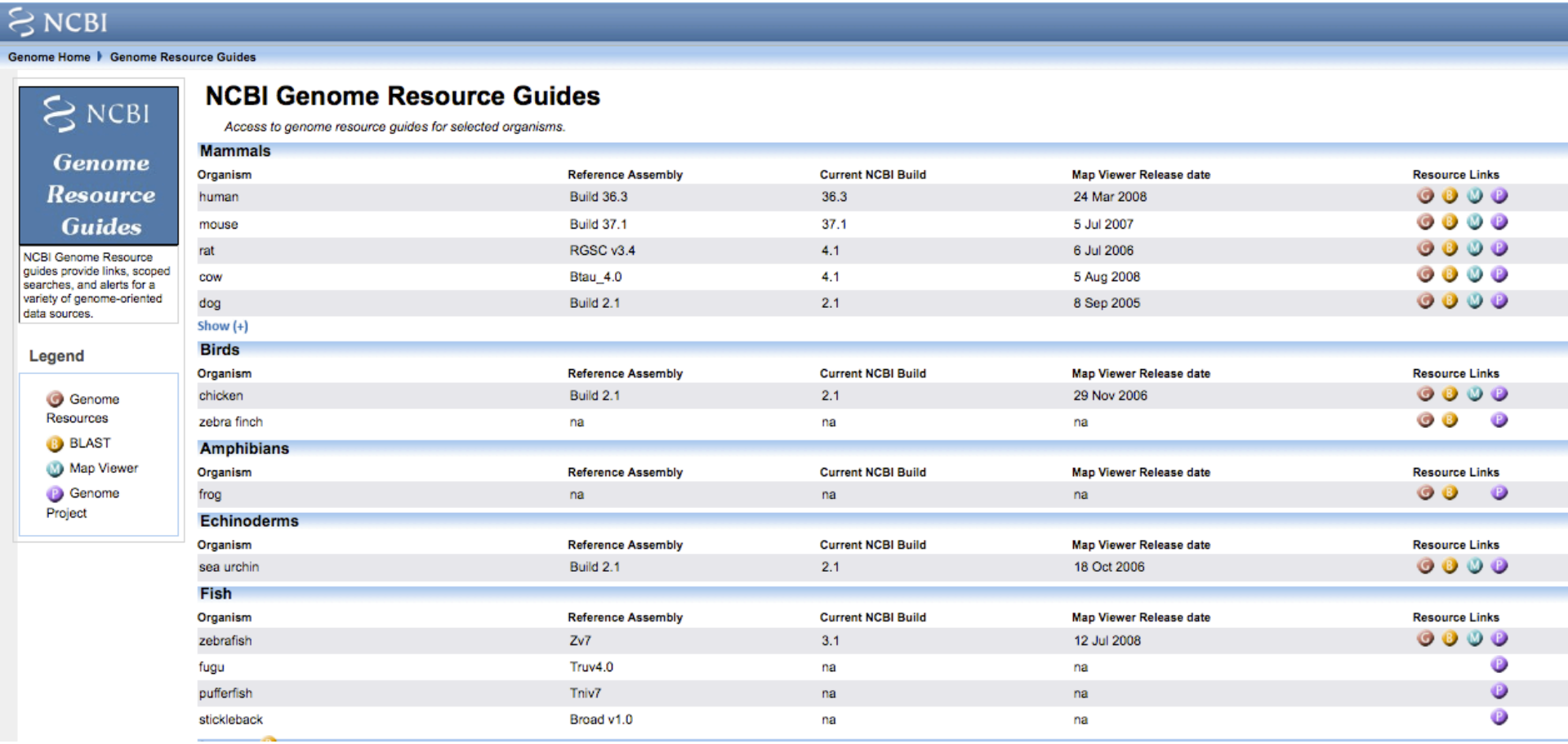
4. Les analyses génomiques



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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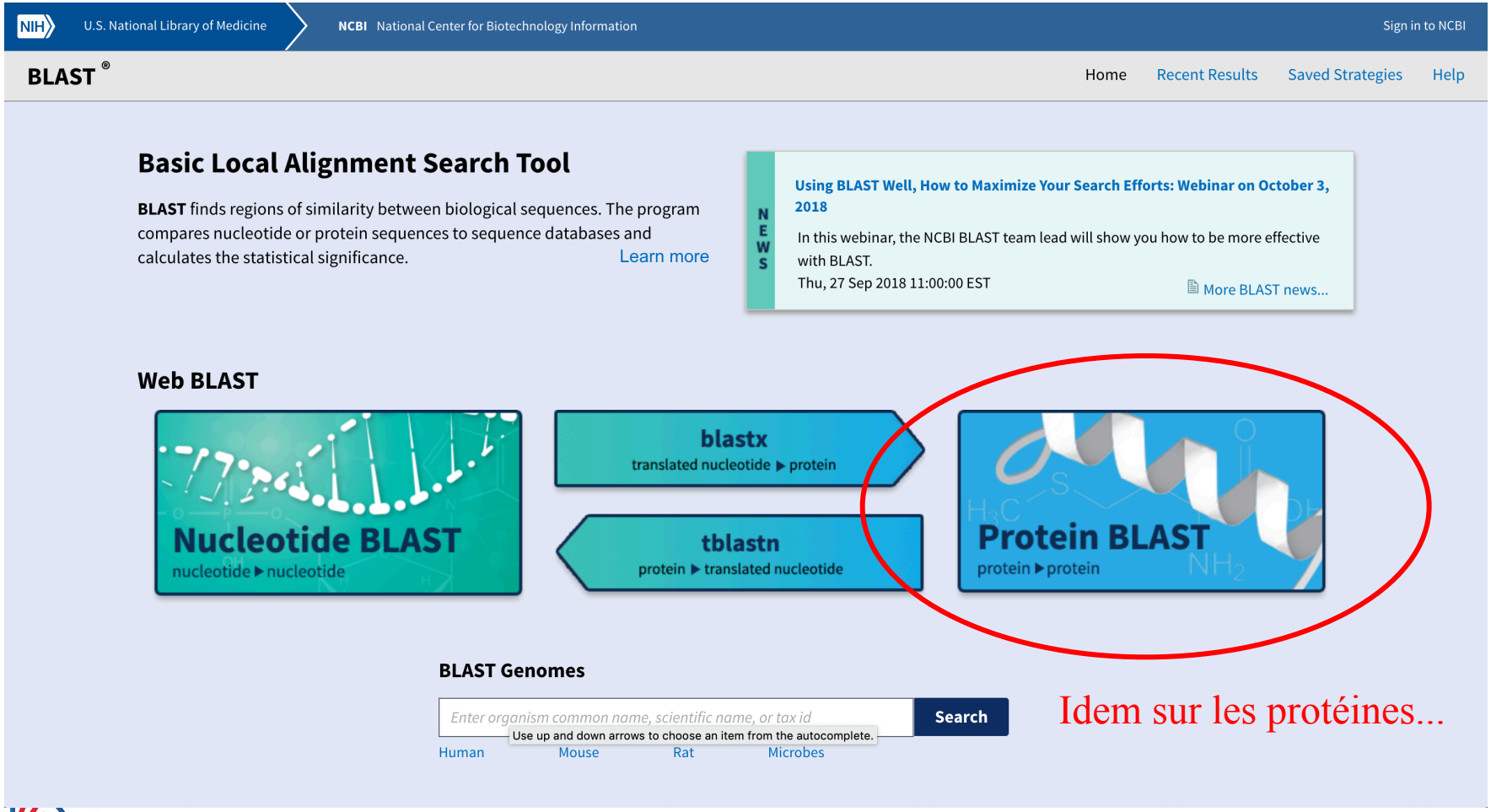
5. Les analyses protéiques



Idem sur les protéines...

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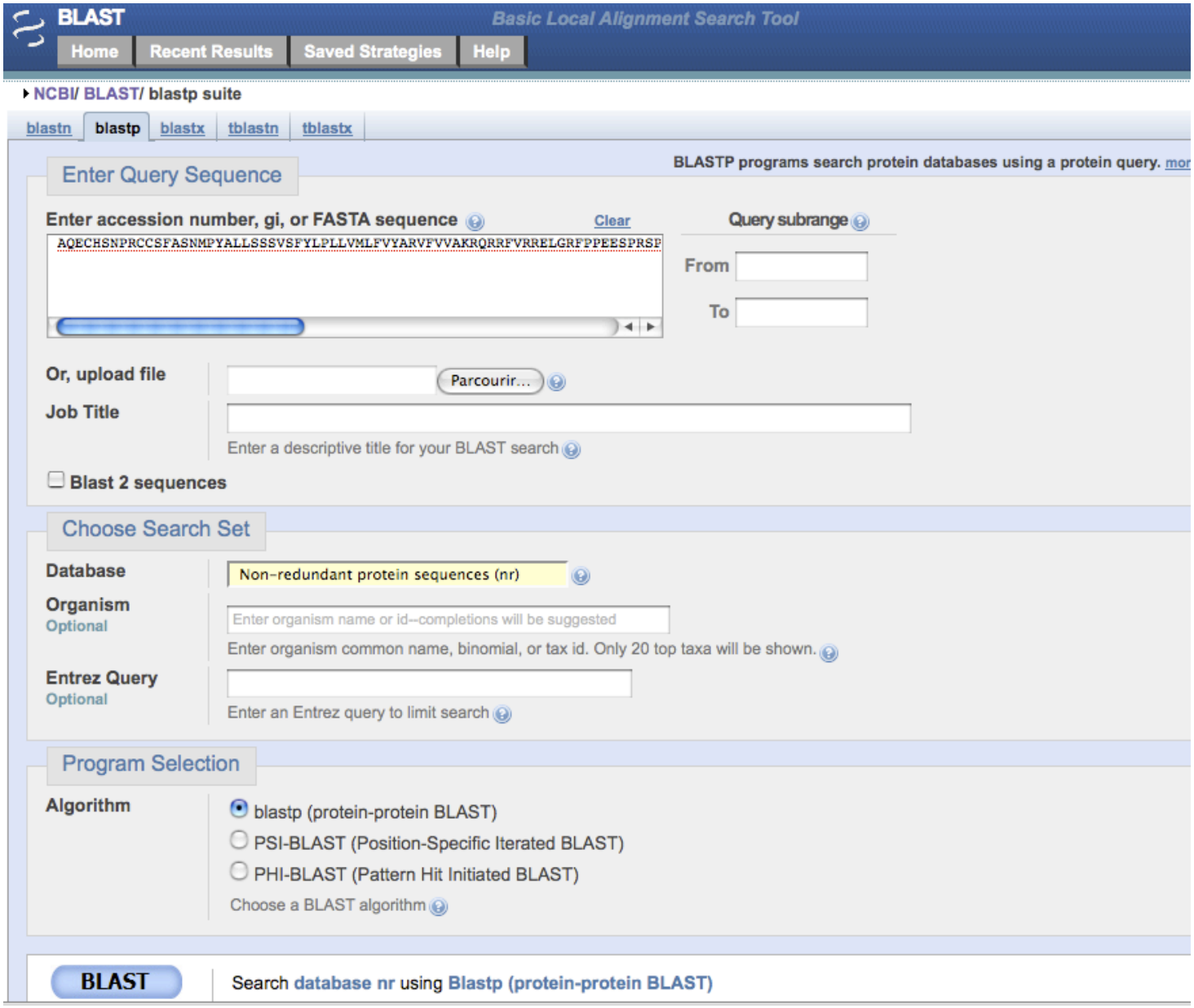
5. Les analyses protéiques



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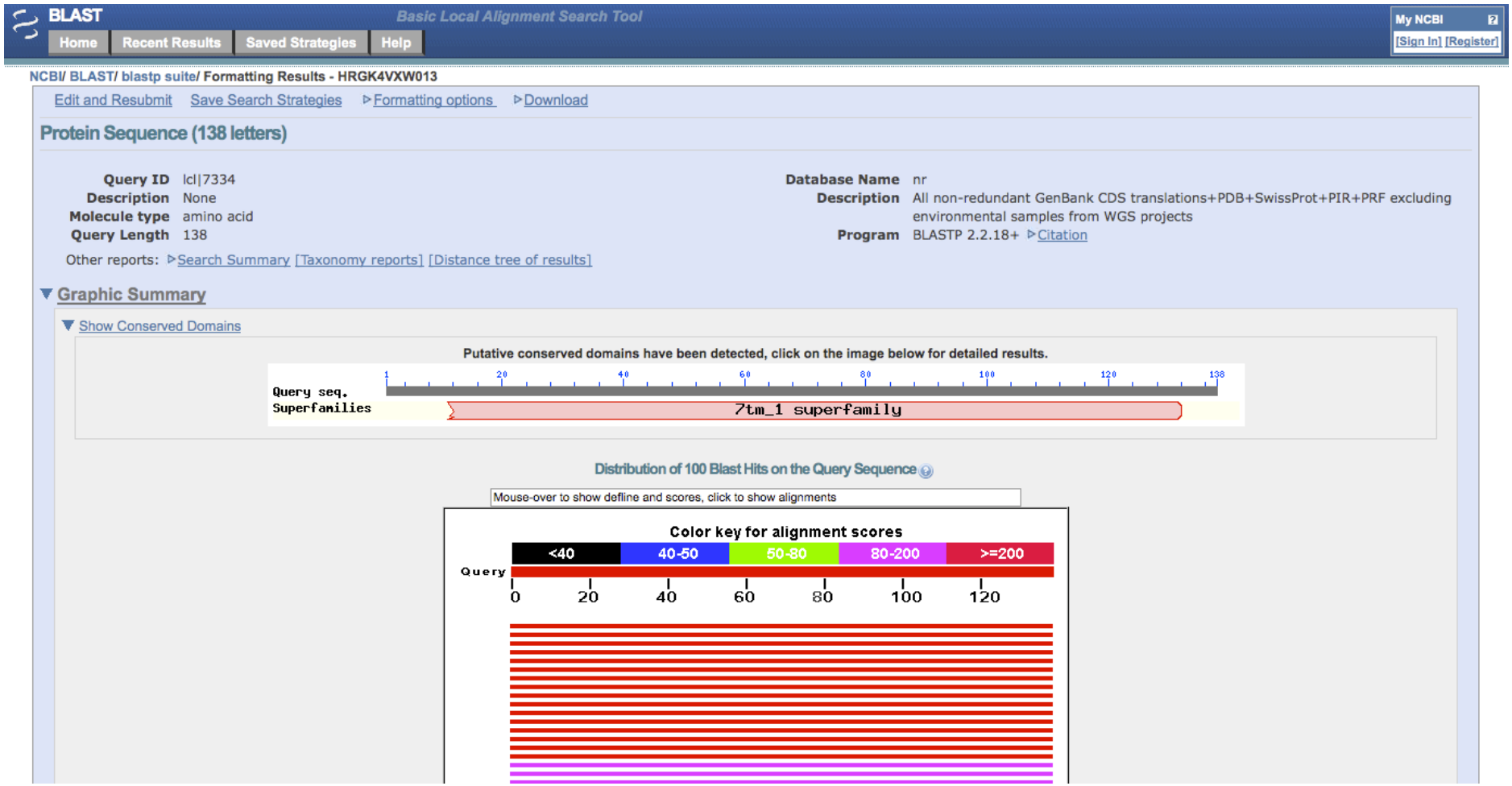
5. Les analyses protéiques



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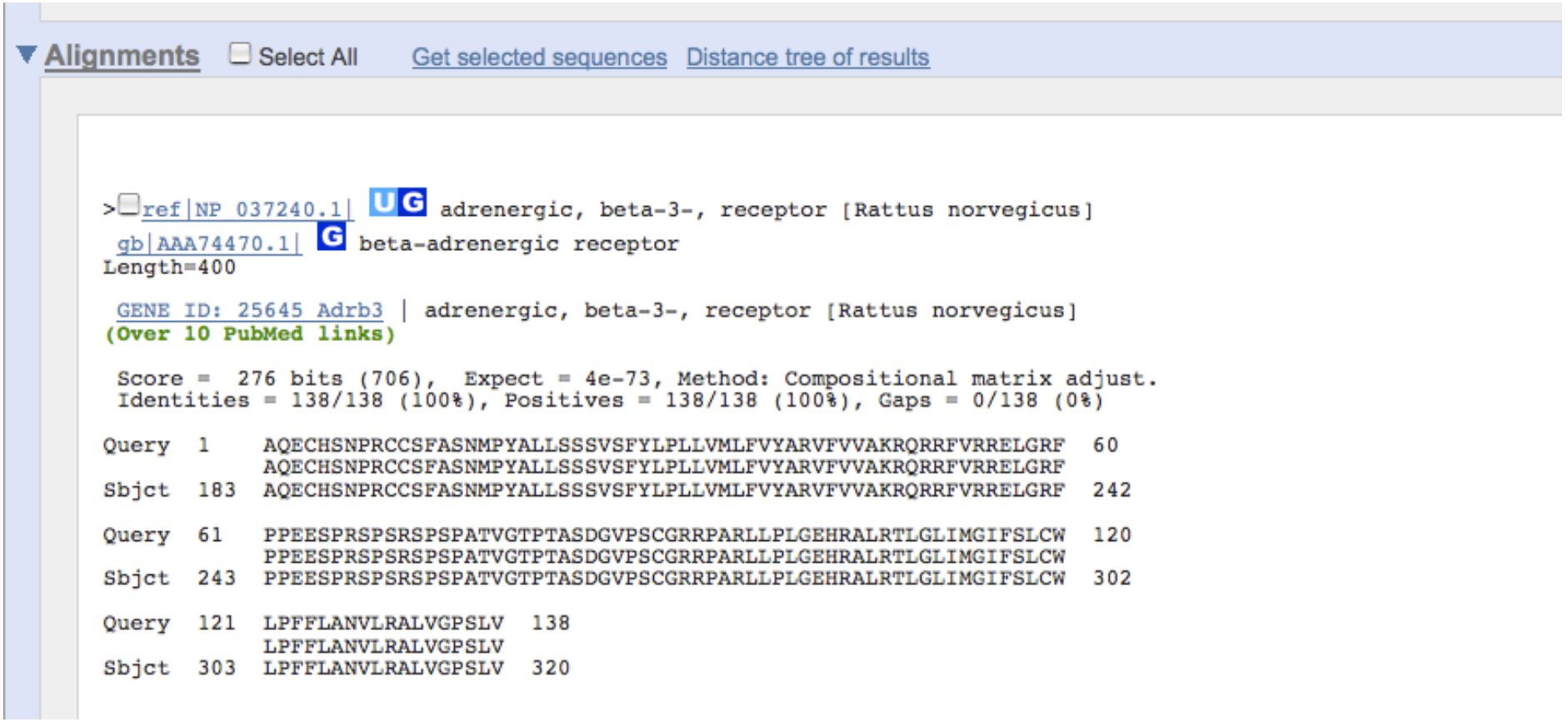
5. Les analyses protéiques



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%)

```
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            AQECHSNPRCCSFASNMPYALLSSSVSFYLPLLVMLFVYARVFVVAKRQRRFVRRELGRF
Sbjct  183  AQECHSNPRCCSFASNMPYALLSSSVSFYLPLLVMLFVYARVFVVAKRQRRFVRRELGRF  242

Query  61   PPEESPRSPSRSPSPATVGTPTASDGVPSCGRRPARLLPLGEHRALRTLGLIMGIFSLCW  120
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Sbjct  243  PPEESPRSPSRSPSPATVGTPTASDGVPSCGRRPARLLPLGEHRALRTLGLIMGIFSLCW  302

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

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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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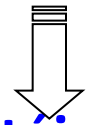
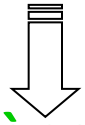
Physiologie « classique »

Fonction



Protéines

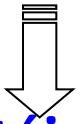


Gènes

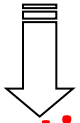
Vision restreinte

Physiologie « inverse »

Gènes



Protéines



Fonction

Vision globale

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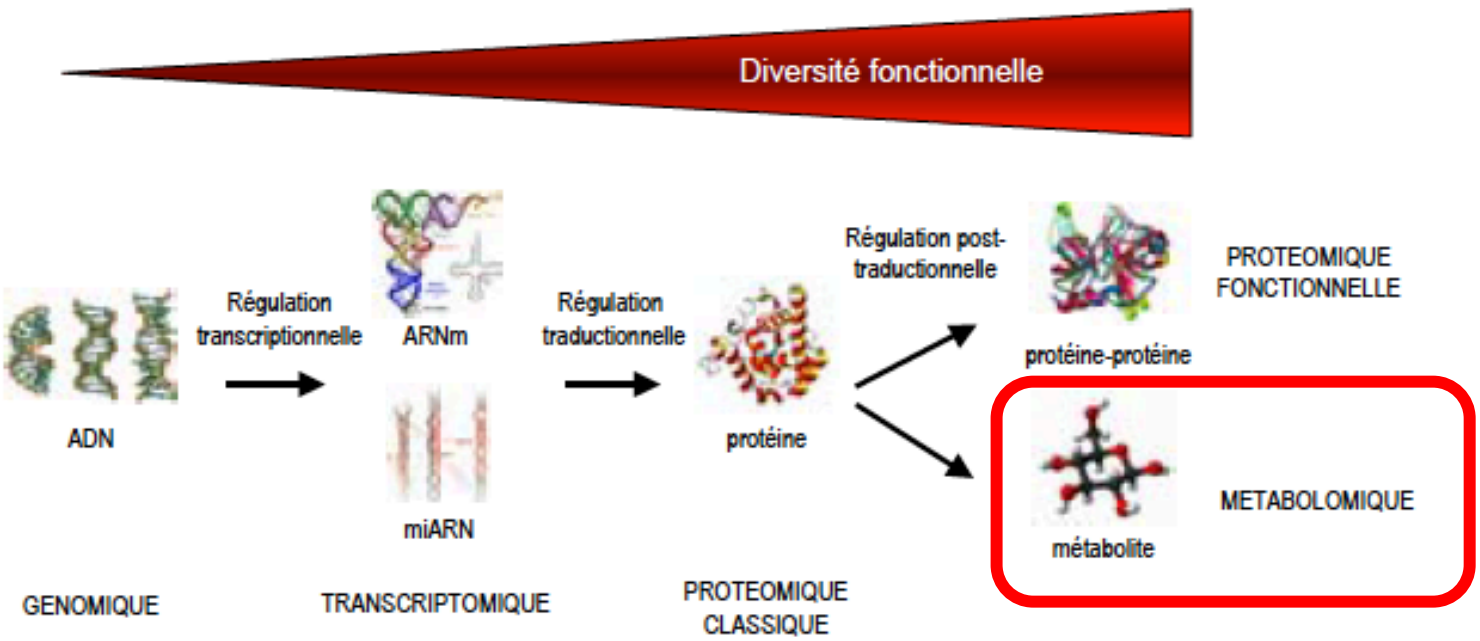
Intérêt de la recherche « OMICS »

❑ 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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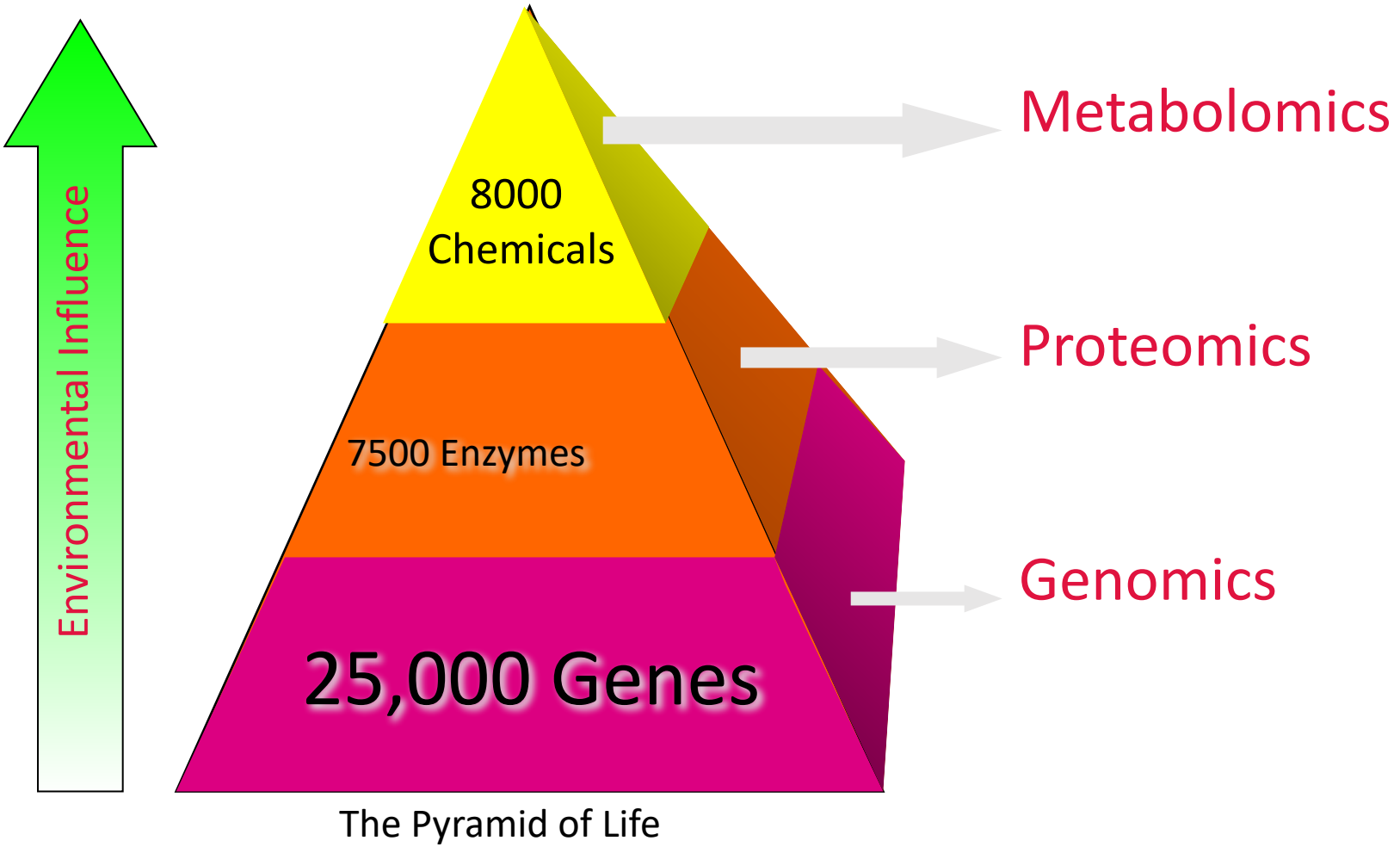

The Pyramid of Life

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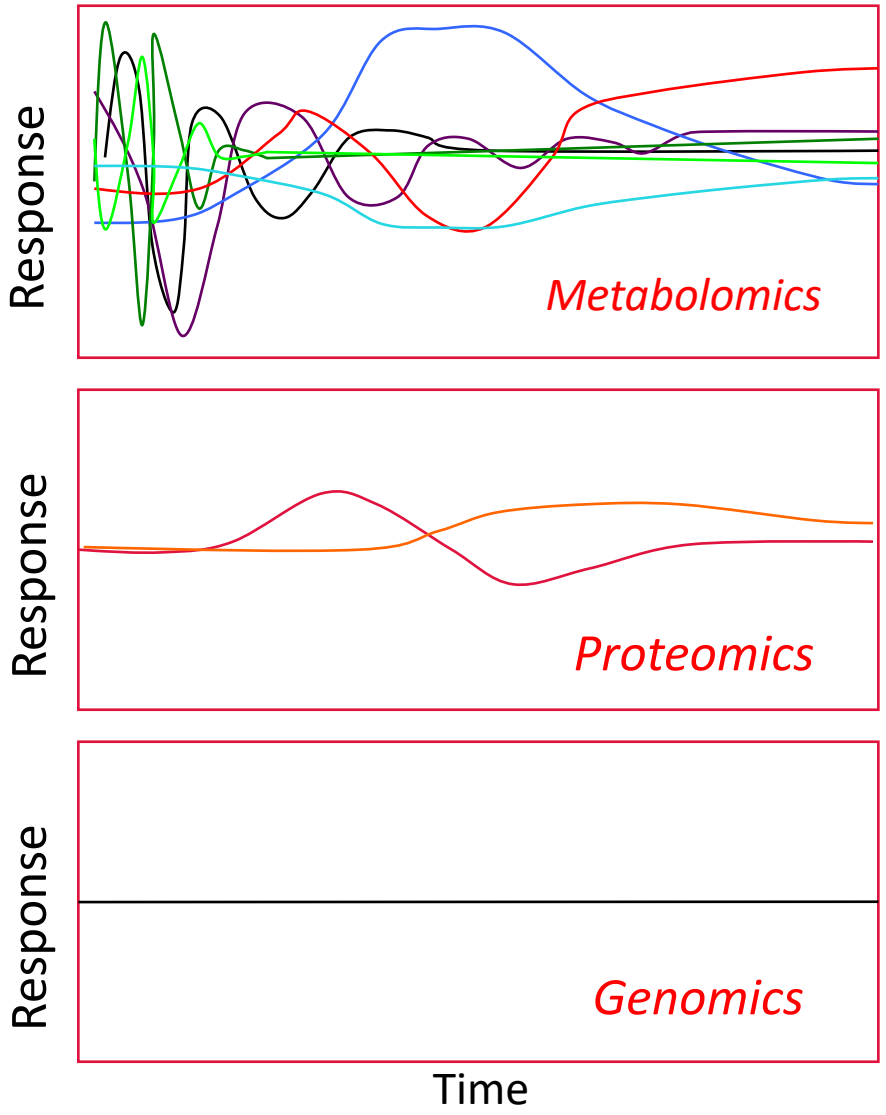

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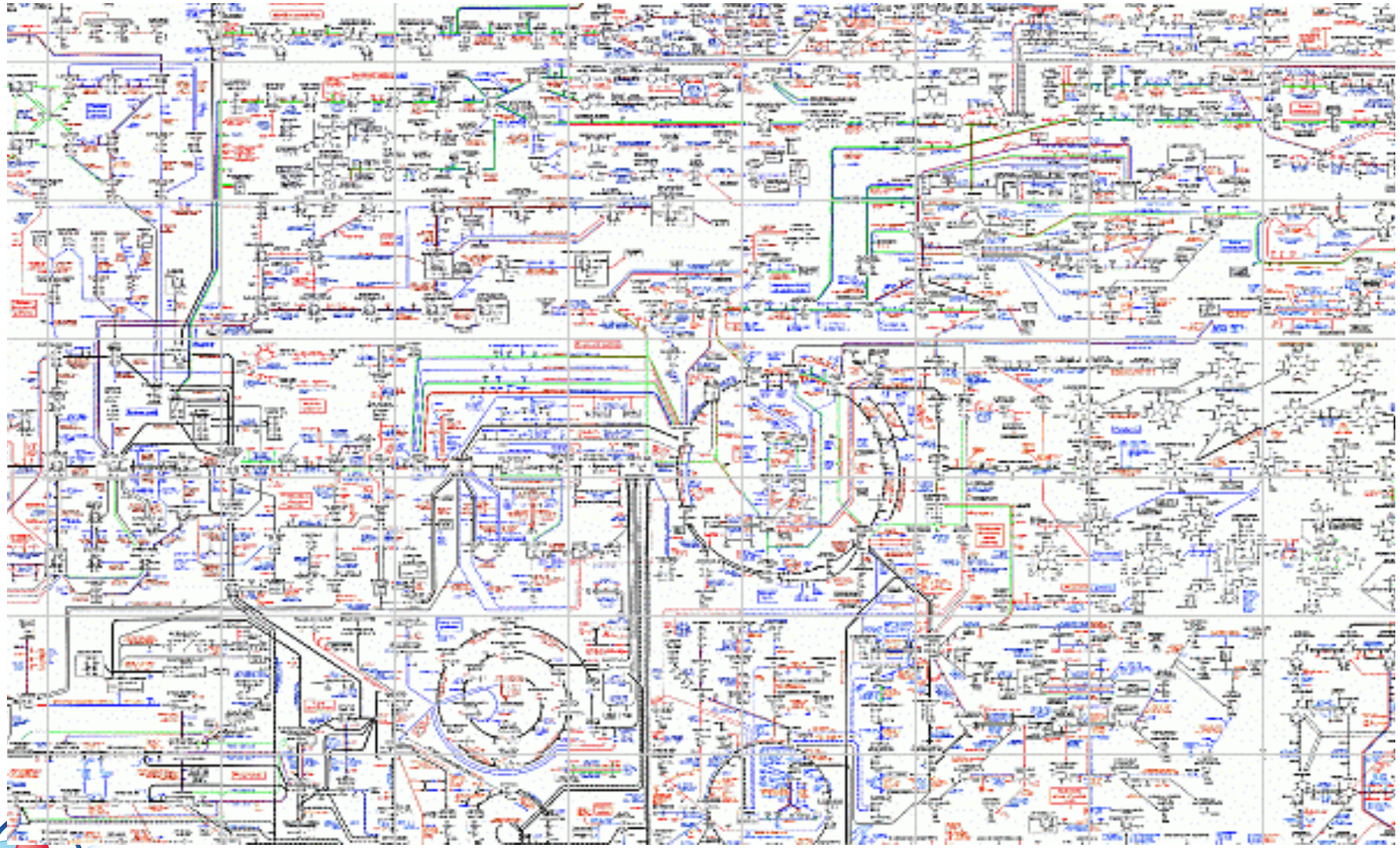

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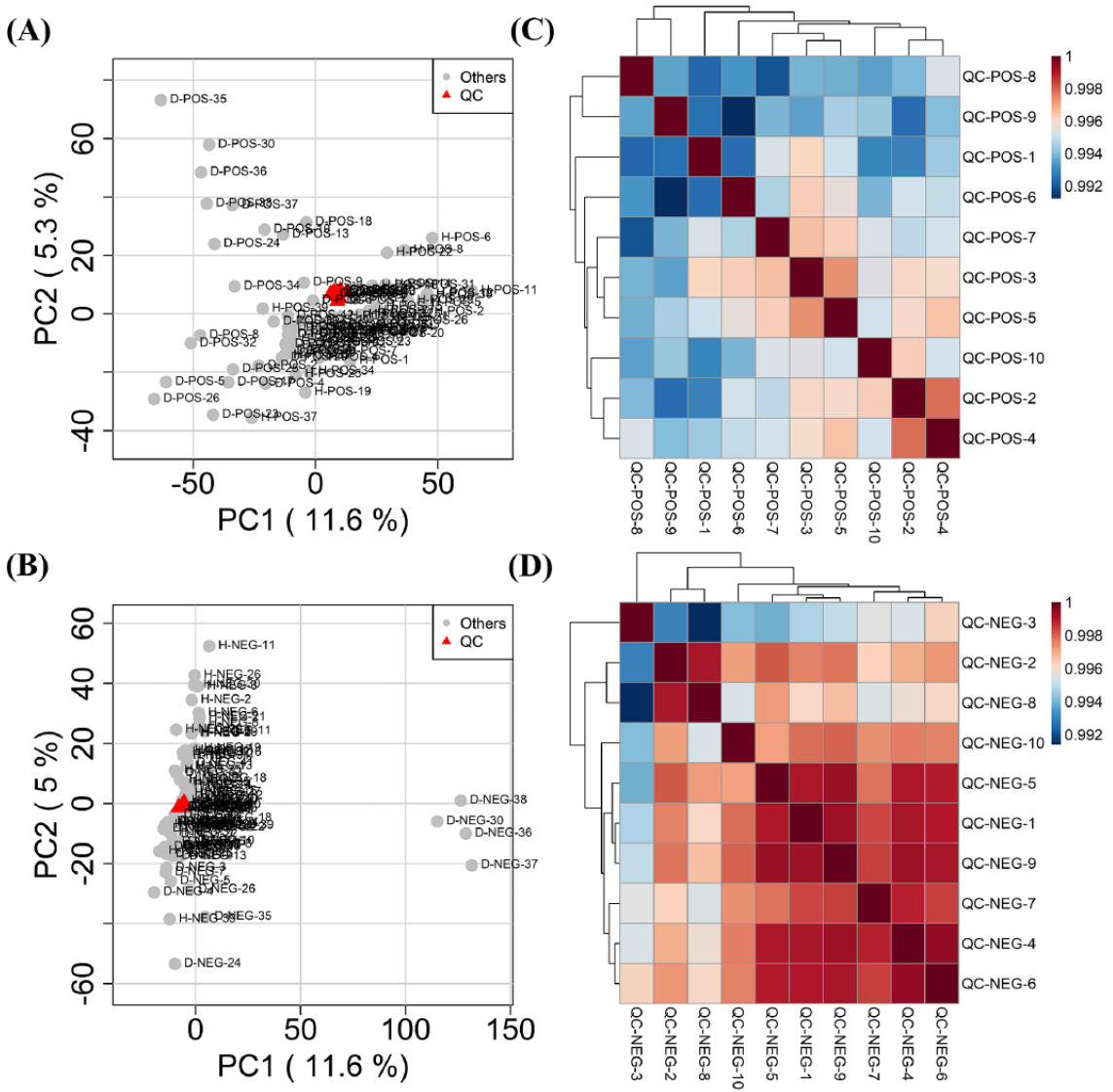

Fig. 1 PCA score plots and correlation analysis of QC samples in ESI+ (**A, C**) and ESI– (**B, D**) scan modes

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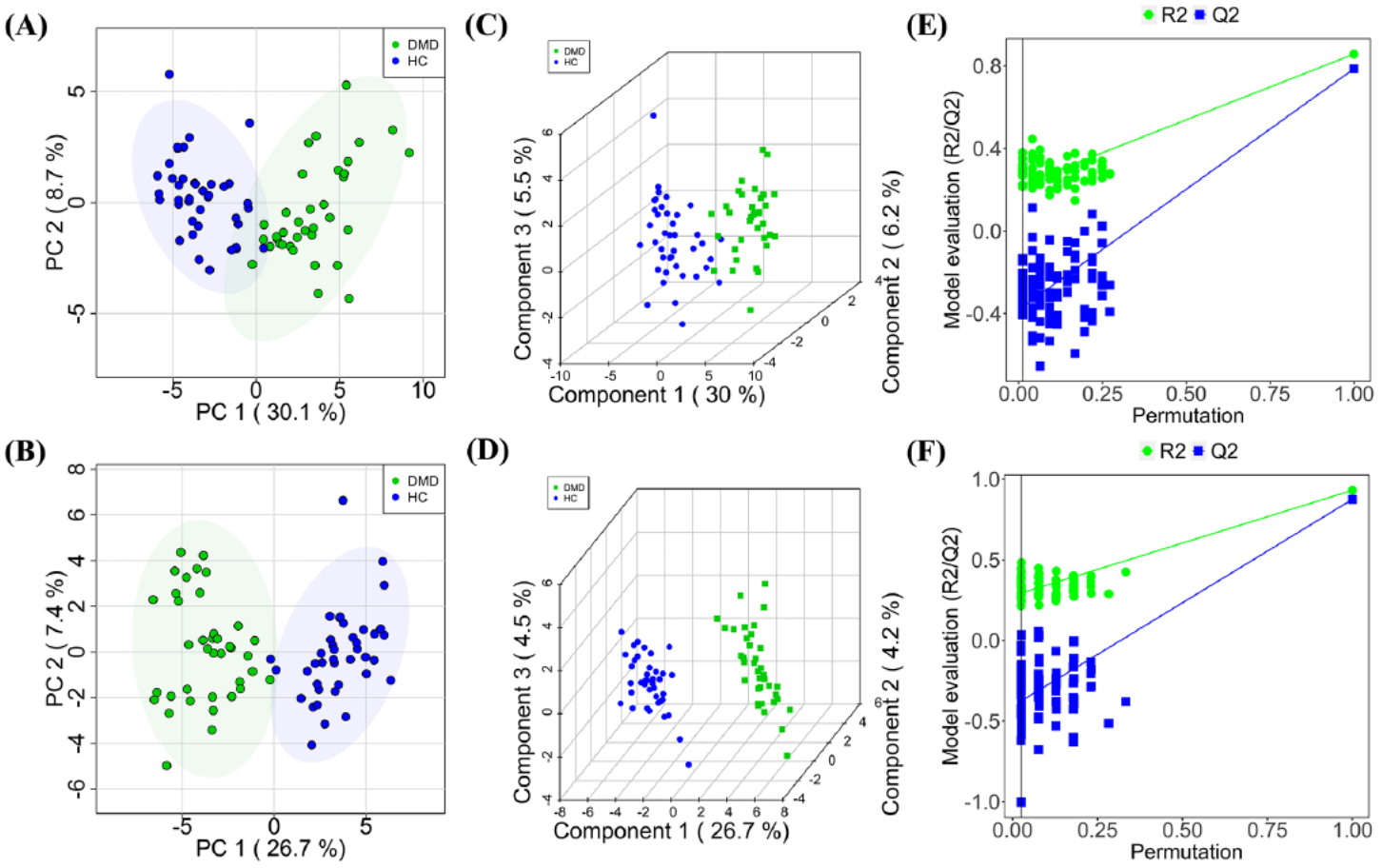

Fig. 2 Plots of PCA (**A, B**) and PLS-DA scores (**C, D**) with permutation testing (**E, F**) for healthy controls and DMD patients comparison in the ESI+and ESI−scan modes

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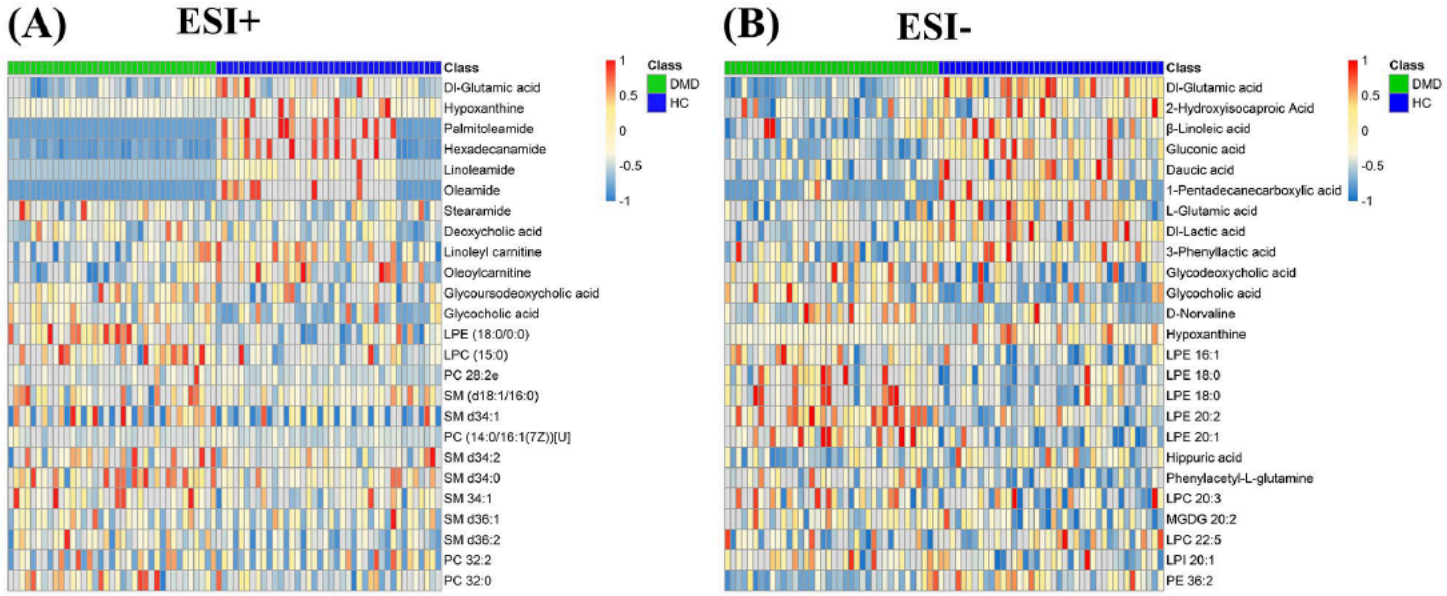

Fig. 3 Differential metabolite heat maps in ESI+ (**A**) and ESI− (**B**) scan modes. The columns represent samples, the rows represent metabolites, and the relative content of the metabolites is displayed by color

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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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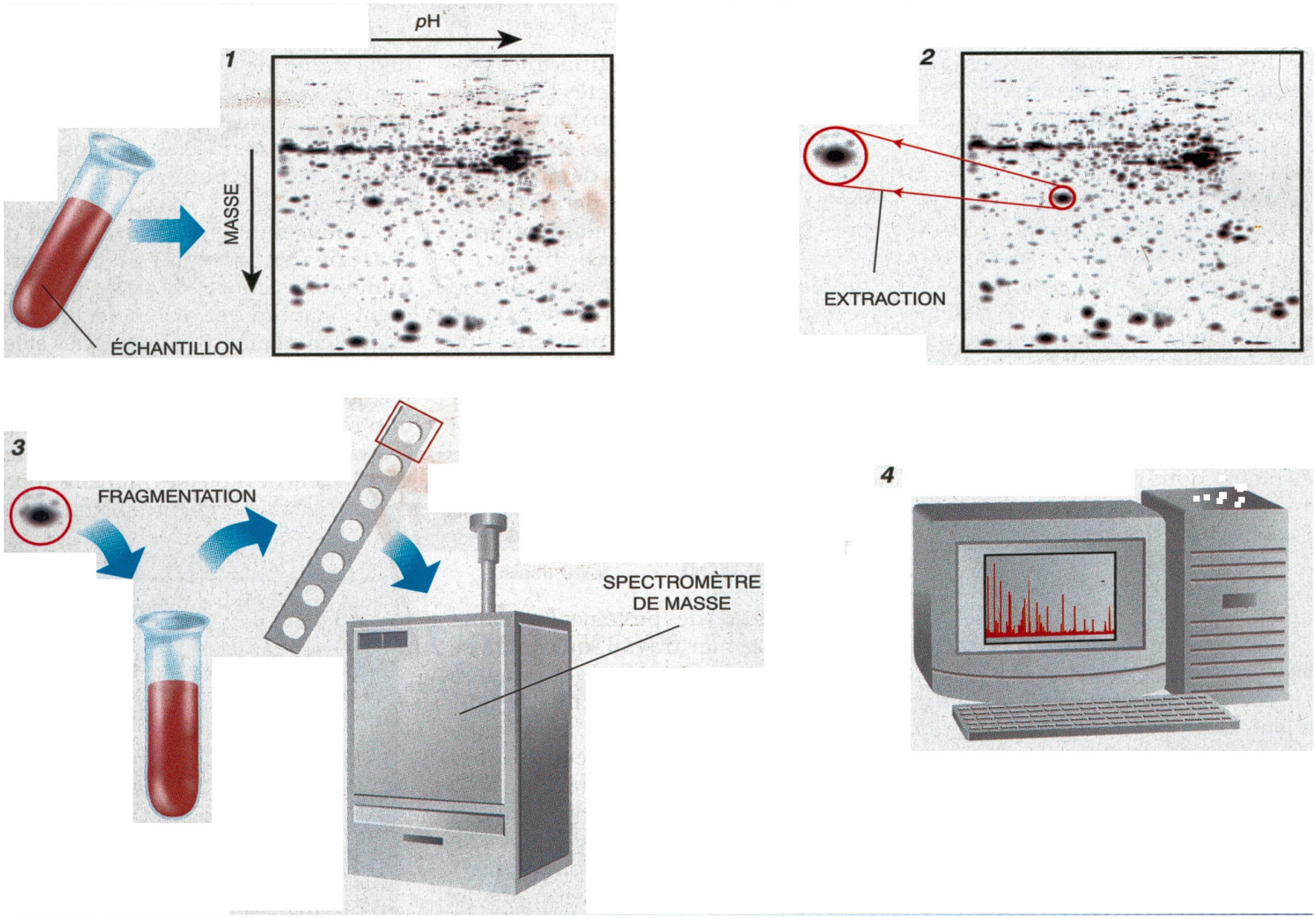

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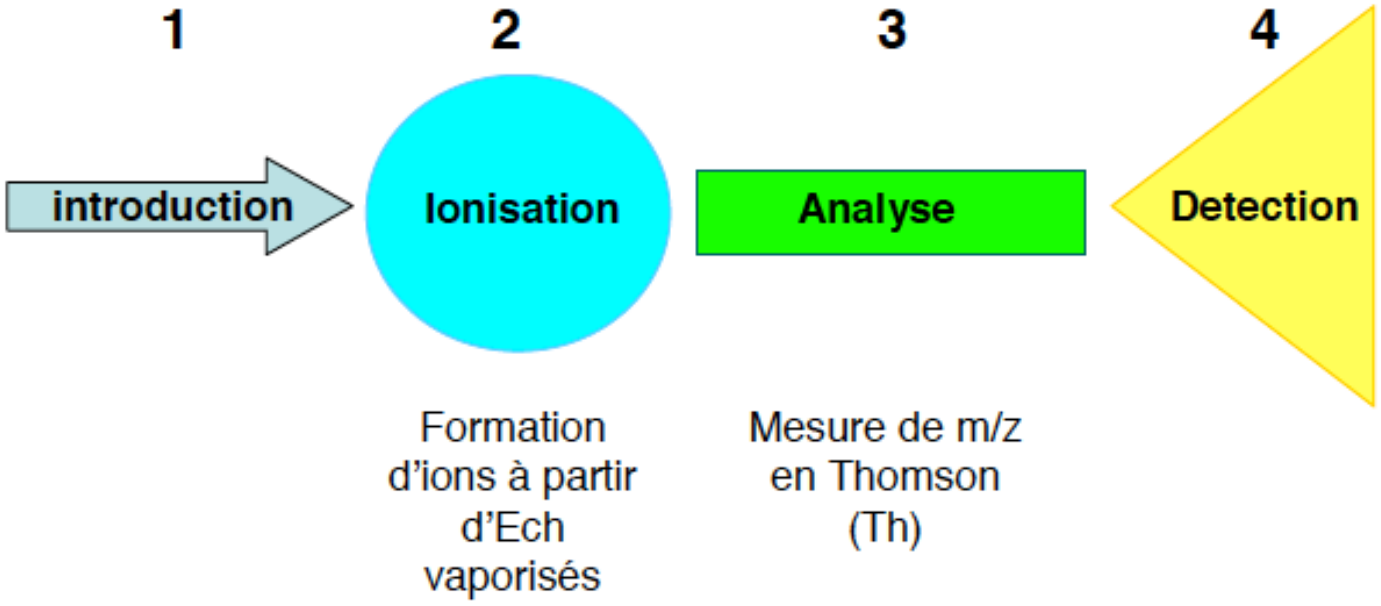
Le spectromètre de masse se compose donc de quatre parties :

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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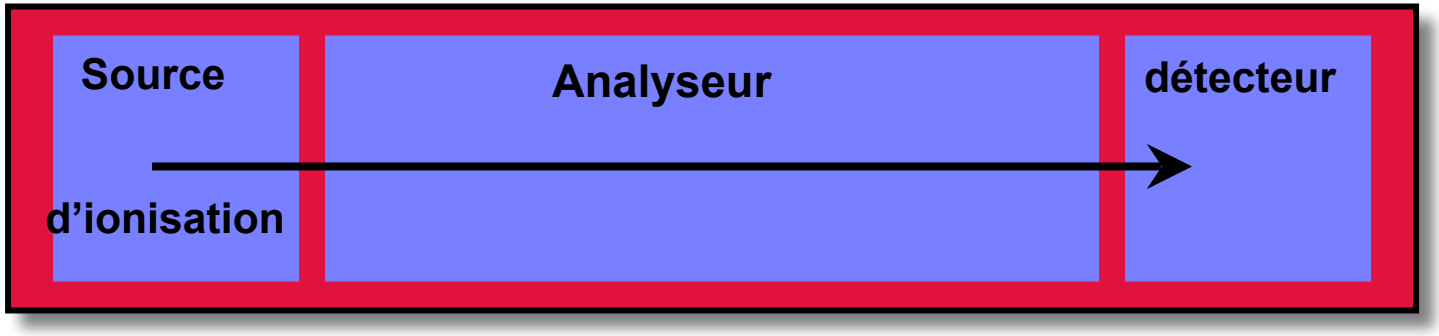
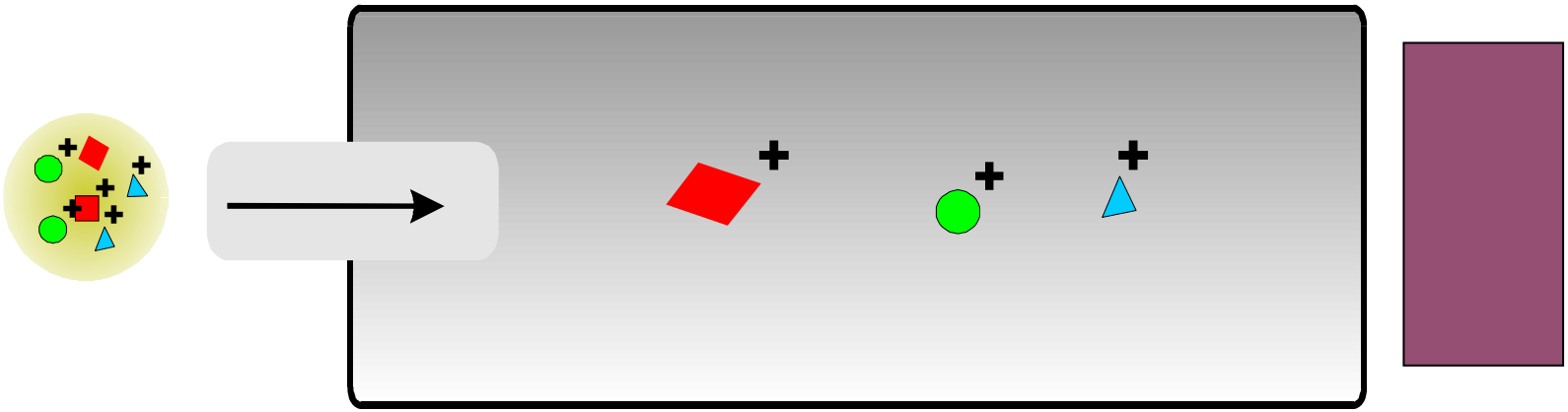


L'analyseur de masse

Détecteur



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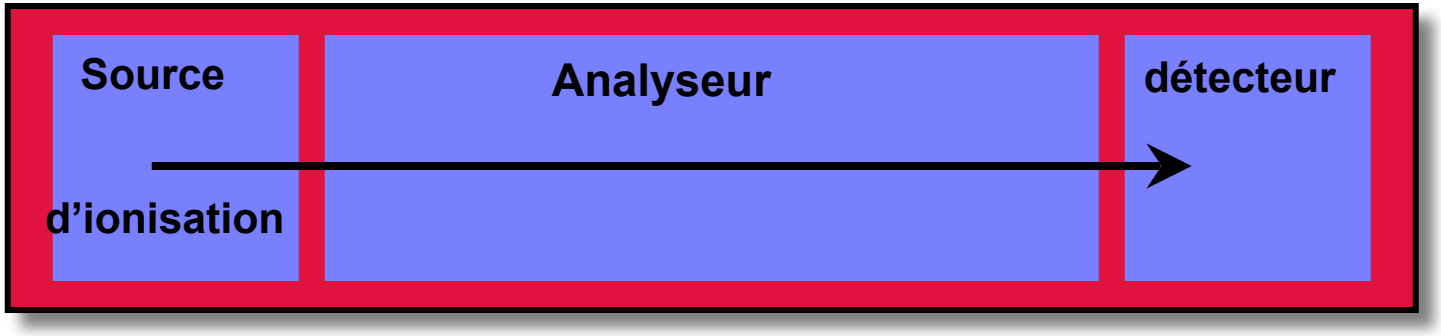
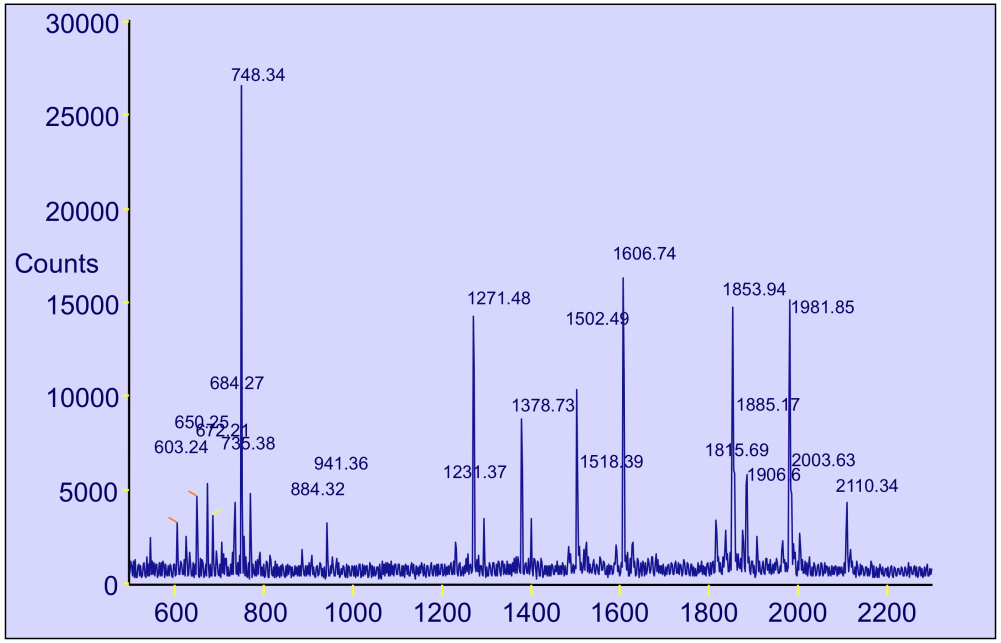


Détecteur



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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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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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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-2H_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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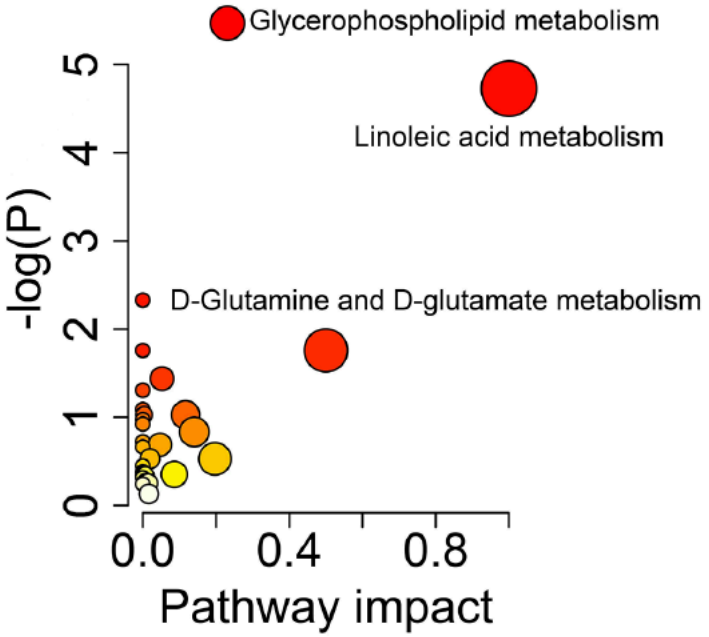

Fig. 5 Bubble diagram of metabolic pathways between DMD and HC groups

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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