



M1 SM THORAX ED TG: Recherche in silico.

Gilles Toumaniantz

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Team IIA

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

1. Les analyses bibliographiques

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Search

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All Resources
Chemicals & Bioassays
Data & Software
DNA & RNA
Domains & Structures
Genes & Expression
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Homology
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Proteins
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NCBI Education
NCBI Help Manual
NCBI Handbook
Training & Tutorials
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Chemicals & Bioassays
Data & Software
DNA & RNA
Domains & Structures
Genes & Expression
Genetics & Medicine
Genomes & Maps

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PubMed Central
BLAST
Nucleotide
Genome
SNP

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GenBank
Reference Sequences
Gene Expression Omnibus
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Gene sequences and annotations used as references for the study of orthologs structure, expression, and evolution

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Collected information about gene loci

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Functional genomics studies

GEO Profiles

Gene expression and molecular abundance profiles

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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

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Museum, herbaria, and other biorepository collections

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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 sequence 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

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Bioactivity screening studies

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Privately and publicly funded clinical studies conducted around the world

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Human variations of clinical significance

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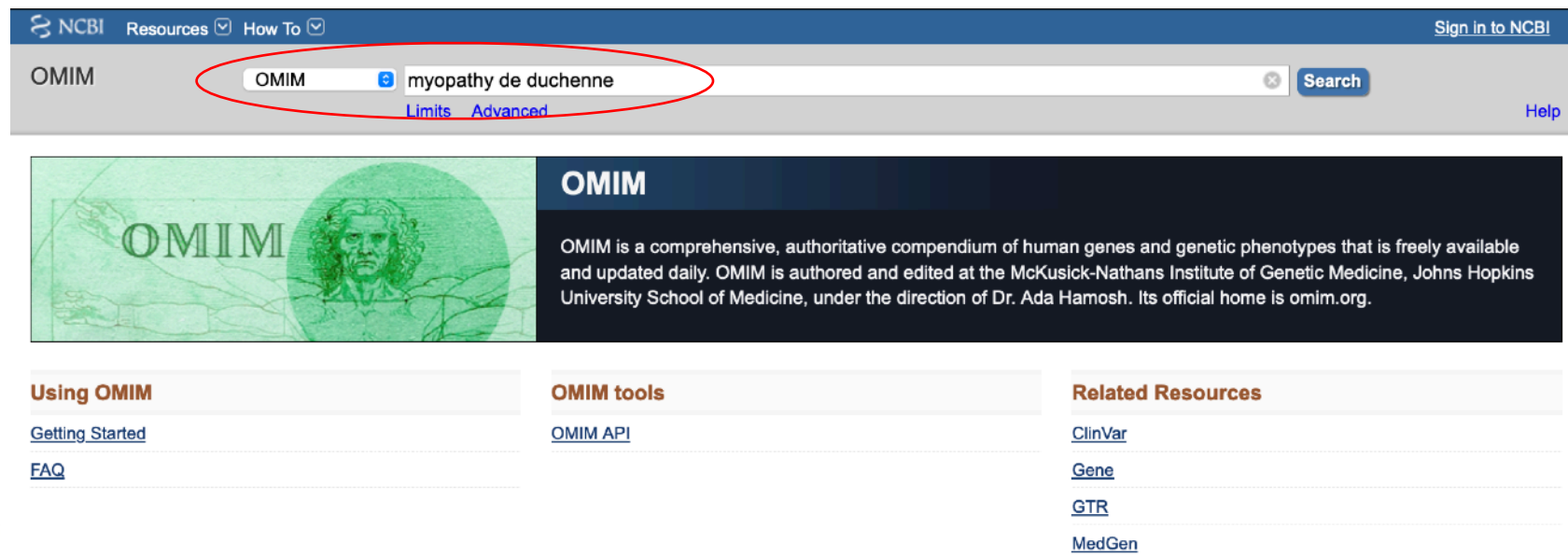
OMIM

Online mendelian inheritance in man

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.

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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OMIM

OMIM is a comprehensive, authoritative compendium of human genes and genetic phenotypes that is freely available and updated daily. OMIM is authored and edited at the McKusick-Nathans Institute of Genetic Medicine, Johns Hopkins University School of Medicine, under the direction of Dr. Ada Hamosh. Its official home is omim.org.

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[FAQ](#)

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[OMIM API](#)

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[Gene](#)

[GTR](#)

[MedGen](#)

Summary 20 per page

Send to: Filter your results:

Search results

Items: 1 to 20 of 26

<< First < Prev Page 1 of 2 Next > Last >>

All (26)

OMIM UniSTS (13)

OMIM dbSNP (12)

Manage Filters

☐ [#253700 - MUSCULAR DYSTROPHY, LIMB-GIRDLE, AUTOSOMAL RECESSIVE 5; LGMDR5](#)

1. Cytogenetic locations: 13q12.12

OMIM: 253700

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☐ [#608099 - MUSCULAR DYSTROPHY, LIMB-GIRDLE, AUTOSOMAL RECESSIVE 3; LGMDR3](#)

2. Cytogenetic locations: 17q21.33

OMIM: 608099

[Gene summaries](#) [Genetic tests](#) [Medical literature](#)

☐ [#310200 - MUSCULAR DYSTROPHY, DUCHENNE TYPE; DMD](#)

3. Cytogenetic locations: Xp21.2-p21.1

OMIM: 310200

[Gene summaries](#) [Genetic tests](#) [Medical literature](#)

☐ [#158810 - BETHLEM MYOPATHY 1; BTHLM1](#)

4. Cytogenetic locations: 21q22.3, 1p36, 21q22.3

OMIM: 158810

[Gene summaries](#) [Genetic tests](#) [Medical literature](#)

☐ [#310400 - MYOPATHY, CENTRONUCLEAR, X-LINKED; CNMX](#)

5. Cytogenetic locations: Xq28

OMIM: 310400

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☐ [#254130 - MIYOSHI MUSCULAR DYSTROPHY 1; MMD1](#)

6. Cytogenetic locations: 2p13.2

OMIM: 254130

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☐ [#310440 - MYOPATHY, X-LINKED, WITH EXCESSIVE AUTOPHAGY; MEAX](#)

7. Cytogenetic locations: Xq28

OMIM: 310440

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☐ [#300257 - DANON DISEASE](#)

8. Cytogenetic locations: Xq24

OMIM: 300257

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Database: Select

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myopathy[All Fields] AND de[All Fields] AND duchenne[All Fields]

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OMIM

myopathy (666)

OMIM

myopathy du chenue (21)

OMIM

dystrophin (135)

OMIM

See more...

#310200

Table of Contents

310200

ICD+

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

▼ External Links

► Protein

▼ Clinical Resources

Clinical Trials
 EuroGentest
 ► Gene Reviews
 Genetic Alliance
 Genetics Home Reference
 GTR
 GARD
 OrphaNet
 POSSUM

► Animal Models

► Cell Lines

Title

Phenotype-Gene Relationships

Clinical Synopsis

Text

Description

Clinical Features

Other Features

Inheritance

Cytogenetics

Mapping

Molecular Genetics

Diagnosis

Clinical Management

Population Genetics

Animal Model

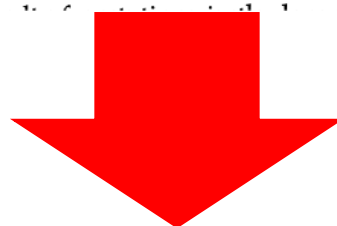
See Also

References

Contributors

Creation Date

Edit History



- Title
- Phenotype-Genes Relationships
- Clinical Synopsis
- Text
 - Description
 - Clinical Features
 - Other Features
 - Inheritance
 - Cytogenetics
 - Mapping
 - Molecular Genetics
 - Diagnosis
 - Clinical Management
 - Population Genetics
 - Animal Model
- See Also
- References
- Contributors
- Creation Date
- Edit History

▼ 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.

▼ External Links

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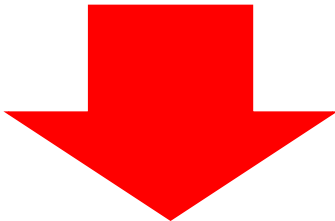
[GARD](#)

[OrphaNet](#)

[POSSUM](#)

▶ Animal Models

▶ Cell Lines





Options ▾

#310200

Table of Contents

Title

Phenotype-Gene
Relationships

Clinical Synopsis

Text

Description

Clinical Features

Other Features

Inheritance

Cytogenetics

Mapping

Molecular Genetics

Diagnosis

Clinical Management

Population Genetics

Animal Model

See Also

References

Contributors

Creation Date

Edit History

▼ REFERENCES

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▼ External Links

► Protein

▼ Clinical Resources

[Clinical Trials](#)
[EuroGentest](#)
► [Gene Reviews](#)
[Genetic Alliance](#)
[Genetics Home](#)
[Reference](#)
[GTR](#)
[GARD](#)
[OrphaNet](#)
[POSSUM](#)

► Animal Models

► Cell Lines

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Chemicals & Bioassays
Data & Software
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Domains & Structures
Genes & Expression
Genetics & Medicine
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Proteins
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Taxonomy
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Data & Software
DNA & RNA
Domains & Structures
Genes & Expression
Genetics & Medicine
Genomes & Maps

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BLAST
Nucleotide
Genome
SNP

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Reference Sequences
Gene Expression Omnibus
Genome Data Viewer
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Resource List (A-Z)

- All Resources
- Chemicals & Bioassays
- Data & Software
- DNA & RNA
- Domains & Structures
- Genes & Expression
- Genetics & Medicine
- Genomes & Maps
- Homology
- Literature
- Proteins
- Sequence Analysis
- Taxonomy
- Training & Tutorials
- Variation

- Genome
- GEO DataSets
- GEO Profiles
- GTR
- HomoloGene
- Identical Protein Groups
- MedGen
- MeSH
- NCBI Web Site
- NLM Catalog
- Nucleotide
- OMIM
- PMC
- PopSet
- Protein
- Protein Clusters
- PubChem BioAssay
- PubChem Compound
- PubChem Substance
- PubMed
- SNP
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- Training & Tutorials
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- Chemicals & Bioassays
- Data & Software
- DNA & RNA
- Domains & Structures
- Genes & Expression
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- Bookshelf
- PubMed Central
- BLAST
- Nucleotide
- Genome
- SNP

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- Reference Sequences
- Gene Expression Omnibus
- Genome Data Viewer
- Human Genome
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☐ 1 **The relationship among fear and anxiety of COVID-19, pregnancy experience, and mental health disorder in pregnant women: A structural equation model.**

Cite Salehi L, Rahimzadeh M, Molaei E, Zaheri H, Esmaelzadeh-Saeieh S.

Brain Behav. 2020 Sep 23:e01835. doi: 10.1002/brb3.1835. Online ahead of print.

Share PMID: 32969190

The eligible individuals entered the study through convenience sampling, and data were collected using five questionnaires including the Fear of COVID-19 Scale, the Anxiety of COVID-19 Scale, the pregnancy experiences Scales, Depression Anxiety Stress ...

☐ 2 **How to restart the interventional activity in the COVID-19 era. The experience of a private Pain Unit in Spain.**

Cite Abejón González D, Monzón EM, Deer T, Hagedorn JM, Araujo R, Abad C, Rios A, Zamora A, Vallejo R.

Share Pain Pract. 2020 Sep 23. doi: 10.1111/papr.12951. Online ahead of print.

PMID: 32969188 Review.

The situation generated in the health system by the COVID-19 pandemic has provoked a crisis involving the necessity to cancel non-urgent and oncologic activity in the operating room and in day-to-day practice. ...We describe procedures to implement these recommendat ...

☐ 3 **Experiences of breastfeeding during COVID-19: Lessons for future practical and emotional support.**

Cite Brown A, Shenker N.



Back to Top

Feedback

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h
Guide

PubMed.gov

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Advanced Create alert Create RSS

User Guide

MY NC

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Email

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Display options

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Page 1 of 29,780

RESULTS BY YEAR



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Abstract

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ARTICLE

ARTICLE ATTRIBUTE

ARTICLE TYPE

Books and Documents

Clinical Trial

Meta-Analysis

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Mental health and sleep habits during preclinical years of medical school.

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PMID: 36148761

Additional assessments evaluated exercise habits, chronic disease, and impact of COVID-19 Pandemic. The COVID-19 Pandemic was evaluated directly in the model (pre- and post-COVID-19 period variable), and through additional questions on th ...

Letter to the Editor: "Respiratory and peripheral muscular ultrasound characteristics in ICU COVID 19 ARDS patients".

Sajid DS.

J Crit Care. 2022 Sep 20;72:154155. doi: 10.1016/j.jcrc.2022.154155. Online ahead of print.

PMID: 36148740

No abstract available.

Risk factors associated with COVID-19 infection and mortality in nursing homes.

Beobide Telleria I, Ferro Uriguen A, Laso Lucas E, Sannino Menicucci C, Enriquez Barroso M, López de Munain Arregui A.

Aten Primaria. 2022 Sep 6;54(10):102463. doi: 10.1016/j.aprim.2022.102463. Online ahead of print.

PMID: 36148713

OBJECTIVE: The aim of this paper was to analyse the association of demographic, clinical and pharmacological risk factors with the presence of SARS-COV-2 virus infection, as well as to know the variables related to mortality from COVID-19 in nur ...

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Back to Top

Feedback

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Search

Advanced Create alert Create RSS

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- ☐ Clinical Trial

☐ 1 **The relationship among fear and anxiety of COVID-19, pregnancy experience, and mental health disorder in pregnant women: A structural equation model.**

Cite Salehi L, Rahimzadeh M, Molaei E, Zaheri H, Esmaelzadeh-Saeieh S.

Brain Behav. 2020 Sep 23:e01835. doi: 10.1002/brb3.1835. Online ahead of print.

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The eligible individuals entered the study through convenience sampling, and data were collected using five questionnaires including the Fear of COVID-19 Scale, the Anxiety of COVID-19 Scale, the pregnancy experiences Scales, Depression Anxiety Stress ...

☐ 2 **How to restart the interventional activity in the COVID-19 era. The experience of a private Pain Unit in Spain.**

Cite Abejón González D, Monzón EM, Deer T, Hagedorn JM, Araujo R, Abad C, Rios A, Zamora A, Vallejo R.

Share Pain Pract. 2020 Sep 23. doi: 10.1111/papr.12951. Online ahead of print.

PMID: 32969188 Review.

The situation generated in the health system by the COVID-19 pandemic has provoked a crisis involving the necessity to cancel non-urgent and oncologic activity in the operating room and in day-to-day practice. ...We describe procedures to implement these recommendat ...

☐ 3 **Experiences of breastfeeding during COVID-19: Lessons for future practical and emotional support.**

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

Cite Buitrago-Garcia D, Egli-Gany D, Counotte MJ, Hossmann S, Imeri H, Ipekci AM, Salanti G, Low N. PLoS Med. 2020 Sep 22;17(9):e1003346. doi: 10.1371/journal.pmed.1003346. eCollection 2020 Sep.

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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-Gany¹, Michel J Counotte¹, Stefanie Hossmann¹, Hira Imeri¹, Aziz Mert Ipekci¹, Georgia Salanti¹, Nicola Low¹

Affiliations + expand

PMID: 32960881 DOI: [10.1371/journal.pmed.1003346](https://doi.org/10.1371/journal.pmed.1003346)

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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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Abstract

Author summary

Introduction

Methods

Results

Conclusions

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)

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Diana Buitrago-Garcia^{1,2}, Dianne Egli-Gany^{1,2}, Michel J. Counotte^{1,2}, Stefanie Hossmann¹, Hira Imeri¹, Aziz Mert Ipekci¹, Georgia Salanti¹, Nicola Low^{1*}

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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, Saqian	2	1	1 F, 0 M	54	3
Jiang, XL [26]	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 [127]	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 [58]	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 [79]	China, Wuxi	15	6	3 F, 3 M	50 IQR 48–51	1, 2
Contact investigation, aggregated						
Hjinen, 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 [77]	China, Wuhan	47	4	NR	NR	1
Wu, J [105]	China, Zhuhai	83	8	NR	NR	1, 2
Luo, L [16]	China, Guangzhou	129	8	NR	NR	1, 2, 3
Bi, Q [40]	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
Boothby, AC [94]	USA	6	3	NR	NR	1
Yang, N [48]	China, Xiaoshan	10	2	1 F, 1 M	NR	1, 2
Schwietzke, V [95]	Germany	12	2	NR	NR	2
Arona, 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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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.

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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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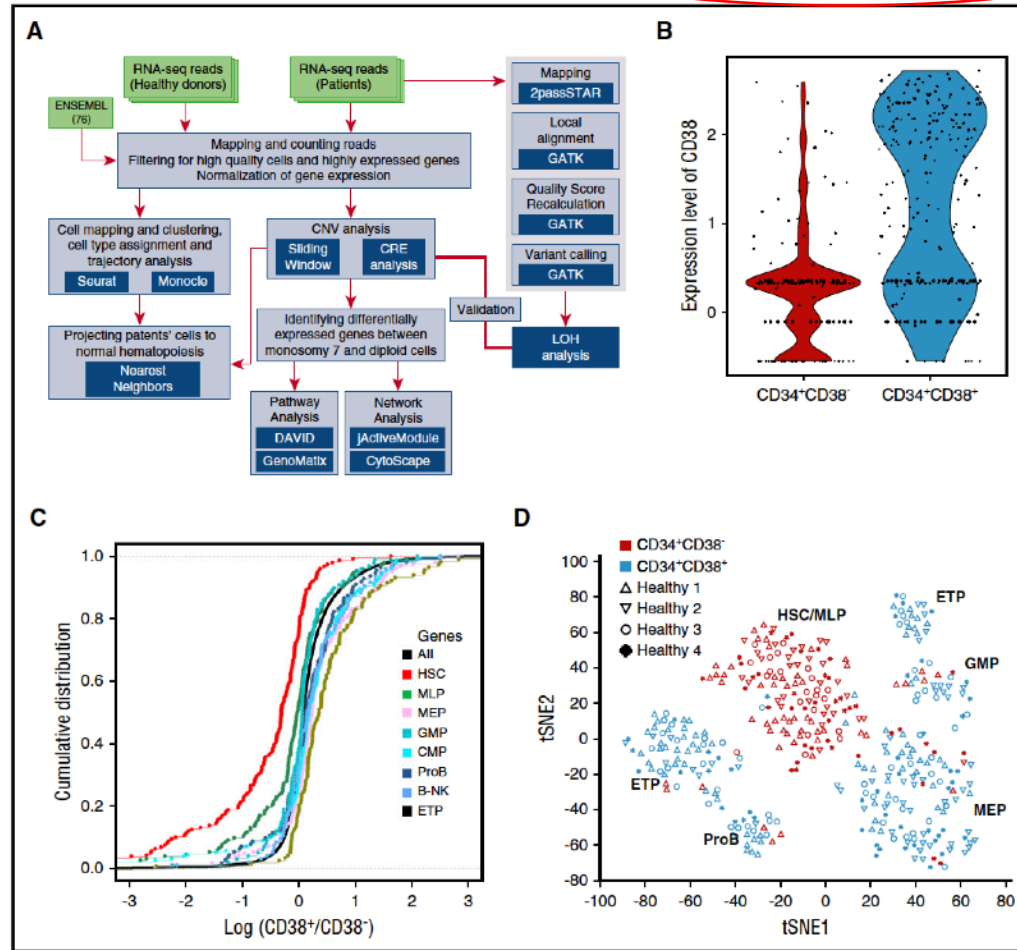


Figure 1. Hematopoietic heterogeneity in healthy donors quantified by scRNA-seq. CD34⁺CD38⁻ and CD34⁺CD38⁺ cells from 4 healthy donors (healthy 1-4) were sorted by surface-membrane markers and subjected to analyses. (A) The schematic pipeline consisting of 3 major analytic components: differentiation analysis with cells from healthy donors, identification and characterization of monosomy 7 cells with gene expression, and validation of monosomy identification with loss of heterozygosity (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, multi-lymphoid progenitor; ProB, pro-B cell. y-axis, cumulative distribution; x-axis, log (marker gene expression levels in CD34⁺CD38⁻ cells/markers 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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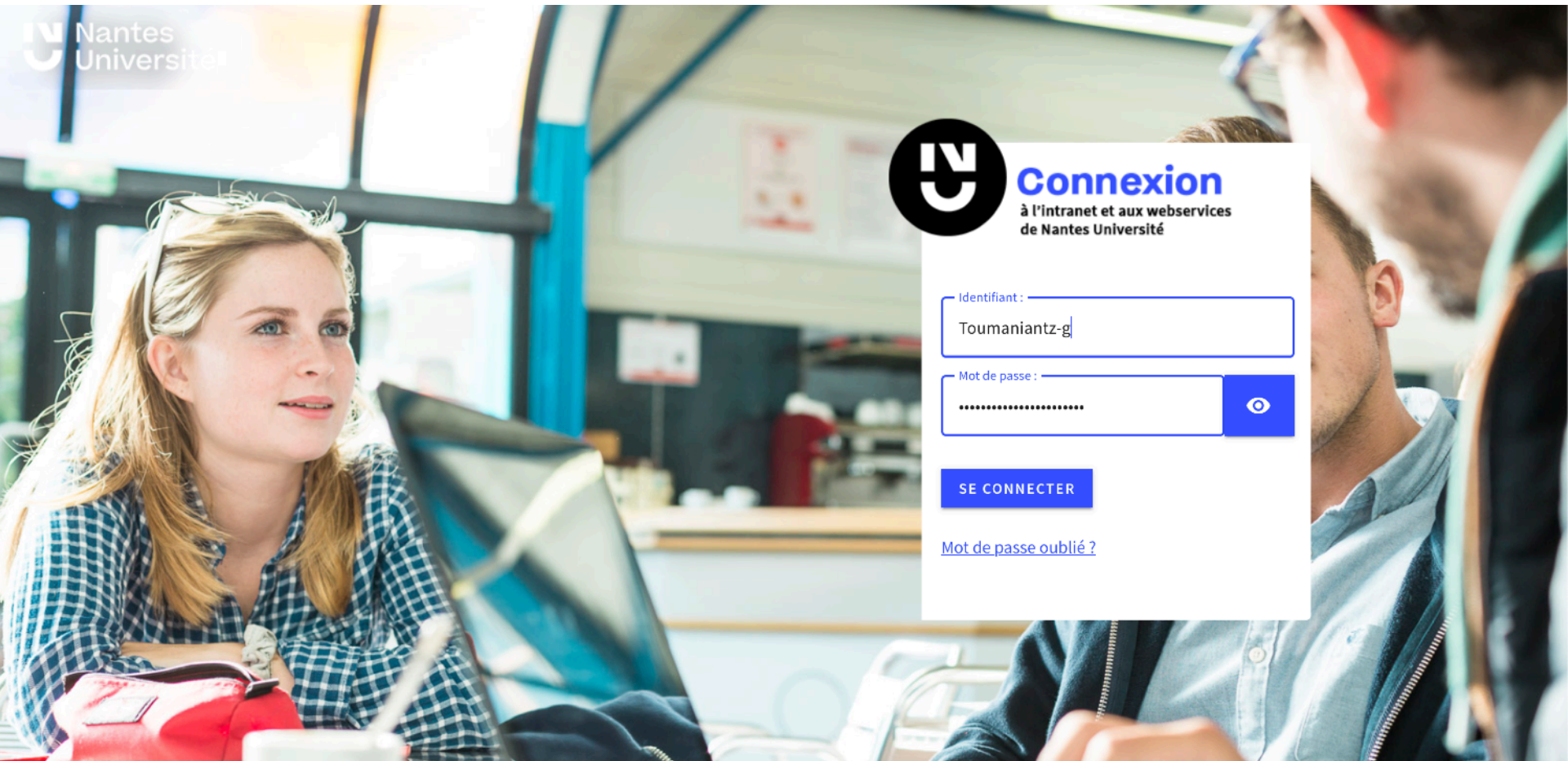
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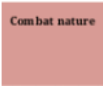
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La bibliothèque possède :
BU Sciences : Vol. 202 (1964) - Vol. 203 (1964) ; Vol. 206 (1965) - Vol. 257 (1975) ; Vol. 259 (1976) - Vol. 312 (1984) ; Vol. 322 (1986) - Vol. 565 (2019)
Egalement en ligne : [En ligne](#) [Via Nature](#)
[Sommaires en ligne](#)
[Revue](#) [Réserver](#) [Ajouter au panier](#) [Ajouter à vos listes](#)

☐ 2  **Nature**
Nature
depuis 1869 jusqu'à 2012
L'accès à cette ressource est contrôlé.
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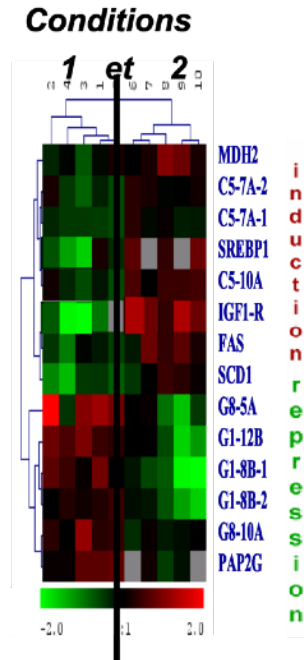
☐ 3  **Combat nature**
Société d'édition pour la nature et l'environnement 1974-2004
La bibliothèque possède :

Au labo : analyse à haut débit de cette bibliographie.

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

sont-elles cohérentes/incohérentes

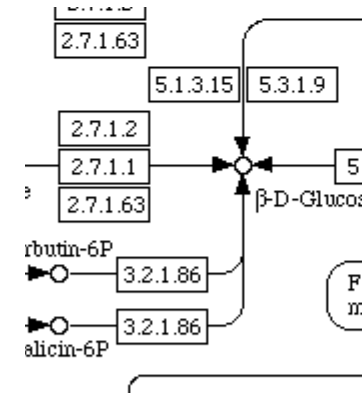
avec les connaissances du moment ?



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

2. Les analyses nucléotidiques

Question à étudier:

2. Les analyses nucléotidiques



NCBI

PubMed

A service of the [U.S. National Library of Medicine](#) and the [National Institutes of Health](#)

[www.pubmed.gov](#)

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

Search PubMed 101 Go Clear [Advanced Search \(beta\)](#)

Limits Preview/Index History Clipboard Details

To get started with PubMed, enter one or more search terms.

Search terms may be [topics](#), [authors](#) or [journals](#).

The NIH Public Access Policy May Affect You

Does NIH fund your work?

Then your manuscript must be made available in PubMed Central

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If you publish in one of [these journals](#), they will take care of the whole process.

If you publish *anywhere else*, deposit the manuscript in PubMed Central via one of the options described at [publicaccess.nih.gov](#).

Note: Other funding organizations, including [HHMI](#), [Wellcome Trust](#) and the [MRC](#) also require papers to be made freely available through PMC.

PubMed is a service of the [U.S. National Library of Medicine](#) that includes over 18 million citations from MEDLINE and other life science journals for biomedical articles back to the 1950s. PubMed includes links to full text articles and other related resources.

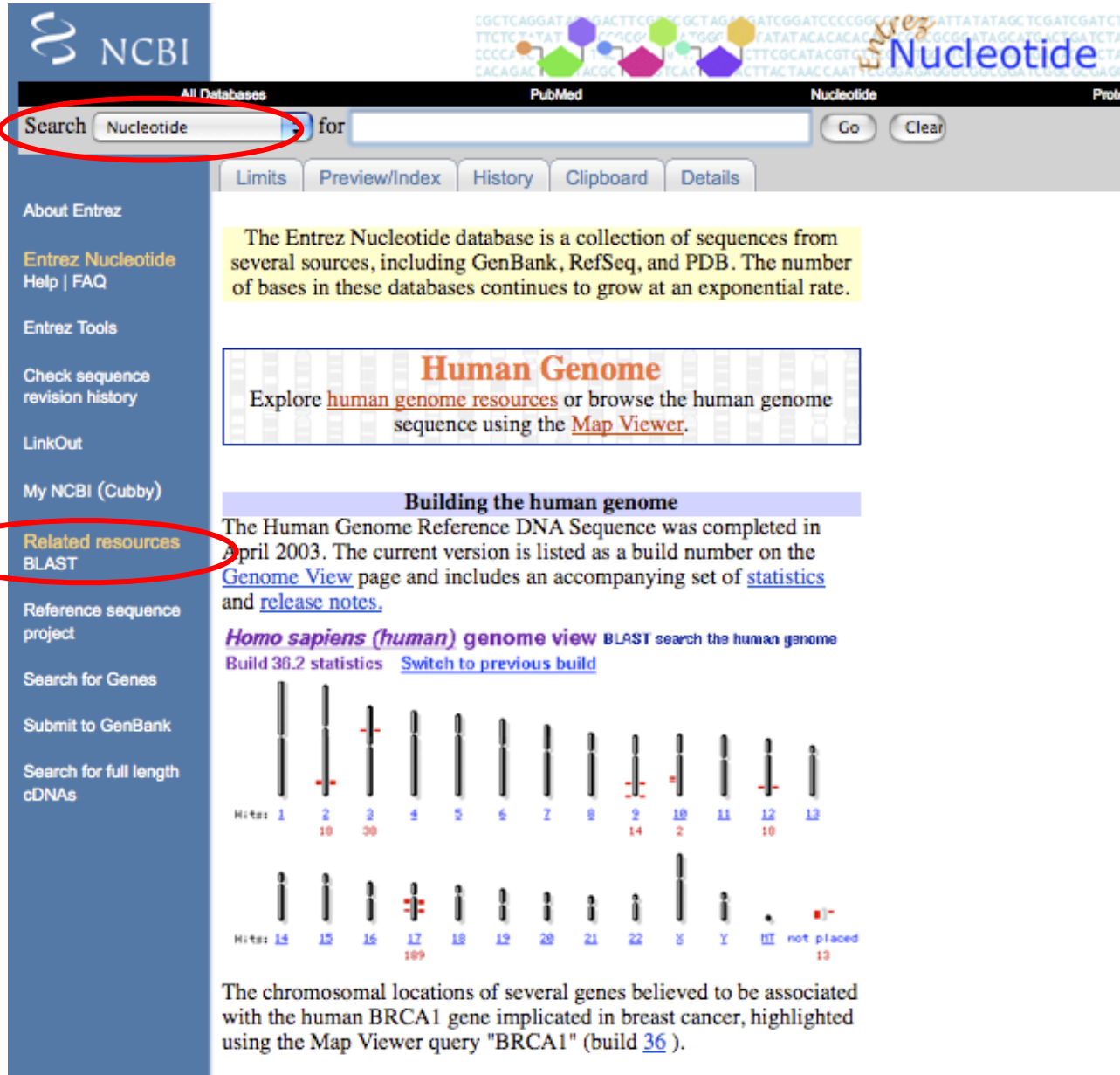
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New/Noteworthy
E-Utilities

PubMed Services
Journals Database
MeSH Database
Single Citation Matcher
Batch Citation Matcher
Clinical Queries
Special Queries
LinkOut
My NCBI

Related Resources
Order Documents
NLM Mobile
NLM Catalog
NLM Gateway
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Consumer Health
Clinical Alerts
ClinicalTrials.gov
PubMed Central

2. Les analyses nucléotidiques



NCBI

Entrez Nucleotide

Search Nucleotide for [] Go Clear

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Entrez Tools

Check sequence revision history

LinkOut

My NCBI (Cubby)

Related resources BLAST

Reference sequence project

Search for Genes

Submit to GenBank

Search for full length cDNAs

The Entrez Nucleotide database is a collection of sequences from several sources, including GenBank, RefSeq, and PDB. The number of bases in these databases continues to grow at an exponential rate.

Human Genome

Explore [human genome resources](#) or browse the human genome sequence using the [Map Viewer](#).

Building the human genome

The Human Genome Reference DNA Sequence was completed in April 2003. The current version is listed as a build number on the [Genome View](#) page and includes an accompanying set of [statistics](#) and [release notes](#).

Homo sapiens (human) genome view BLAST search the human genome

Build 38.2 statistics [Switch to previous build](#)

Hits: 1 2 3 4 5 6 7 8 9 10 11 12 13

10 30 14 2 10

Hits: 14 15 16 17 18 19 20 21 22 23 Y III not placed 13

109

The chromosomal locations of several genes believed to be associated with the human BRCA1 gene implicated in breast cancer, highlighted using the Map Viewer query "BRCA1" (build 36).

2. Les analyses nucléotidiques

NIH U.S. National Library of Medicine NCBI National Center for Biotechnology Information Sign in to NCBI

BLAST® Home Recent Results Saved Strategies Help

Basic Local Alignment Search Tool

BLAST finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance. [Learn more](#)


NEWS

Using BLAST Well, How to Maximize Your Search Efforts: Webinar on October 3, 2018

In this webinar, the NCBI BLAST team lead will show you how to be more effective with BLAST.

Thu, 27 Sep 2018 11:00:00 EST [More BLAST news...](#)

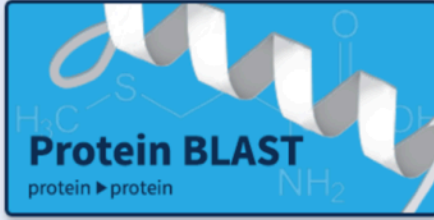
Web BLAST



Nucleotide BLAST
nucleotide ► nucleotide

blastx
translated nucleotide ► protein

tblastn
protein ► translated nucleotide



Protein BLAST
protein ► protein

BLAST Genomes

Enter organism common name, scientific name, or tax id

Use up and down arrows to choose an item from the autocomplete.

Human Mouse Rat Microbes **Search**

2. Les analyses nucléotidiques

BLAST Basic Local Alignment Search Tool

Home Recent Results Saved Strategies Help

NCBI/ BLAST/ blastn suite

blastn blastp blastx tblastn tblastx

BLASTN programs search nucleotide databases using a nucleotide query.

Enter Query Sequence

Enter accession number, gi, or FASTA sequence [Clear](#)

tcgtctgctgctccagccagcgagggtcagcgccgctgtcgcagcagtgagccgagggtatgggcctac

Query subrange

From

To

Or, upload file [Parcourir...](#)

Job Title

Enter a descriptive title for your BLAST search

☐ Blast 2 sequences

Choose Search Set

Database

☐ Human genomic + transcript ☐ Mouse genomic + transcript ☒ Others (nr etc.):

Nucleotide collection (nr/nt)

Organism Optional

Enter organism name or id--completions will be suggested

Enter organism common name, binomial, or tax id. Only 20 top taxa will be shown.

Entrez Query Optional

Enter an Entrez query to limit search

Program Selection

Optimize for

☒ Highly similar sequences (megablast)

☐ More dissimilar sequences (discontiguous megablast)

☐ Somewhat similar sequences (blastn)

Choose a BLAST algorithm

2. Les analyses nucléotidiques

Sequence input area with a text box and a "From" "To" range selector.

Or, upload file

Job Title

Enter a descriptive title for your BLAST search

☐ Blast 2 sequences

Choose Search Set

Database

☐ Human genomic + transcript ☐ Mouse genomic + transcript ☒ Others (nr etc.):

Nucleotide collection (nr/nt)

Organism

Optional

Enter organism name or id--completions will be suggested

Enter organism common name, binomial, or tax id. Only 20 top taxa will be shown.

Entrez Query

Optional

Enter an Entrez query to limit search

Program Selection

Optimize for

☒ Highly similar sequences (megablast)

☐ More dissimilar sequences (discontiguous megablast)

☐ Somewhat similar sequences (blastn)

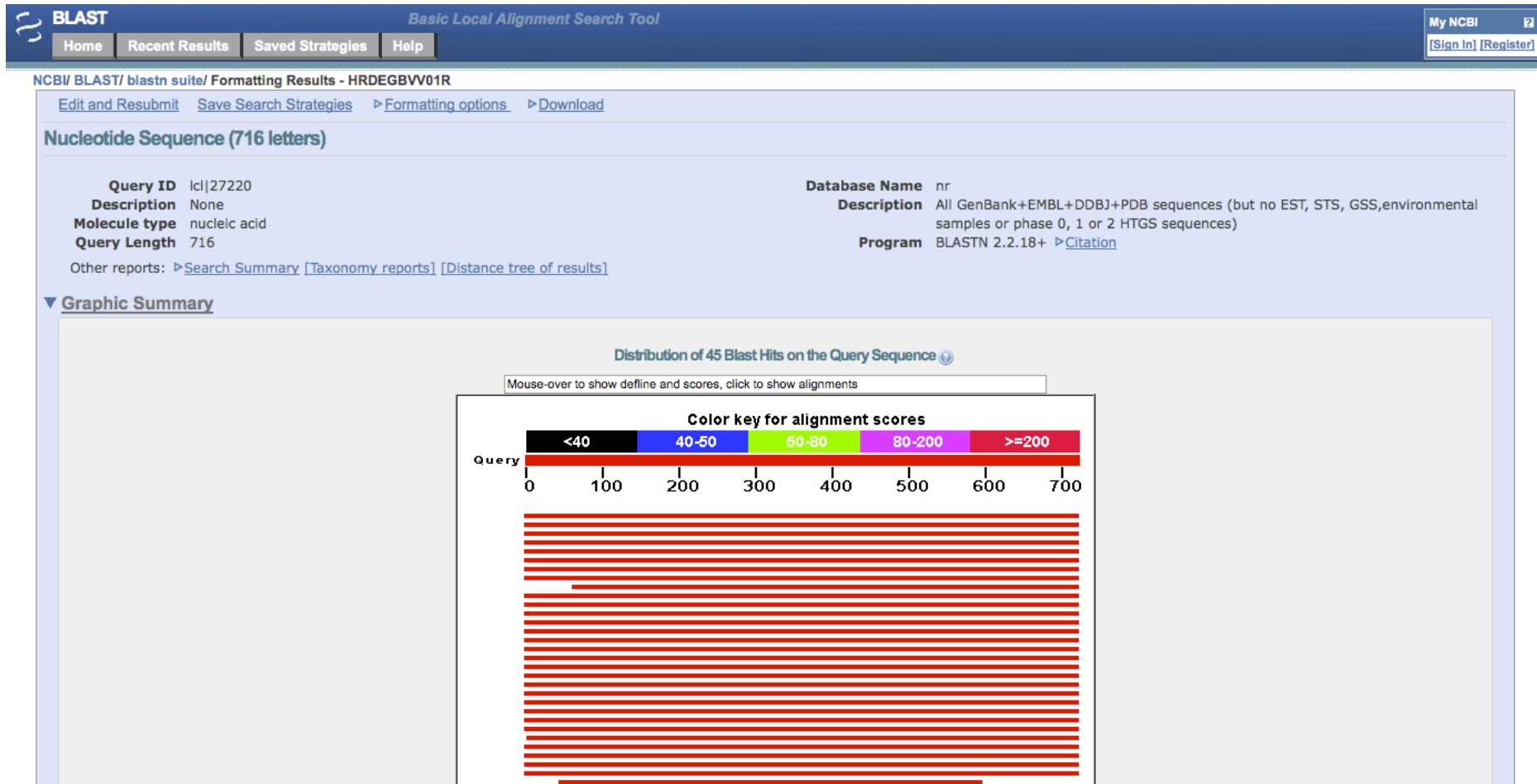
Choose a BLAST algorithm

BLAST

Search database nr using Megablast (Optimize for highly similar sequences)

☐ Show results in a new window

2. Les analyses nucléotidiques



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 column)

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
J05501.1	R.norvegicus beta-1-adrenergic receptor gene, complete cds	1317	1317	100%	0.0	99%	U E G
D00634.1	Rattus norvegicus gene for beta-1 adrenergic receptor, complete cds	1299	1299	100%	0.0	99%	E G
BC147435.1	Mus musculus adrenergic receptor, beta 1, mRNA (cDNA clone MGC:182135 IMAG	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, clon	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

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

GENE ID: 24925 Adrb1 | adrenergic, beta-1-, receptor [Rattus norvegicus]
(Over 10 PubMed links)

Score = 1317 bits (713), Expect = 0.0
Identities = 715/716 (99%), Gaps = 0/716 (0%)
Strand=Plus/Plus

```
Query 1 TCGCTGCTGCCTCCAGCCAGCGAGGGCTCAGCGCCGCTGTCGCGAGCAGTGGACCGGGGT 60
Sbjct 121 TCGCTGCTGCCTCCAGCCAGCGAGGGCTCAGCGCCGCTGTCGCGAGCAGTGGACCGGGGT 180
Query 61 ATGGGCCTACTCCTGGCGCTCATCGTCTGCTCATCGTAGTGGGCAACGTGTTGGTGATC 120
Sbjct 181 ATGGGCCTACTCCTGGCGCTCATCGTCTGCTCATCGTAGTGGGCAACGTGTTGGTGATC 240
Query 121 GTGGCCATCGCCAAGACCCCGCGGCTGCAGACGCTCACCAACCTCTTCATCATGTCCCTG 180
Sbjct 241 GTGGCCATCGCCAAGACCCCGCGGCTGCAGACGCTCACCAACCTCTTCATCATGTCCCTG 300
Query 181 GCCAGCGCCGATCTGGTCATGGGACTGCTGGTGGTGCCTTTGCGGGCCACCATTGTGGTG 240
Sbjct 301 GCCAGCGCCGATCTGGTCATGGGACTGCTGGTGGTGCCTTTGCGGGCCACCATTGTGGTG 360
Query 241 TGGGGCCGCTGGGAGTACGGCTCCTTCTCTGTGAGCTCTGGACTTCGGTAGACGTGCTA 300
Sbjct 361 TGGGGCCGCTGGGAGTACGGCTCCTTCTCTGTGAGCTCTGGACTTCGGTAGACGTGCTA 420
Query 301 TGTGTGACGGCCAGCATCGAGACCCCTGTGTGTCATCGCCCTGGAGCGCTTCCTCGGCATC 360
Sbjct 421 TGTGTGACGGCCAGCATCGAGACCCCTGTGTGTCATCGCCCTGGAGCGCTTCCTCGGCATC 480
Query 361 ACGCTGCCCTTTTCGCTACCAGAGCCTGCTGACGCGCGCGGAGCGCGGGCCCTCGTGTGC 420
```

Position 470/début séquence référencée

2. Les analyses nucléotidiques

NCBI Nucleotide

Search Nucleotide for [] Go Clear

Display GenBank Show 20 Send to Hide sequence all but gene, CDS and mRNA feat

Range: from begin to end Reverse complemented strand Features: STS Refresh

1: NM_012701. Reports Rattus norvegicus...[gi:6978458]

Comment Features Sequence

LOCUS NM_012701 1401 bp mRNA linear ROD 10-OCT-2008

DEFINITION Rattus norvegicus adrenergic, beta-1-, receptor (Adrb1), mRNA.

ACCESSION NM_012701 XM_001063787

VERSION NM_012701.1 GI:6978458

KEYWORDS

SOURCE Rattus norvegicus (Norway rat)

ORGANISM Rattus norvegicus

Chordata; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Glires; Rodentia; Sciurognathi; Muroidea; Muridae; Murinae; Rattus.

REFERENCE 1 (bases 1 to 1401)

AUTHORS Bidasee,K.R., Zheng,H., Shao,C.H., Parbhu,S.K., Rozanski,G.J. and Patel,K.P.

TITLE Exercise training initiated after the onset of diabetes preserves myocardial function: effects on expression of beta-adrenoceptors

JOURNAL J. Appl. Physiol. 105 (3), 907-914 (2008)

PUBMED 18583384

REMARK GeneRIF: Myocardial Adrb1 reduction in type 1 diabetes is prevented using exercise training.

REFERENCE 2 (bases 1 to 1401)

AUTHORS Fu,A., Li,X. and Zhao,B.

TITLE Role of betal-adrenoceptor in the basolateral amygdala of rats with anxiety-like behavior

JOURNAL Brain Res. 1211, 85-92 (2008)

PUBMED 18423428

REMARK GeneRIF: results suggested that the betal-AR played an important role in anxiety-like behavior

REFERENCE 3 (bases 1 to 1401)

AUTHORS Abraham,P.A., Xing,G., Zhang,L., Yu,E.Z., Post,R., Gamble,E.H. and Li,H.

TITLE betal- and beta2-adrenoceptor induced synaptic facilitation in rat basolateral amygdala

JOURNAL Brain Res. 1209, 65-73 (2008)

PUBMED 18396264

REMARK GeneRIF: These data suggest that beta-adrenoceptor mediated synaptic facilitation in the amygdala is mediated by both betal and beta2-adrenoceptor activation.

REFERENCE 4 (bases 1 to 1401)

AUTHORS Plante,E., Lachance,D., Champetier,S., Drolet,M.C., Roussel,E., Arsenault,M. and Couet,J.

TITLE Benefits of long-term beta-blockade in experimental chronic aortic regurgitation

JOURNAL Am. J. Physiol. Heart Circ. Physiol. 294 (4), H1888-H1895 (2008)

PUBMED 18296565

REMARK GeneRIF: Long-term beta-blockade in chronic aortic regurgitation improved heart function and restored betal/2 adrenergic receptor

Identité

Bibliographie

2. Les analyses nucléotidiques

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                        /db_xref="RATMAP:34960"
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                        VTNRAYAIASSVVSFFYVPLCIMA FVYLRVVFREAQKQVKKIDSCERRFLTGP RPSPSPA
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                        VKAFHRDLVPDRLFVFFNWLG YANSAFNP I IYCRSPDPRKAFQRLCCARRAACRRRA
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                        /gene_synonym="BIAR"
                        /gene_synonym="RATBIAR"
                        /standard_name="Adrb1"
                        /db_xref="UniSTS:256461"
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                        /gene_synonym="BIAR"
                        /gene_synonym="RATBIAR"
                        /standard_name="Adrb1"
                        /db_xref="UniSTS:141043"
ORIGIN
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61 ccgctgcccc acggcgcggc caccgcggca cgactgctg tgctcgctc gctcccgcc
121 tcgctgctgc ctccagccag cgaggctcga gcgcgctgt cgcagcagt gaccgcgggt
181 atgggcctac tcctggcgct catcgtgctg ctcactgtg tgggcaacgt gttggtgat
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481 acgctgcctt ttcgctacca gacgctgctg acgcgcgcgc gacgcggggc cctcgtgtgc
541 acagtgtggg ccatctccgc gctggtgtcc ttctgcccc tctcatgca ctggtggcgg
```

Phase ouverte de lecture

Protéine

Séquence nucléotidique

Défaut en position
470/début
séquence
référéncée

2. Les analyses nucléotidiques

Question à étudier:

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

2. Les analyses nucléotidiques

Question à étudier:

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

Basic BLAST

Choose a BLAST program to run.

nucleotide blast	Search a nucleotide database using a nucleotide query <i>Algorithms: blastn, megablast, discontinuous megablast</i>
protein blast	Search protein database using a protein query <i>Algorithms: blastp, psi-blast, phi-blast</i>
blastx	Search protein database using a translated nucleotide query
tblastn	Search translated nucleotide database using a protein query
tblastx	Search translated nucleotide database using a translated nucleotide query

2. Les analyses nucléotidiques

BLAST Basic Local Alignment Search Tool

Home Recent Results Saved Strategies Help

► NCBI/ BLAST/ tblastx

blastn blastp blastx **tblastx**

TBLASTX search translated nucleotide database using a translated nucleotide query

Enter Query Sequence

Enter accession number, gi, or FASTA sequence [Clear](#)

tcgctgctgcctccagccagcgagggtcagcgccgctgtcgcagcagtgagaccgagggtatgggctac

Query subrange

From

To

Or, upload file [Parcourir...](#)

Genetic code

Job Title

Enter a descriptive title for your BLAST search

☐ Blast 2 sequences

Choose Search Set

Database

Organism Optional

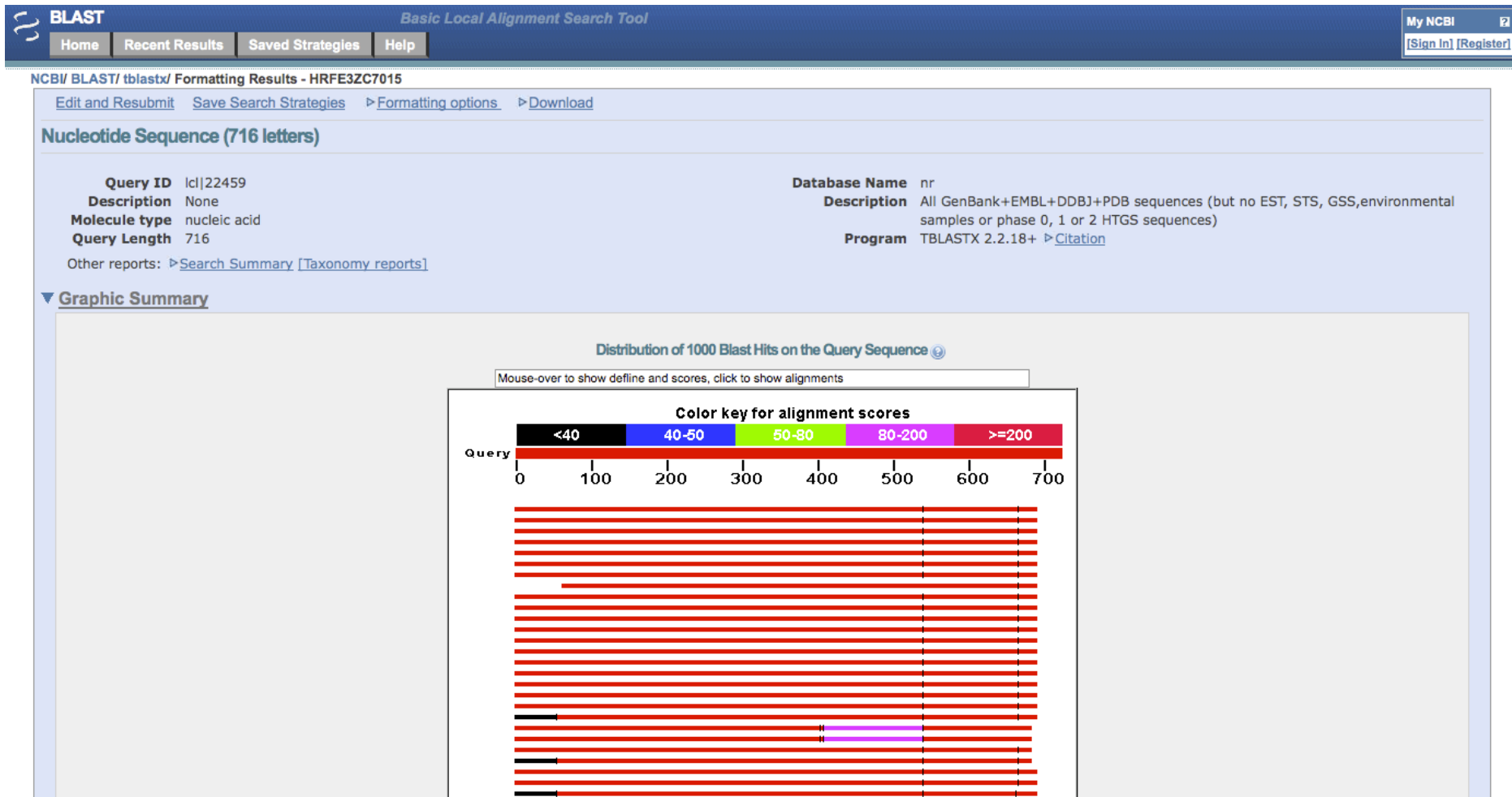
Enter organism common name, binomial, or tax id. Only 20 top taxa will be shown.

Entrez Query Optional

BLAST Search database nr using Tblastx (Search translated nucleotide database using a translated nucleotide query)

☐ Show results in a new window

2. Les analyses nucléotidiques



2. Les analyses nucléotidiques

▼ **Alignments** ☐ Select All [Get selected sequences](#) [Distance tree of results](#)

> ☐ gb|J05561.1|RATB1AR **G** R.norvegicus beta-1-adrenergic receptor gene, complete cds
Length=1645

[GENE ID: 24925 Adrb1](#) | adrenergic, beta-1-, receptor [Rattus norvegicus]
(Over 10 PubMed links)

Score = 439 bits (952), Expect = 6e-154
Identities = 177/178 (99%), Positives = 177/178 (99%), Gaps = 0/178 (0%)
Frame = -3/-3

Query	534	EIAALGVVVAARFVALGPPPVHEDGQEGHQRGDGP	355
		CAHEGPRSRARQQALVAKGQRDG	
Sbjct	722	EIAALGVVVAARFVALGPPPVHEDGQEGHQRGDGP	543
		CAHEGPRSRARQQALVAKGQRDG	
Query	354	EEAVQGDDTQGLDAGRHT*HVYRSP	175
		ELTEEGAVLPAAPHHNGGPERHHQQSHDQIGAGQG	
Sbjct	542	EEAVQGDDTQGLDAGRHT*HVYRSP	363
		ELTEEGAVLPAAPHHNGGPERHHQQSHDQIGAGQG	
Query	174	HDEEVGERLQPRGLGDGHDHQAHAHYDEQHDERQE*AHTRGPLLRQRR*ALAGWRQQR	1
		HDEEVGERLQPRGLGDGHDHQAHAHYDEQHDERQE*AHTRGPLLRQRR*ALAGWRQQR	
Sbjct	362	HDEEVGERLQPRGLGDGHDHQAHAHYDEQHDERQE*AHTRGPLLRQRR*ALAGWRQQR	189

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 ???

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

NC_005100.2

[263925655] 5' [263927955] 3'

NP_012701.1 NP_012702.1

■ = coding region ■ = untranslated region

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
- Probe
- Protein
- PubMed
- PubMed (GeneRIF)
- Taxonomy
- UniSTS
- Ensembl
- Evidence Viewer
- KEGG
- ModelMaker
- RATMAP
- RGD
- UniGene
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Entrez Gene Info

2. Les analyses nucléotidiques

Legend for links to other resources: [U](#) UniGene [E](#) GEO [G](#) Gene [S](#) Structure [M](#) Map Viewer

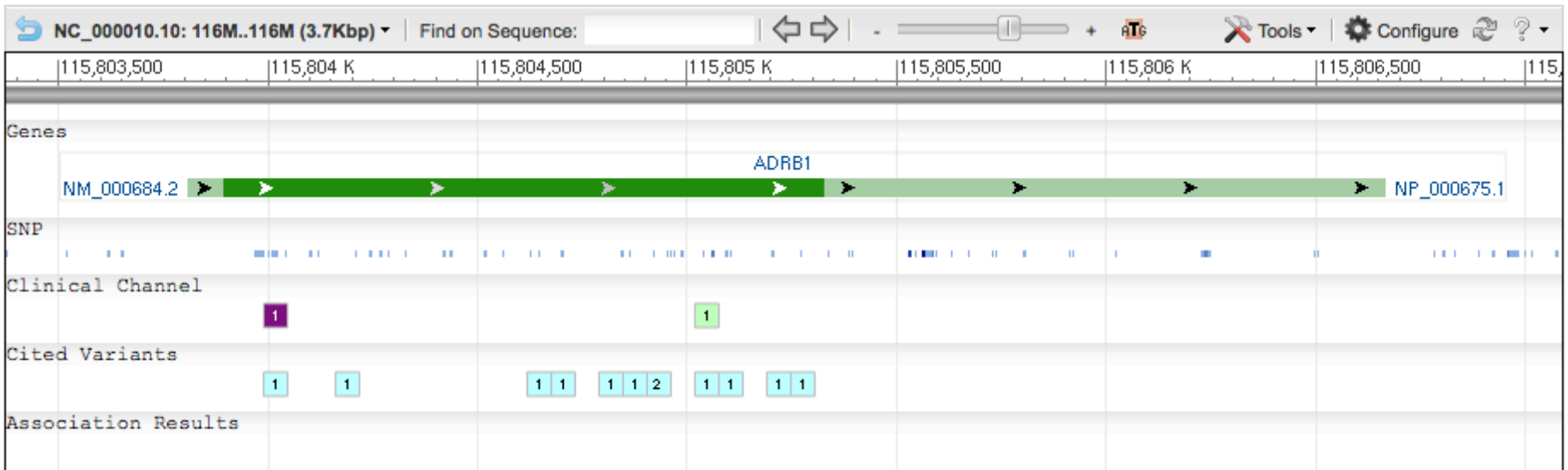
Position sur le génome ???

Genomic regions, transcripts, and products

Genomic Sequence [NC_000010 chromosome 10 reference GRCh37.p10 Primary Assembly](#)

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Go to nucleotide [Graphics](#) [FASTA](#) [GenBank](#)



Exons, introns, SNP, etc...

2. Les analyses nucléotidiques

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NCBI  **NCBI Map Viewer**

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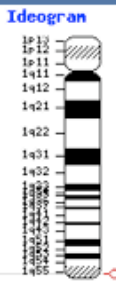
Map Viewer Home

Map Viewer Help
Rat Maps Help
FTP
Data As Table View
[Maps & Options](#)

Compress Map ☐

Region Shown:
263,025,480
263,027,230

You are here:
Ideogram



☐ default
☐ master

Rattus norvegicus (rat) RGSC v3.4

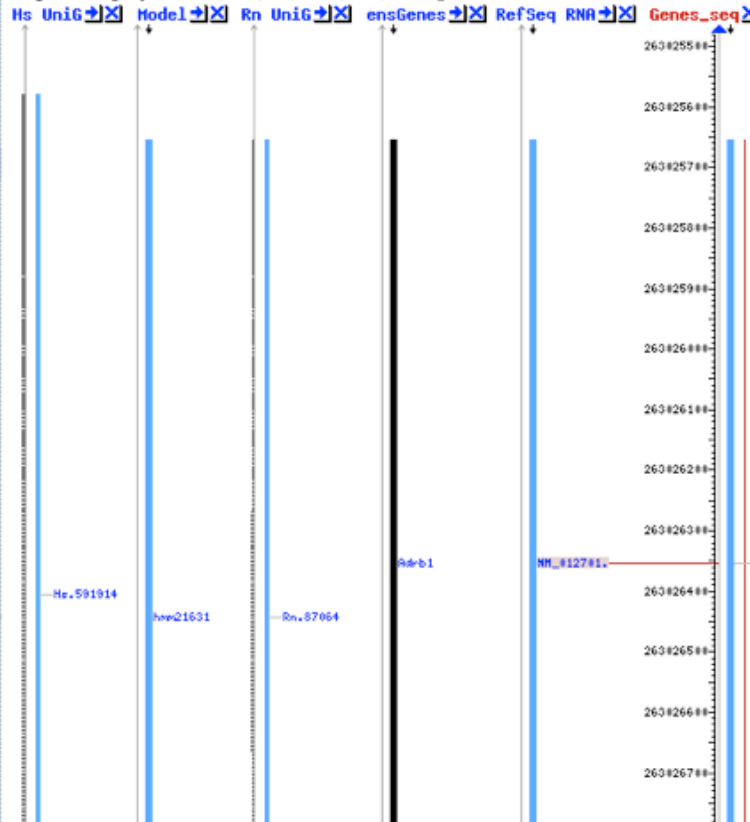
Chromosome: [1] [2](#) [3](#) [4](#) [5](#) [6](#) [7](#) [8](#) [9](#) [10](#) [11](#) [12](#) [13](#) [14](#) [15](#) [16](#) [17](#) [18](#) [19](#) [20](#) [X](#) [Y](#) [MT](#)

Query: 24925[[gene_id](#)]

Master Map: Genes On Sequence [Summary of Maps](#)

Region Displayed: 263,025,480-263,027,230 bp

[Hs](#) [UniG](#) [Model](#) [Rn](#) [UniG](#) [ensGenes](#) [RefSeq](#) [RNA](#) [Genes_seq](#) Symbol [Links](#) Cyto [E](#) Description





263#255##
263#256##
263#257##
263#258##
263#259##
263#260##
263#261##
263#262##
263#263##
263#264##
263#265##
263#266##
263#267##

Adrb1 + [sv pr dlev mm hm rgs sts](#) 1q55 best RefSeq adrenergic receptor, beta 1

3. Les pathologies héréditaires

3. Les pathologies héréditaires



All Databases

PubMed

Nucleotide

Protein

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Limits

Preview/Index

History

Clipboard

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cDNAs

The Entrez Nucleotide database is a collection of sequences from several sources, including GenBank, RefSeq, and PDB. The number of bases in these databases continues to grow at an exponential rate.

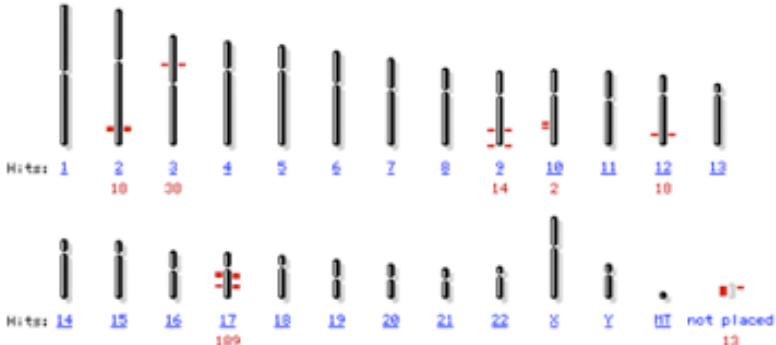
Human Genome

Explore [human genome resources](#) or browse the human genome sequence using the [Map Viewer](#).


Building the human genome

The Human Genome Reference DNA Sequence was completed in April 2003. The current version is listed as a build number on the [Genome View](#) page and includes an accompanying set of [statistics](#) and [release notes](#).

[Homo sapiens \(human\) genome view](#) BLAST search the human genome
[Build 36.2 statistics](#) [Switch to previous build](#)



Chromosome	Hit
1	1
2	10
3	30
4	4
5	5
6	6
7	7
8	8
9	9
10	14
11	2
12	10
13	13
14	14
15	15
16	16
17	109
18	18
19	19
20	20
21	21
22	22
X	X
Y	Y
not placed	13



l'institut
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3. Les pathologies héréditaires

NCBI OMIM Online Mendelian Inheritance in Man Johns Hopkins University

All Databases PubMed Nucleotide Protein Genome

Search OMIM for beta drenergic receptor Go Clear Save Search

Limits Preview/Index History Clipboard Details

The following term was not found: drenergic.
See [Details](#).

Did you mean: [beta adrenergic receptor](#) (99 items)

Display Titles Show 20 Send to


All: 1464 OMIM UniSTS: 190 OMIM dbSNP: 227

Items 1 - 20 of 1464

- ☐ 1: [+141900](#)
HEMOGLOBIN--BETA LOCUS; HBB
BETA-THALASSEMIA, INCLUDED
Gene map locus [11p15.5](#)
- ☐ 2: [+109690](#)
BETA-2-ADRENERGIC RECEPTOR; ADRB2
BETA-2-ADRENORECEPTOR AGONIST, REDUCED RESPONSE TO, INCLUDED
Gene map locus [5q32-q34](#)
- ☐ 3: [*608886](#)
PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA, COACTIVATOR 1, BETA; PPARGC1B
Gene map locus [5q33](#)
- ☐ 4: [*104760](#)
AMYLOID BETA A4 PRECURSOR PROTEIN; APP
Gene map locus [21q21](#)

L'onglet OMIM est un outils de synthèse

3. Les pathologies héréditaires



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

Entrez Gene
Nomenclature
RefSeq
GenBank
Protein
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OMIM
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All DatabasesPubMedNucleotideProteinGenomeStructurePMCOMIM

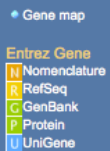
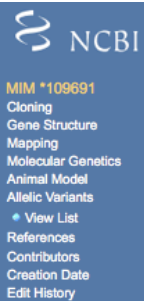
Search OMIM for [] Go Clear

LimitsPreview/IndexHistoryClipboardDetails

Display Detailed Show 20 Send to

***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

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. 🗨

4. Les analyses génomiques




4. Les analyses génomiques

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4. Les analyses génomiques

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4. Les analyses génomiques

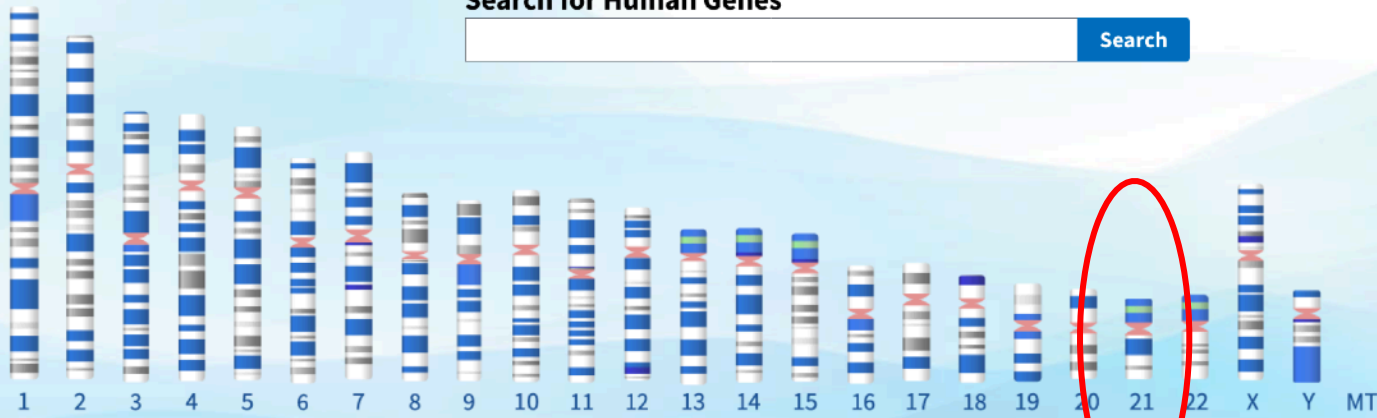
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1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 X Y MT

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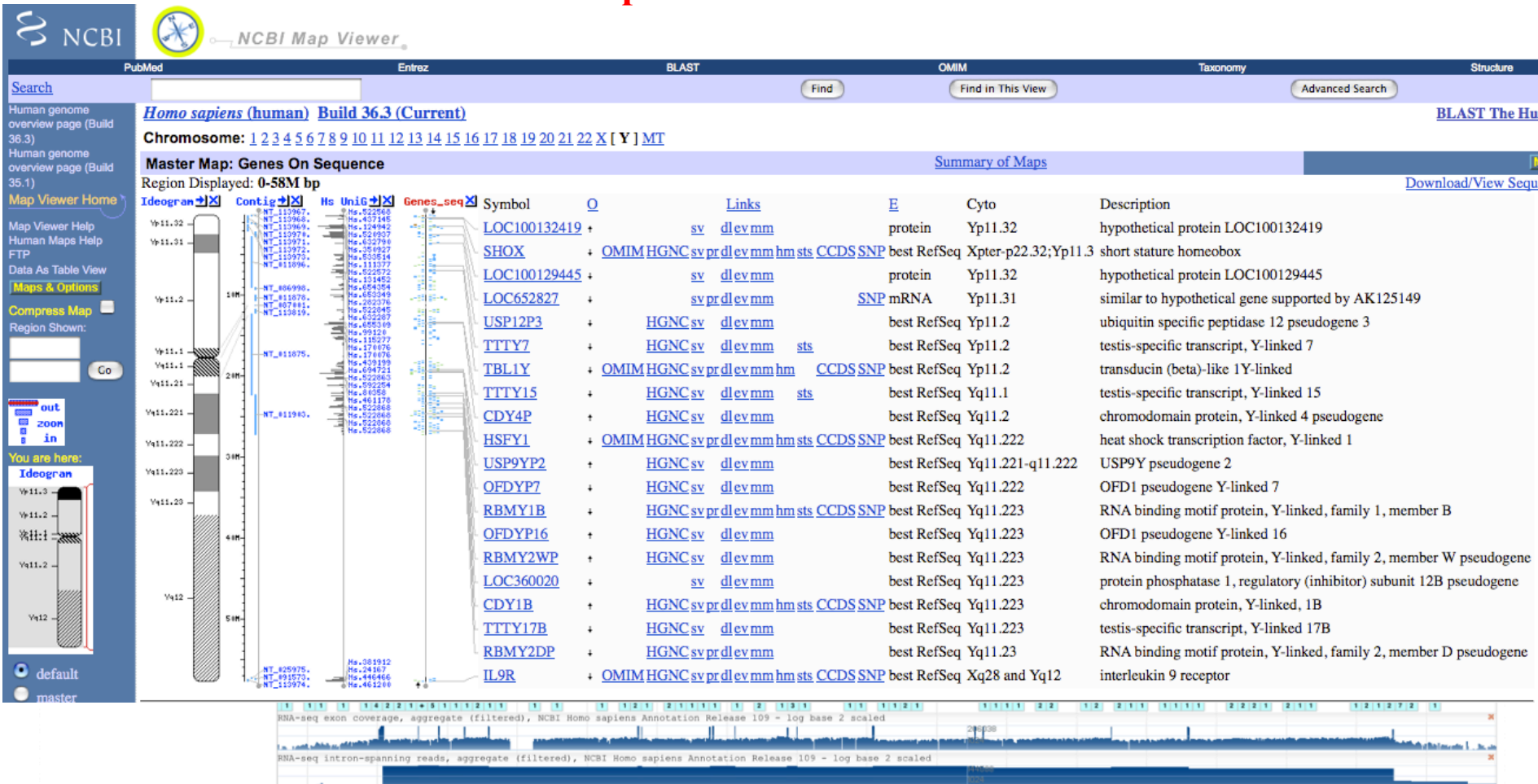
	GRCh38	GRCh37
Reference Genome Sequence	Fasta	Fasta
RefSeq Reference Genome Annotation	gff3	gff3

4. Les analyses génomiques




4. Les analyses génomiques


Ici un Map Viewer sur le chromosome Y.



4. Les analyses génomiques







Genome Home ▸ Genome Resource Guides



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Legend

-  Genome Resources
-  BLAST
-  Map Viewer
-  Genome Project

NCBI Genome Resource Guides








Access to genome resource guides for selected organisms.

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...

5. Les analyses protéiques

5. Les analyses protéiques

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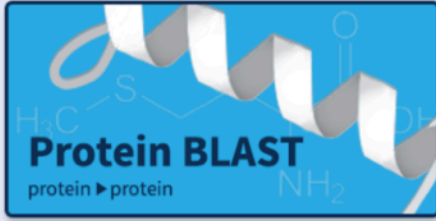
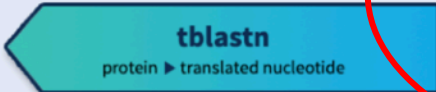

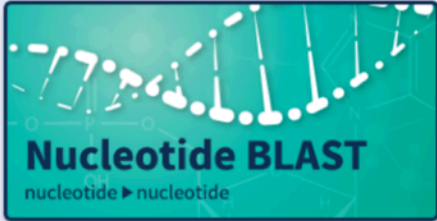
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Basic Local Alignment Search Tool

BLAST finds regions of similarity between biological sequences. The program compares nucleotide or protein sequences to sequence databases and calculates the statistical significance. [Learn more](#)

NEWS
Using BLAST Well, How to Maximize Your Search Efforts: Webinar on October 3, 2018
In this webinar, the NCBI BLAST team lead will show you how to be more effective with BLAST.
Thu, 27 Sep 2018 11:00:00 EST [More BLAST news...](#)

Web BLAST




BLAST Genomes

Enter organism common name, scientific name, or tax id
Use up and down arrows to choose an item from the autocomplete.
Human Mouse Rat Microbes **Search**

Idem sur les protéines...

5. Les analyses protéiques

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blastnblastptblastxtblastntblastx

BLASTP programs search protein databases using a protein query. [more](#)

Enter Query Sequence

Enter accession number, gi, or FASTA sequence  [Clear](#)


AQECHSNPRCCSFASNMPYALLSSSVFYLP LLVMLFVYARVFVAKRQRRFVRRELGRFPPEESPRSP

Query subrange 


From

To

Or, upload file

Parcourir... 


Job Title

Enter a descriptive title for your BLAST search 

☐ Blast 2 sequences

Choose Search Set


Database

Non-redundant protein sequences (nr) 

Organism


Optional

Enter organism name or id—completions will be suggested

Enter organism common name, binomial, or tax id. Only 20 top taxa will be shown. 

Entrez Query

Optional

Enter an Entrez query to limit search 


Program Selection

Algorithm

☒ blastp (protein-protein BLAST)

☐ PSI-BLAST (Position-Specific Iterated BLAST)

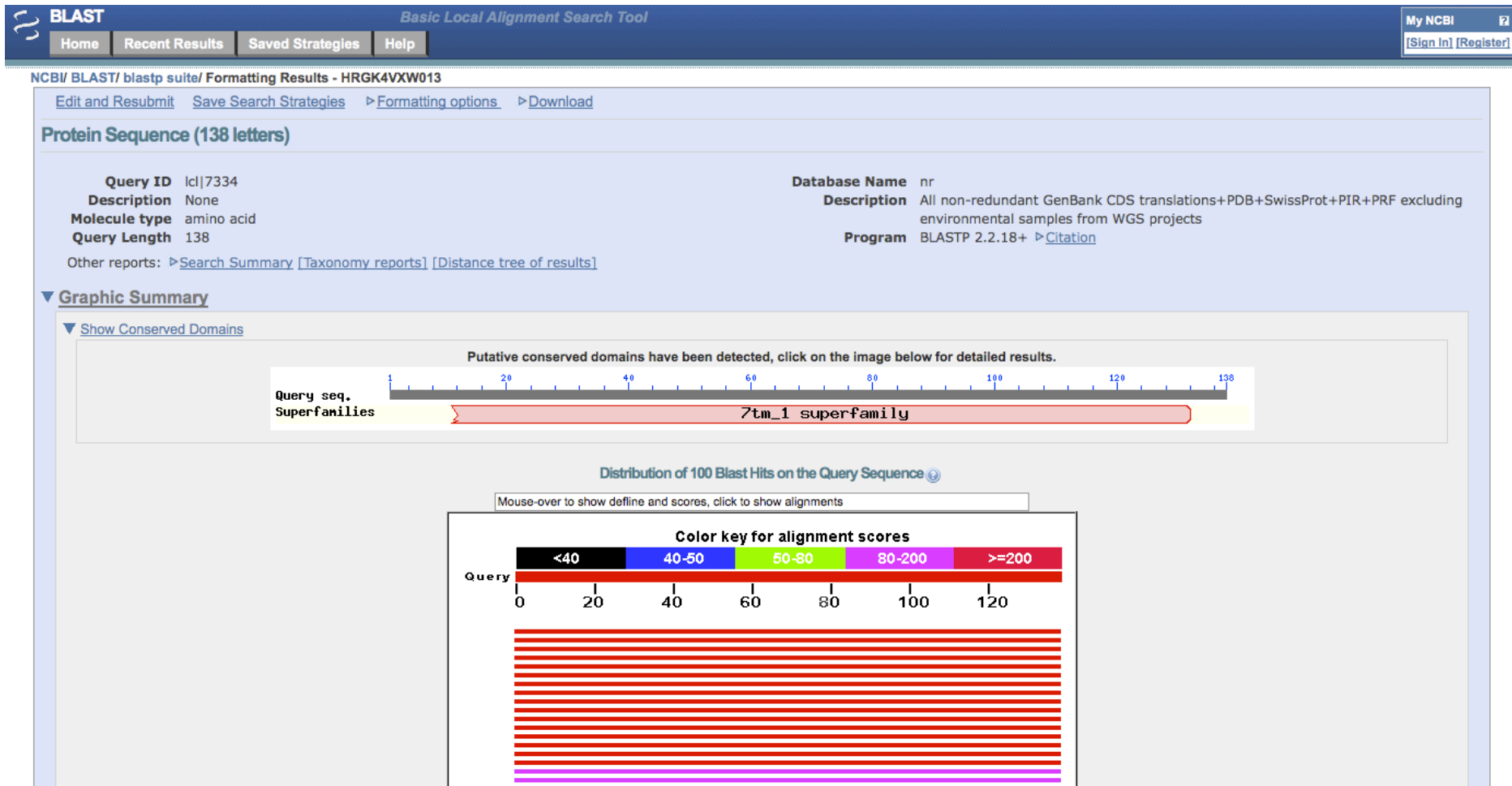
☐ PHI-BLAST (Pattern Hit Initiated BLAST)

Choose a BLAST algorithm 

BLAST

Search database nr using Blastp (protein-protein BLAST)

5. Les analyses protéiques



5. Les analyses protéiques

▼ **Alignments** ☐ Select All [Get selected sequences](#) [Distance tree of results](#)

```
> ☐ ref|NP_037240.1| UG adrenergic, beta-3-, receptor [Rattus norvegicus]
  gb|AAA74470.1| G 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 AQECHSNPRCCSFASNMPYALLSSSVSFYLLVLMFVYARVFVVAKRQRRFVRRELGRF 60
      AQECHSNPRCCSFASNMPYALLSSSVSFYLLVLMFVYARVFVVAKRQRRFVRRELGRF
Sbjct 183 AQECHSNPRCCSFASNMPYALLSSSVSFYLLVLMFVYARVFVVAKRQRRFVRRELGRF 242

Query 61 PPEESPRSPSRSPSPATVGTPTASDGVPSGRRPARLLPLGEHRALRTLGLIMGIFSLCW 120
      PPEESPRSPSRSPSPATVGTPTASDGVPSGRRPARLLPLGEHRALRTLGLIMGIFSLCW
Sbjct 243 PPEESPRSPSRSPSPATVGTPTASDGVPSGRRPARLLPLGEHRALRTLGLIMGIFSLCW 302

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


6. Exemple publication utilisant la bioinfo

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A Rapid Screening Assay to Search for Phosphorylated Proteins in Tissue Extracts

Ignazio Garaguso, Juergen Borlak*

Centre for Pharmacology and Toxicology, Hannover Medical School, Hannover, Germany

Abstract

Reversible protein phosphorylation is an essential mechanism in the regulation of diverse biological processes, nonetheless is frequently altered in disease. As most phosphoproteome studies are based on optimized *in-vitro* cell culture studies new methods are in need to improve *de novo* identification and characterization of phosphoproteins in extracts from tissues. Here, we describe a rapid and reliable method for the detection of phosphoproteins in tissue extract based on an experimental strategy that employs 1D and 2D SDS PAGE, Western immunoblotting of phosphoproteins, in-gel protease digestion and enrichment of phosphopeptides using metal oxide affinity chromatography (MOAC). Subsequently, phosphoproteins are identified by MALDI-TOF-MS/MS with the CHCA-TL or DHB ML sample matrix preparation method and further characterized by various bioinformatic software tools to search for candidate kinases and phosphorylation-dependent binding motifs. The method was applied to mouse lung tissue extracts and resulted in an identification of 160 unique phosphoproteins. Notably, TiO₂ enrichment of pulmonary protein extracts resulted in an identification of additional 17 phosphoproteins and 20 phosphorylation sites. By use of MOAC, new phosphorylation sites were identified as evidenced for the advanced glycosylation end product-specific receptor. So far this protein was unknown to be phosphorylated in lung tissue of mice. Overall the developed methodology allowed efficient and rapid screening of phosphorylated proteins and can be employed as a general experimental strategy for an identification of phosphoproteins in tissue extracts.

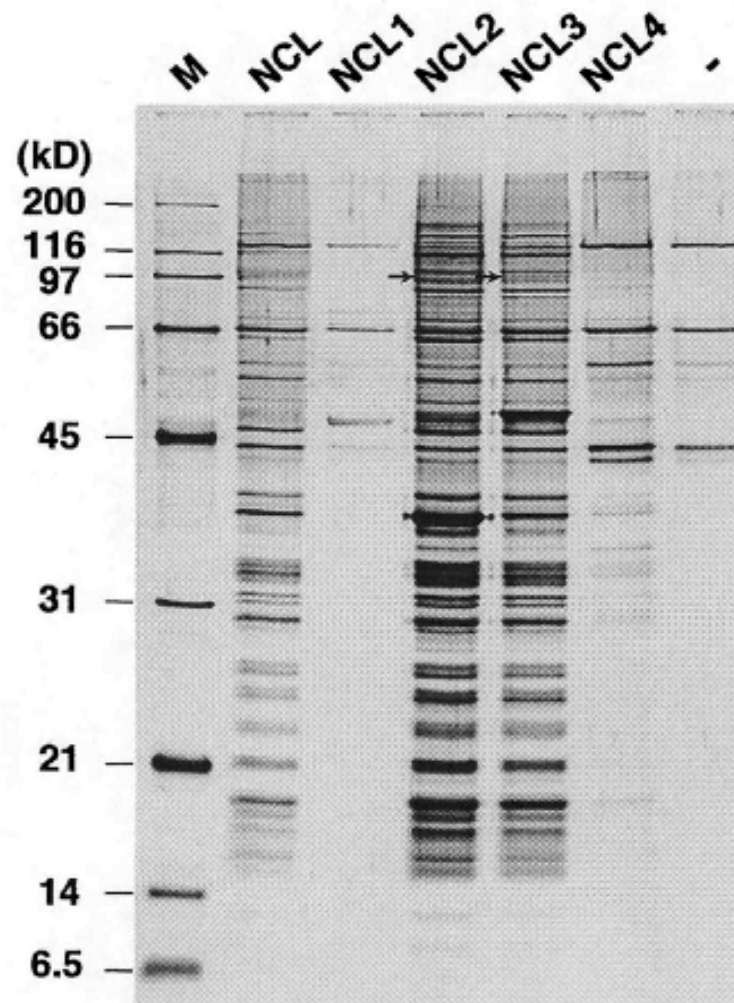
Citation: Garaguso I, Borlak J (2012) A Rapid Screening Assay to Search for Phosphorylated Proteins in Tissue Extracts. PLoS ONE 7(11): e50025. doi:10.1371/journal.pone.0050025

Editor: Christina Lynn Addison, Ottawa Hospital Research Institute, Canada

Received: August 30, 2012; **Accepted:** October 19, 2012; **Published:** November 15, 2012

5. Les analyses protéiques

Migration de protéines: Gel en 1 dimension



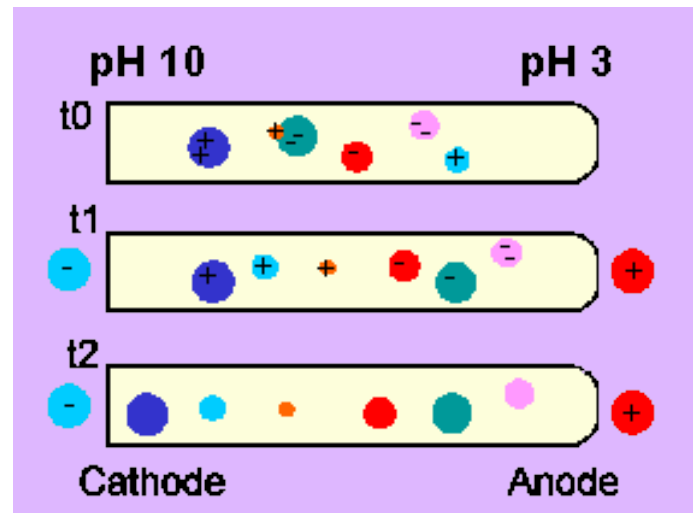
Les protéines migrent selon leur poids moléculaire

5. *Les analyses protéiques*

- L'électrophorèse bidimensionnelle consiste à séparer les protéines :
 - dans une première dimension par focalisation isoélectrique (IEF) selon leur pI
 - dans une deuxième direction, perpendiculaire à la première, selon leur poids moléculaire.

5. Les analyses protéiques

- Première dimension : IEF (électrofocalisation)
 - Gradient de pH sous l'effet d'un champ électrique
 - Migration des protéines à travers le gradient de pH jusqu'à une charge nette nulle lorsqu'elles atteignent leur pI



5. Les analyses protéiques

1ère dimension :
Électrofocalisation
(gradient de pH)

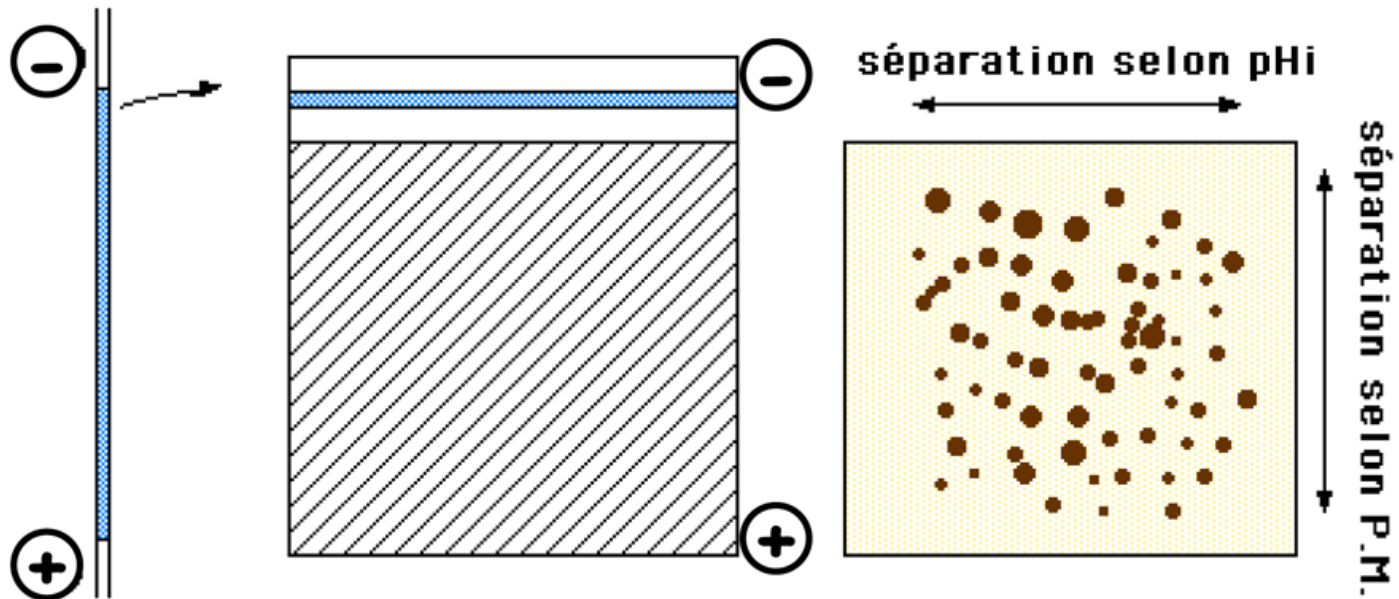


5. Les analyses protéiques

1ère dimension : Électrofocalisation
(gradient de pH)

2ème dimension : Gel dénaturant
(SDS-PAGE)

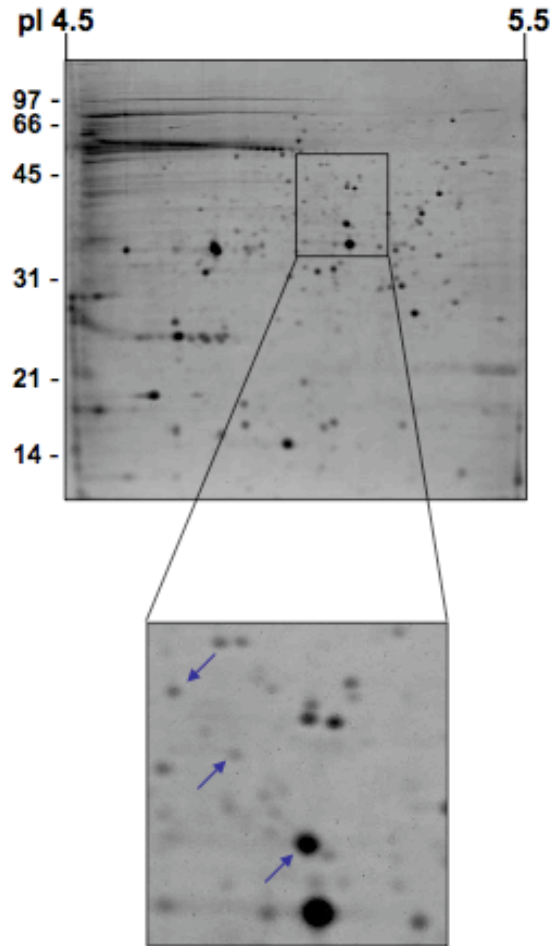
Coloration
(bleu de Coomassie;
 AgNO_3)



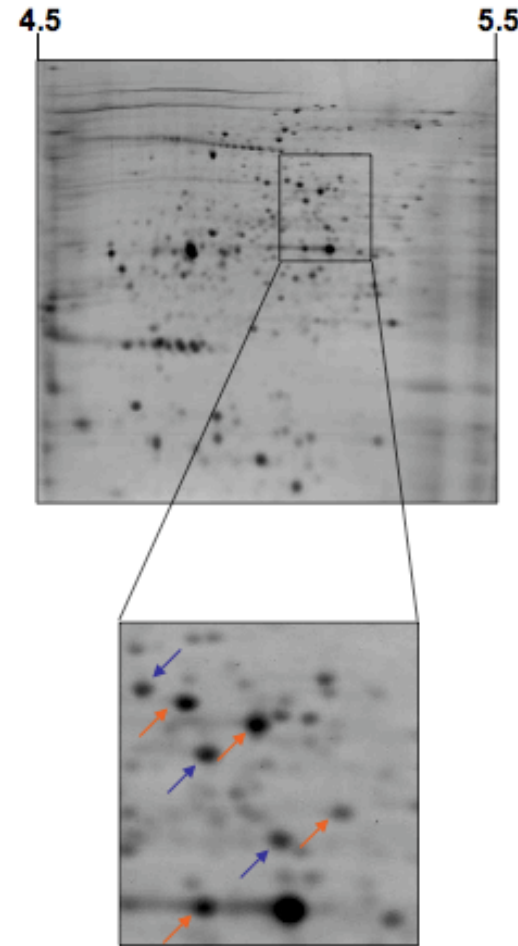
5. Les analyses protéiques

Etudes différentielles

Condition 1



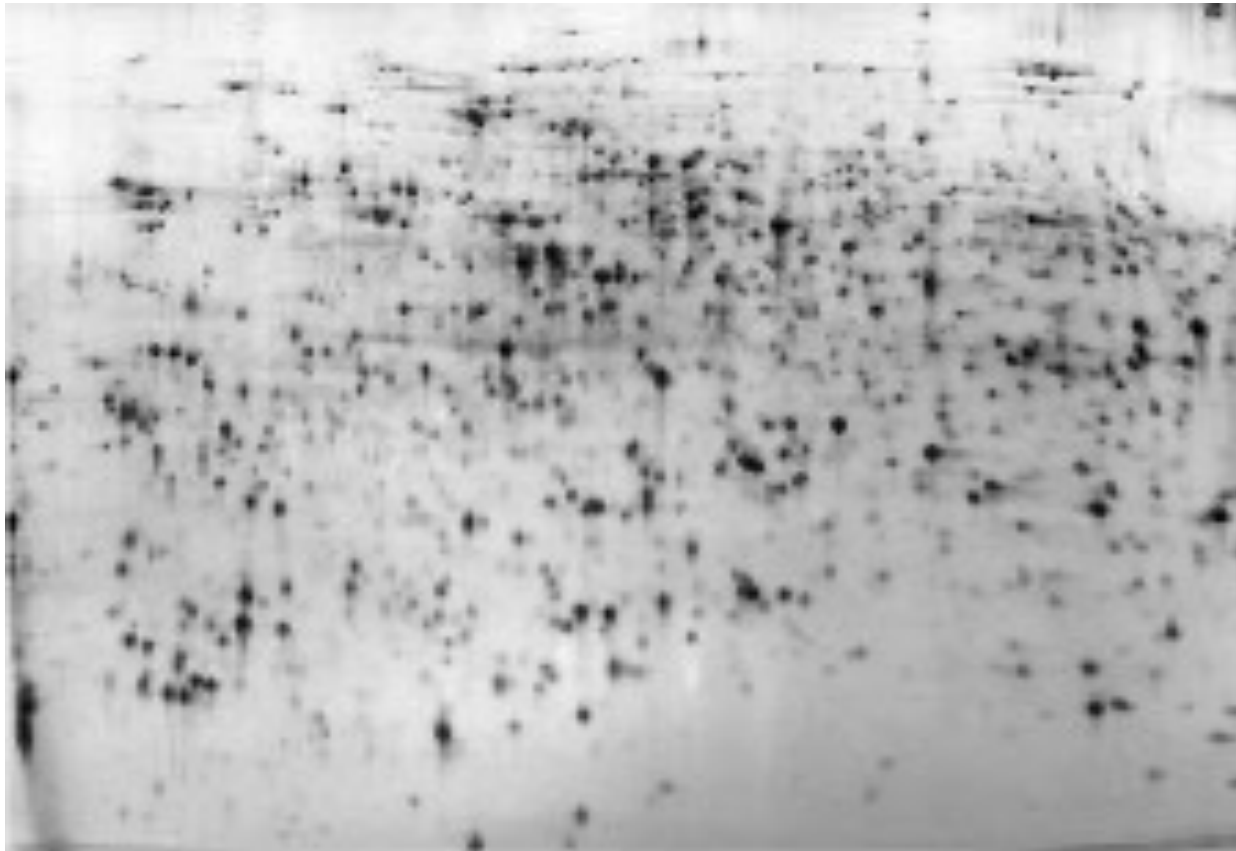
Condition 2



↗ stage-specific
↙ altered expression level

5. Les analyses protéiques

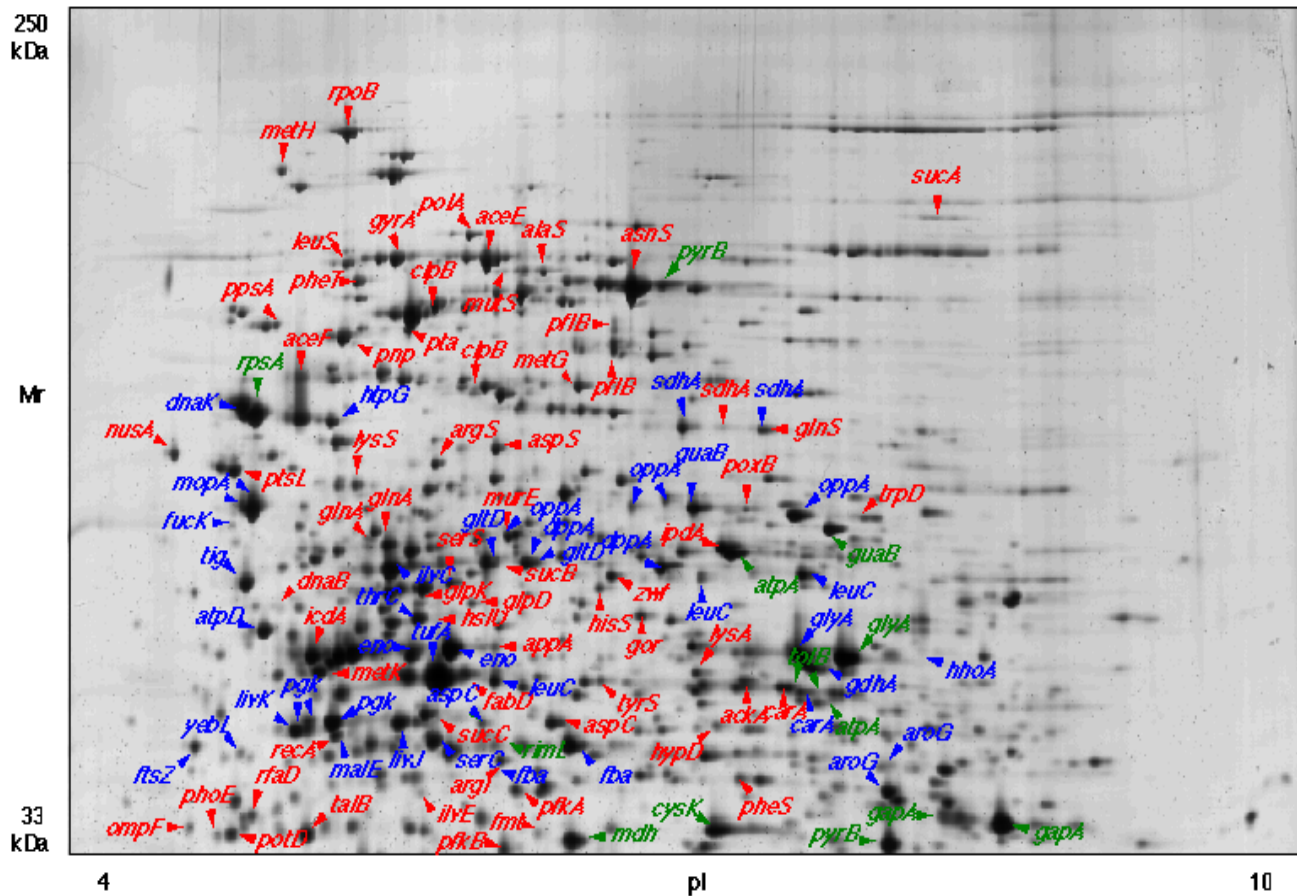
- Il existe des banques de données de résultats



E. coli

5. Les analyses protéiques

- Il existe des banques de données de résultats




E. coli


5. Les analyses protéiques

<http://expasy.org/ch2d/>

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**SWISS-2DPAGE**
Two-dimensional polyacrylamide gel electrophoresis database

**SIB** 10
Pioneers at the heart of science
2008 - 10th Anniversary

Discover the
Chromosome
Walk

SWISS-2DPAGE contains data on proteins identified on various 2-D PAGE and SDS-PAGE reference maps. You can locate these proteins on the 2-D PAGE maps or display the region of a 2-D PAGE map where one might expect to find a protein from UniProtKB/Swiss-Prot [[More details](#) / [References](#) / [Linking to SWISS-2DPAGE](#) / [Commercial users](#) / [Disclaimer](#)].

Release 18.6, September 2006 and updates up to 31-January-2008 (contains 1265 entries in 36 reference maps from human, mouse, *Arabidopsis thaliana*, *Dictyostelium discoideum*, *Escherichia coli*, *Saccharomyces cerevisiae*, and *Staphylococcus aureus* (N315)).

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Access to SWISS-2DPAGE

- [by description](#) (any word in the DE, OS, GN and ID lines)
- [by accession number](#) (AC lines)
- [by clicking on a spot](#): select one of our 2-D PAGE or SDS-PAGE reference maps, click on a spot and then get the corresponding information from the SWISS-2DPAGE database.
- [by author](#) (RA lines)
- [by spot serial number](#) (2D and 1D lines)
- [by experimental pI/Mw range](#)
- [by experimental identification methods](#)
- [by full text search](#)
- [retrieve all the protein entries identified on a given reference map](#)
- [complex queries](#) (SRS like)
- [compute estimated location on reference maps for a user-entered sequence](#)

SWISS-2DPAGE documents

- [User manual](#)
- [Release notes](#) (September 26, 2006)
- [FAQ](#) (Frequently Asked Questions about SWISS-2DPAGE)
- **Protocols:**
 - [Technical information](#) about 2-D PAGE (IPG's, silver staining, protocols, etc)
 - [High performance 2-D gel comparison](#)
- **Figure captions of SWISS-2DPAGE maps available from publications:**
 - Human CSF, ELC, HEPG2, HEPG2SP, LIVER, LYMPHOMA, PLASMA, PLATELET, RBC, U937, CEC, KIDNEY.
 - *Dictyostelium discoideum*, *Escherichia coli*, *Saccharomyces cerevisiae*.

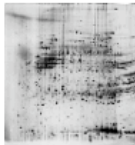
5. Les analyses protéiques

<http://expasy.org/ch2d/>

Homo sapiens (Human)

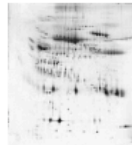
CEC_HUMAN

{ Colorectal epithelia cells }
Tissue: Colon epithelium



CSF_HUMAN

{ Cerebrospinal Fluid }
Tissue: Cerebrospinal fluid



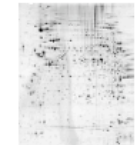
DLD1_HUMAN

{ Colorectal adenocarcinoma cell line (DL-1) }
Tissue: Colon adenocarcinoma



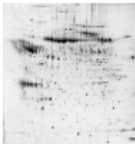
ELC_HUMAN

{ Erythroleukemia Cell }
Tissue: Erythroleukemia



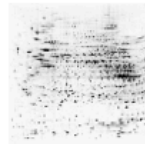
HEPG2SP_HUMAN

{ HepG2 Secreted Proteins }
Tissue: Hepatoblastoma



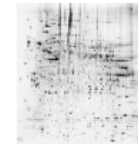
HEPG2_HUMAN

{ HepG2 }
Tissue: Hepatoblastoma



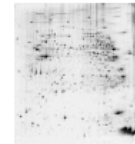
HL60_HUMAN

{ Promyelocytic leukemia cells }
Tissue: Promyelocytic leukemia



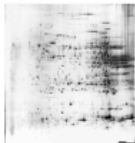
KIDNEY_HUMAN

{ Kidney }
Tissue: Kidney



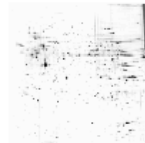
LIVER_HUMAN

{ Liver }
Tissue: Liver



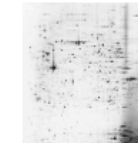
LYMPHOCYTE_HUMAN

{ Lymphocytes }
Tissue: Lymphocyte



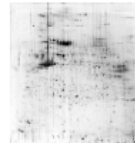
LYMPHOMA_HUMAN

{ Lymphoma }
Tissue: Lymphoma



NUCLEI_LIVER_HUMAN

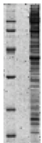
{ Soluble nuclear proteins and matrix from liver tissue }
Tissue: Liver



NUCLEOLI_HELA_1D_HUMAN

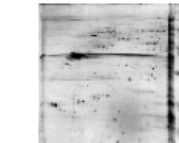
{ SDS-PAGE of nucleolar proteins from Human HeLa cells } { 2D-PAGE of nucleolar proteins from Human HeLa cells }

Tissue: Cervix carcinoma



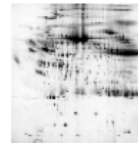
NUCLEOLI_HELA_2D_HUMAN

{ 2D-PAGE of nucleolar proteins from Human HeLa cells }



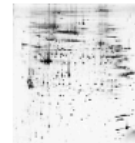
PLASMA_HUMAN

{ Plasma }
Tissue: Plasma



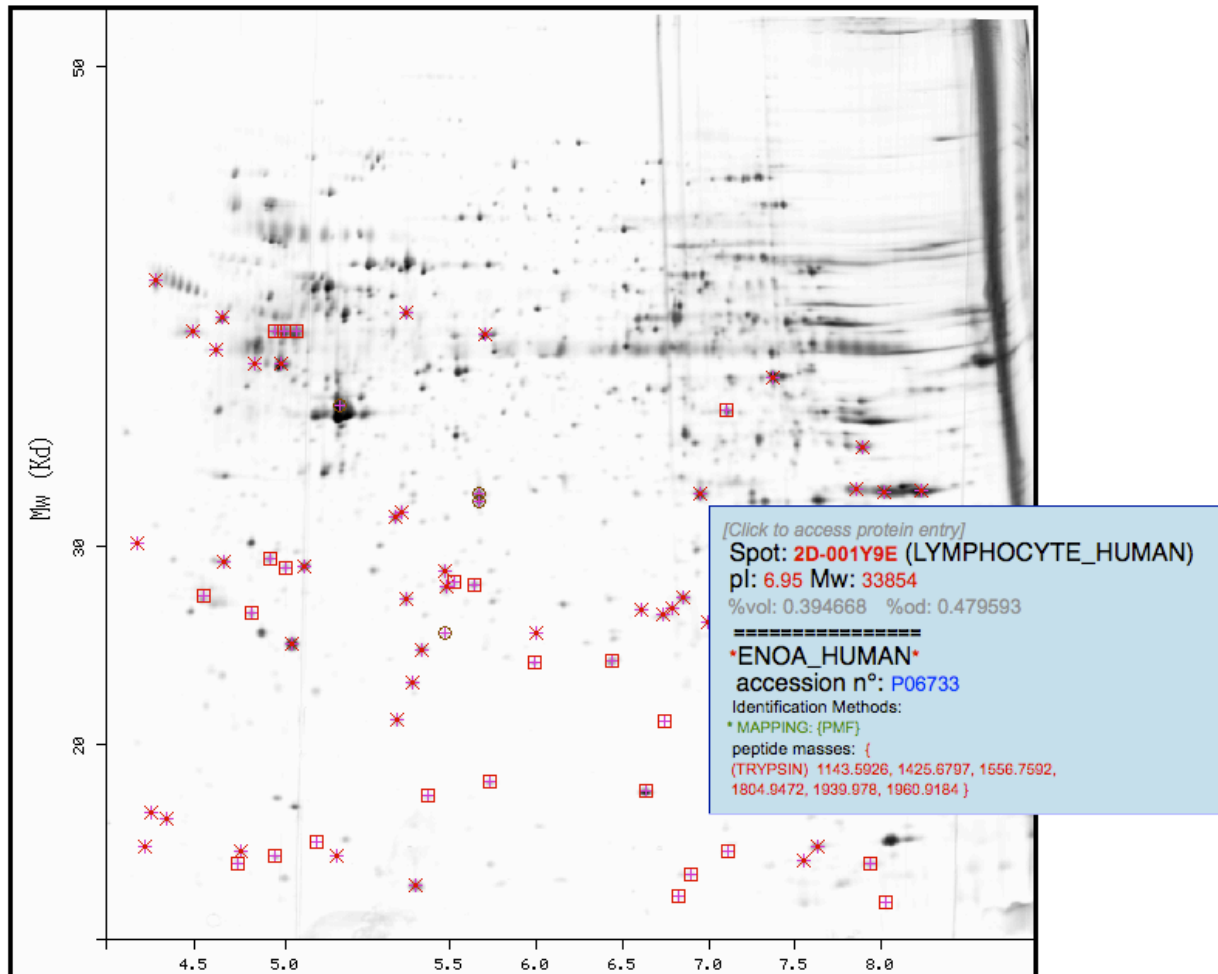
PLATELET_HUMAN

{ Platelet }
Tissue: Platelet

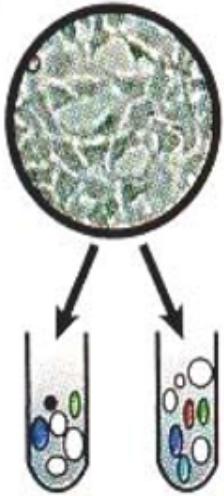


5. Les analyses protéiques

Get more information by dragging your mouse pointer over any spot, or click on a spot to access all its associated protein entries.



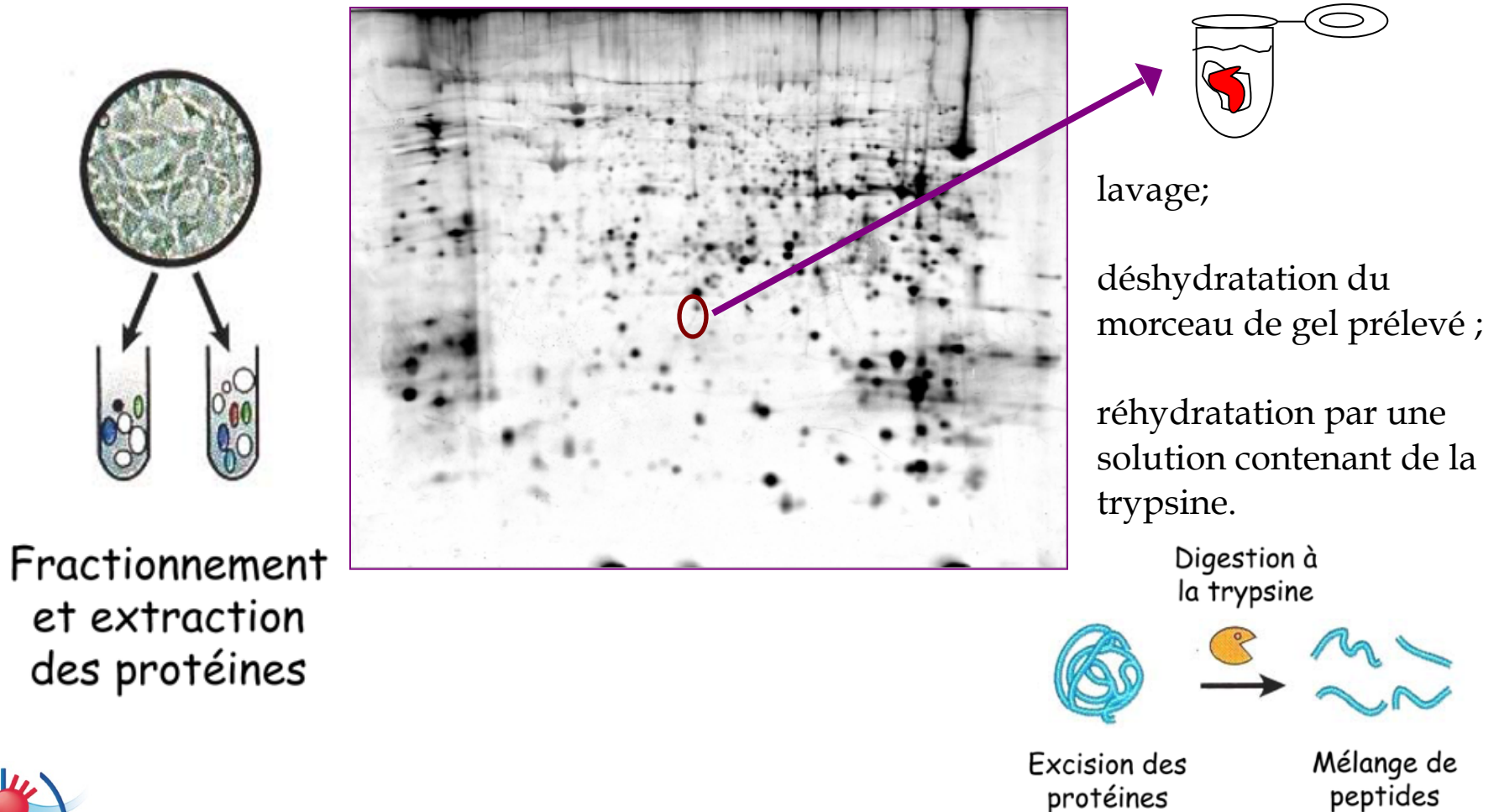
5. Les analyses protéiques



Fractionnement
et extraction
des protéines

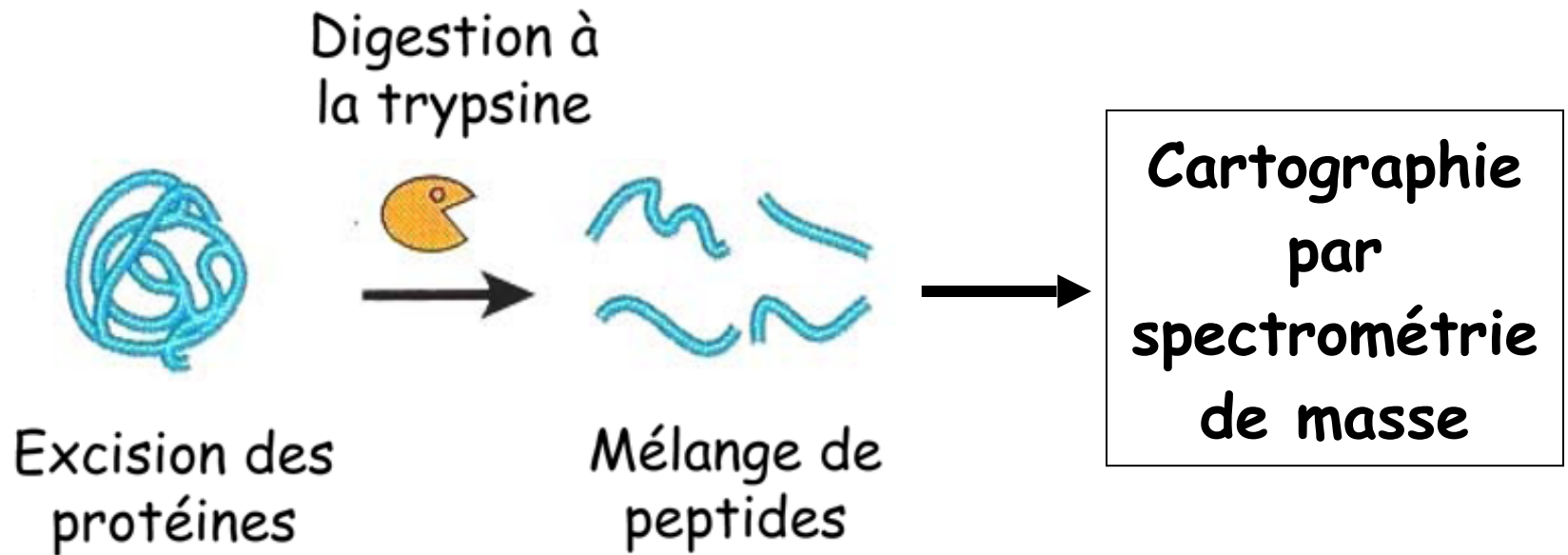
5. Les analyses protéiques

Après avoir repéré la protéine d'intérêt sur le gel 2D, on excise le spot



Une série de peptides résultant de la digestion de la protéine

5. Les analyses protéiques



5. Les analyses protéiques

- Définition

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.

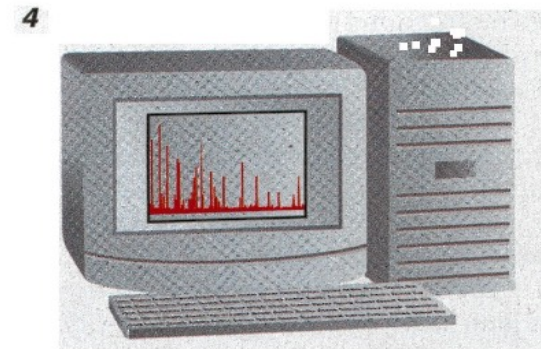
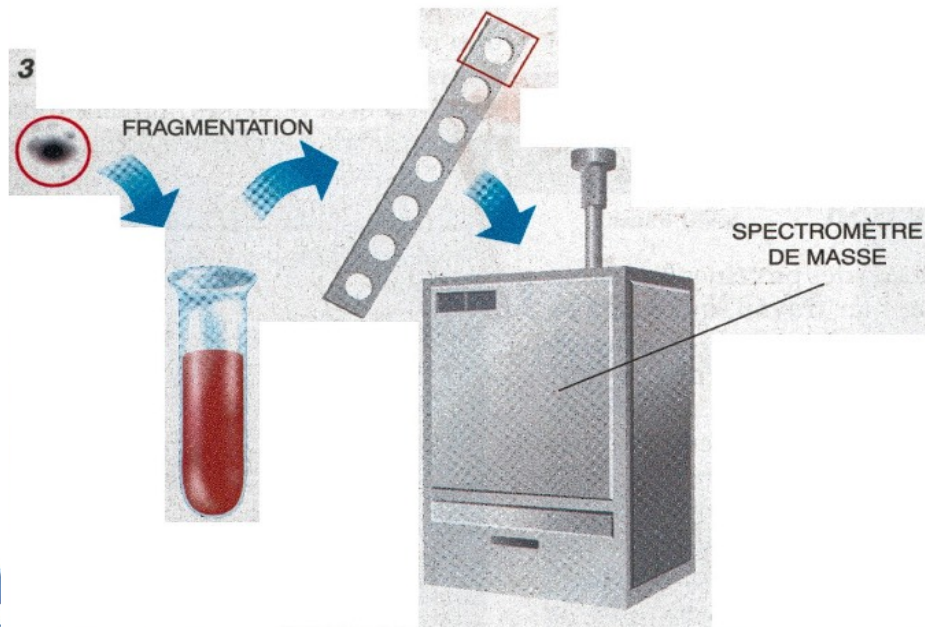
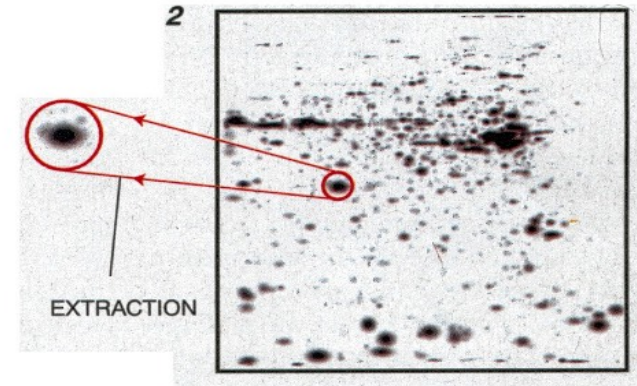
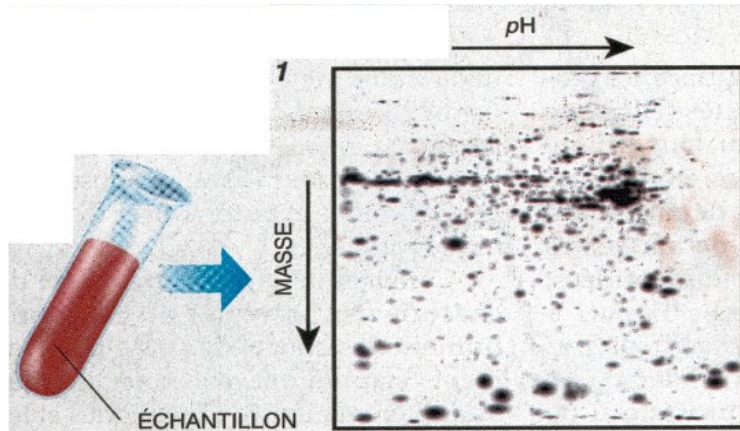
5. Les analyses protéiques

- La spectrométrie de masse
 - Utilisée pour identifier une protéine, ou suivre ses modifications,
 - Mesure la masse des peptides issus d'une digestion trypsique,
 - Les bases de données de séquences permettent de prédire la masse théorique des fragments de protéolyse : on peut identifier une protéine d'après le spectre de masse de ses fragments de protéolyse (il faut disposer de la séquence).

5. Les analyses protéiques

- Principe : Son principe réside dans la **séparation** en phase gazeuse de **molécules chargées** (ions) en fonction de leur rapport **masse/charge** (m/z). La spectrométrie de masse est utilisée dans pratiquement tous les domaines scientifiques : physique, astrophysique, chimie en phase gazeuse, chimie organique, dosages, biologie, médecine...
 - Substance analysée en phase gazeuse (diff RMN subst condensée)
 - Importance des paramètres de la phase de vaporisation de l'échantillon
 - Mesure du déplacement de particules chargées dans un champs électromagnétique
 - Importance des paramètres définissant l'ionisation de l'échantillon
 - Obtention d'un spectre de masse qui montre la variation d'un courant ionique en fonction de m/z
 - **Attention destruction de l'échantillon analysé !**

5. Les analyses protéiques



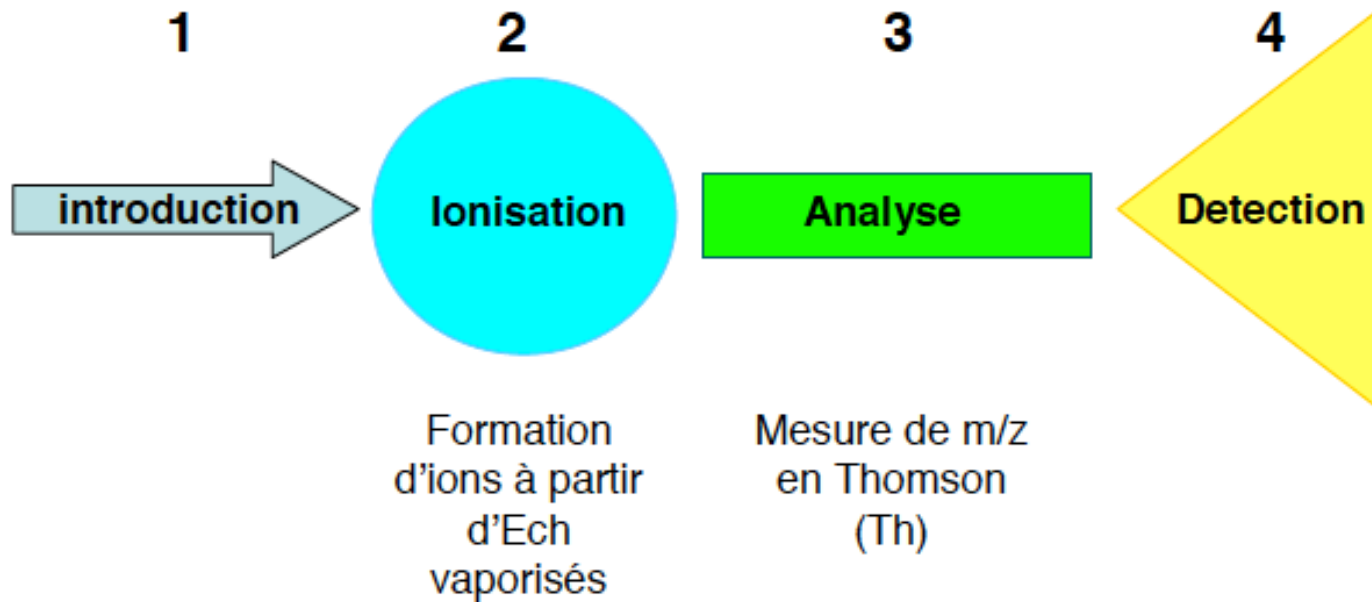
La spectrométrie de masse

5. Les analyses protéiques

La spectrométrie de masse

Le spectromètre de masse se compose donc de quatre parties :

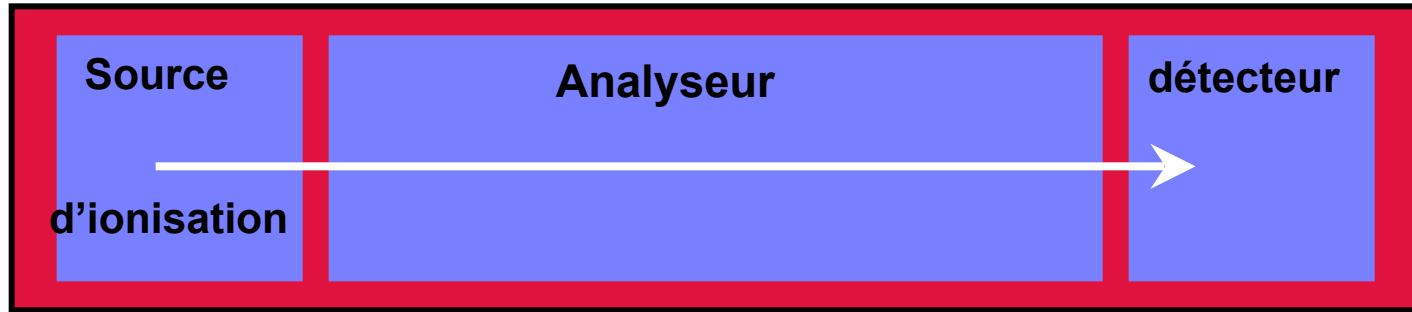
- 1- Le système d'introduction de l'échantillon
- 2- La source d'ionisation: elle consiste à vaporiser les molécules et à les ioniser.
- 3- L'analyseur
- 4- Le détecteur et système de traitement



5. Les analyses protéiques

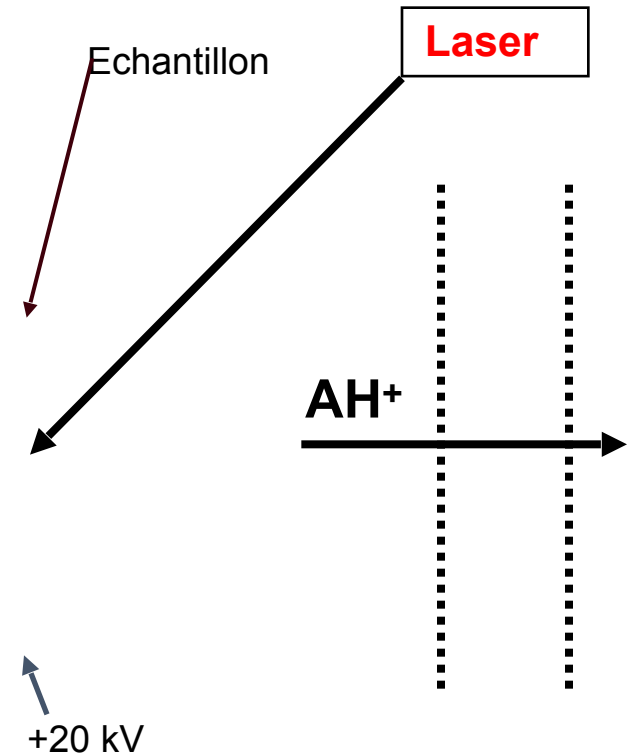
La spectrométrie de masse

1/2



Source d'ionisation :

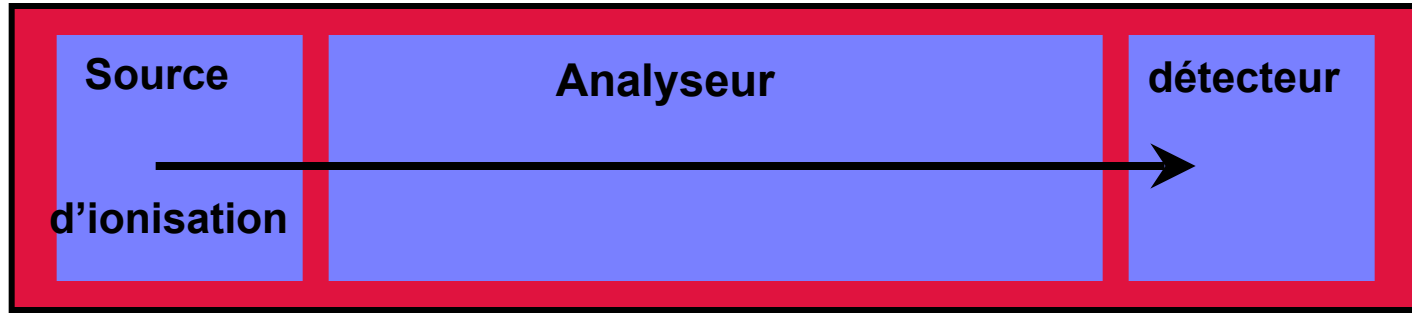
Les molécules doivent passer en phase gazeuse et s'ioniser



5. Les analyses protéiques

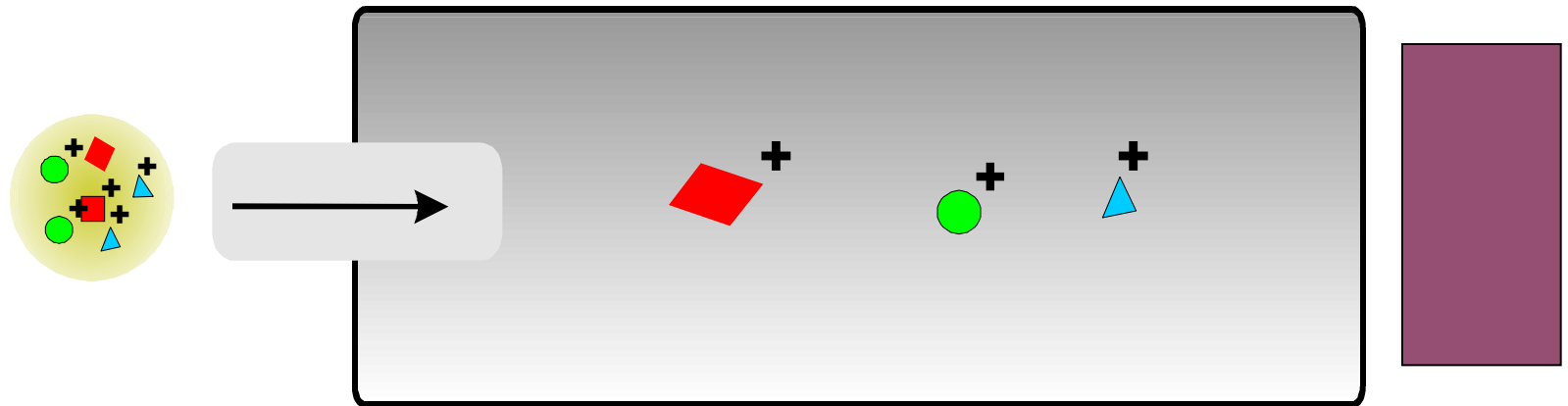
3

La spectrométrie de masse



L'analyseur de masse

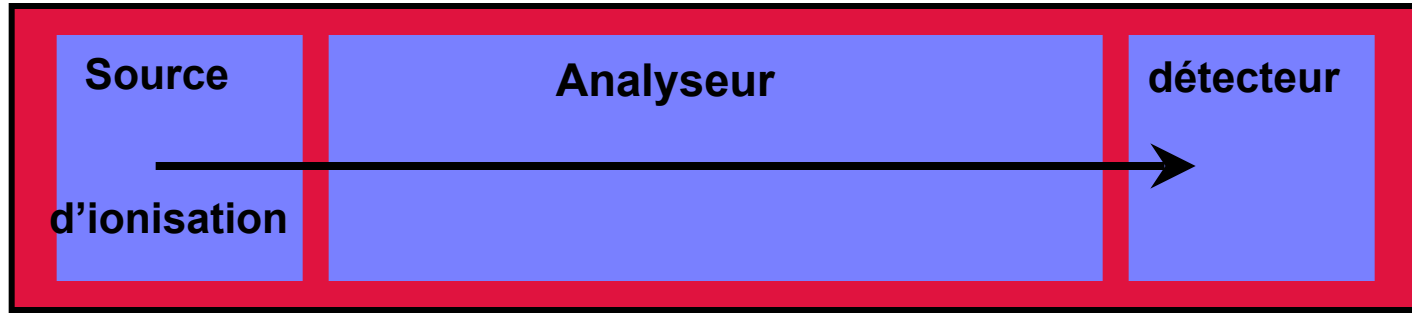
Détecteur



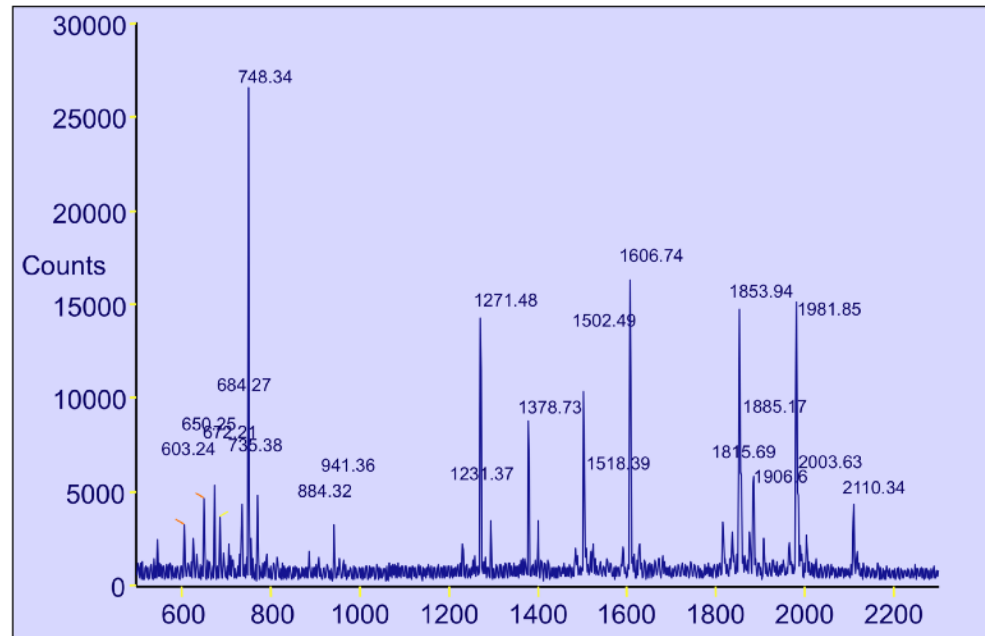
5. Les analyses protéiques

4

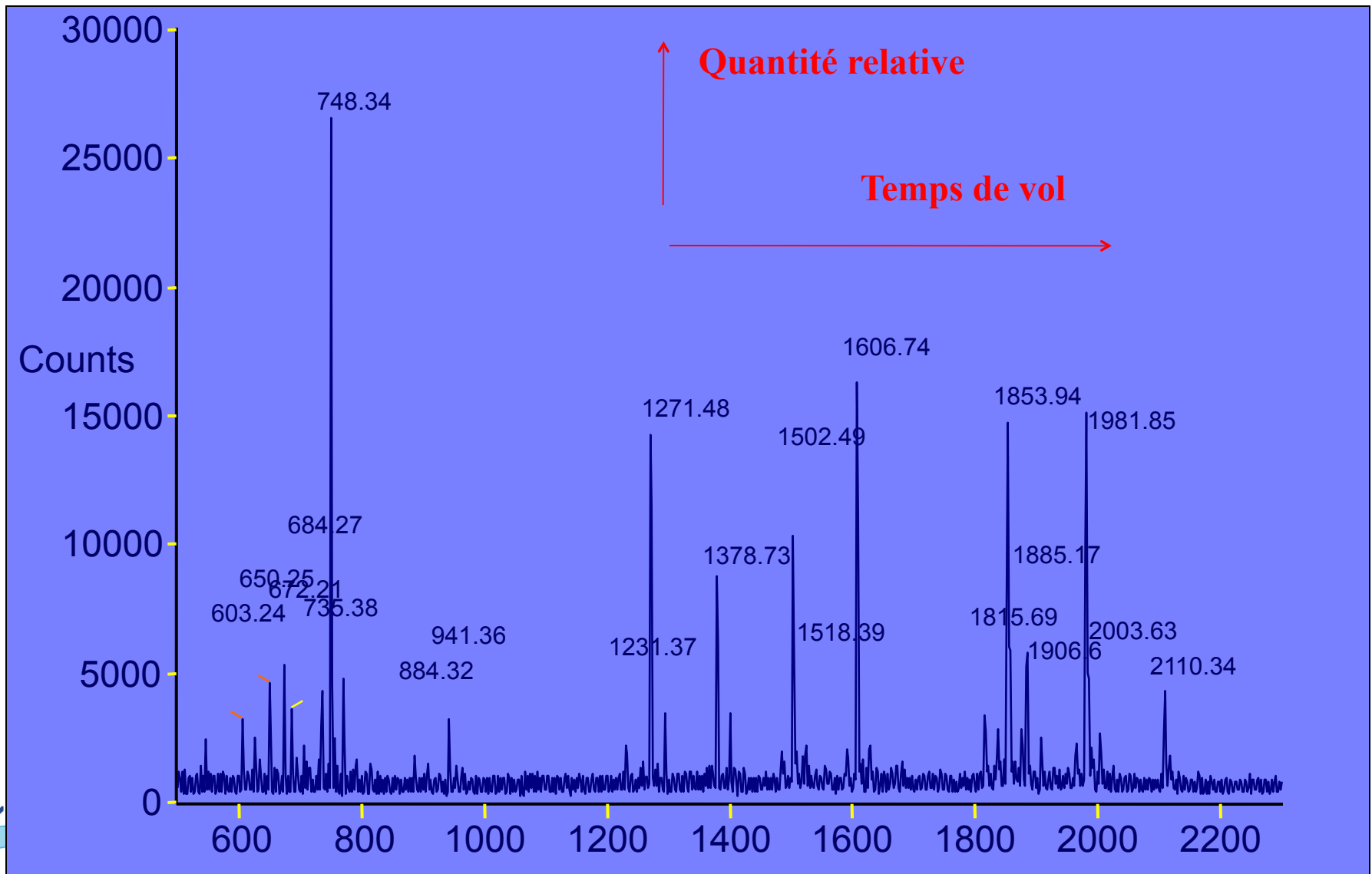
La spectrométrie de masse



Détecteur

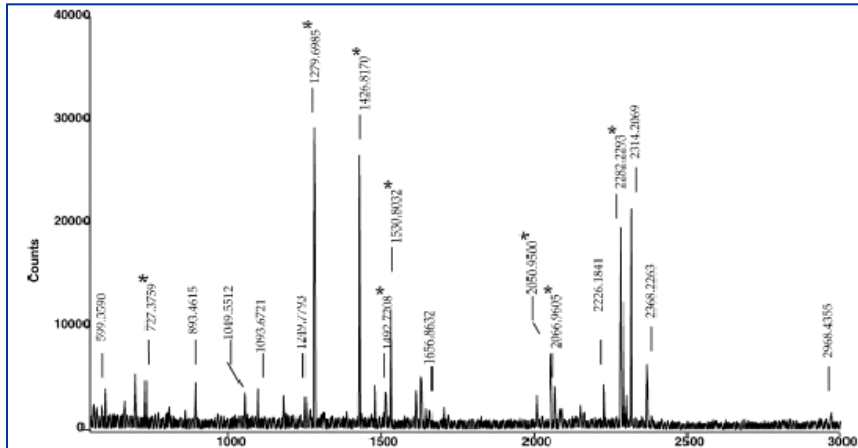


5. Les analyses protéiques



5. Les analyses protéiques

Cartographie massique par SM

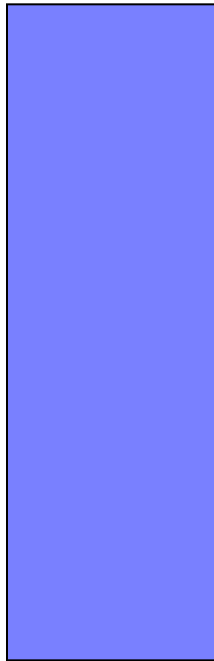


4148.1061
3221.5113
3392.5756
2993.3522
2468.2415
2325.0207
2144.9770
1948.9585
2005.9800
1906.8817
1883.0497
1721.7765
1618.7577
1732.8006
1508.7889
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1007.4714
880.4159
832.3658
792.3709

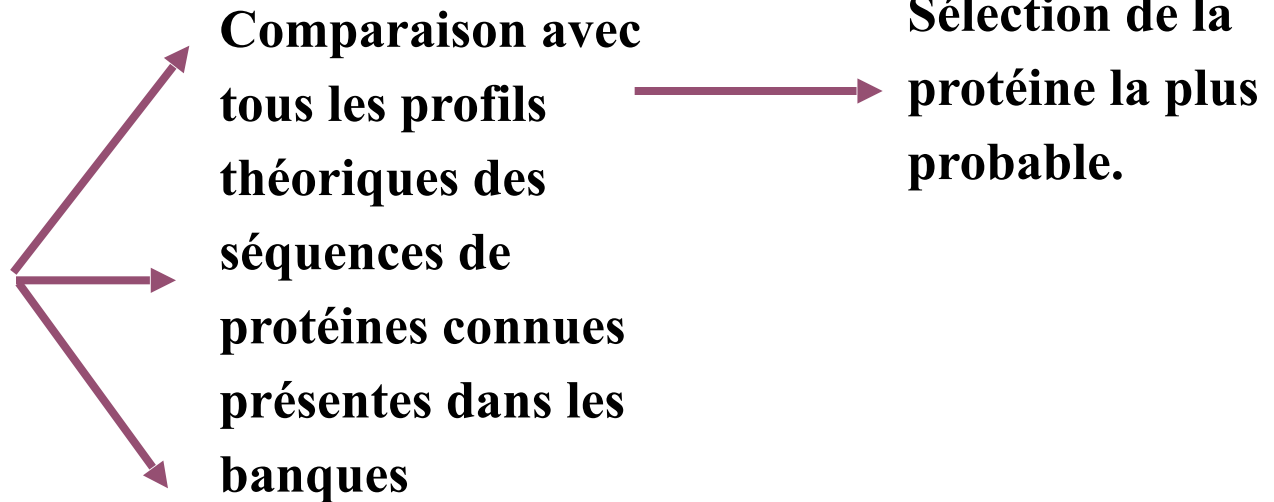
La carte massique obtenue est **l'empreinte massique** de la protéine. Elle est très spécifique.

5. Les analyses protéiques

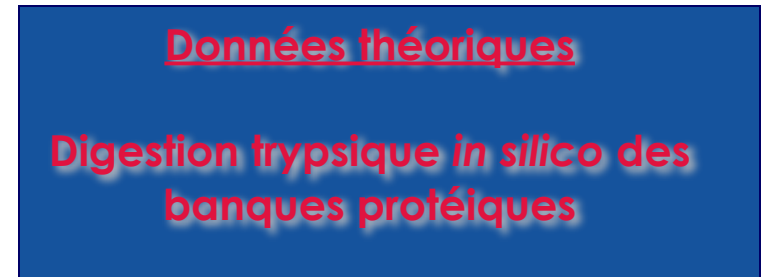
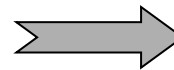
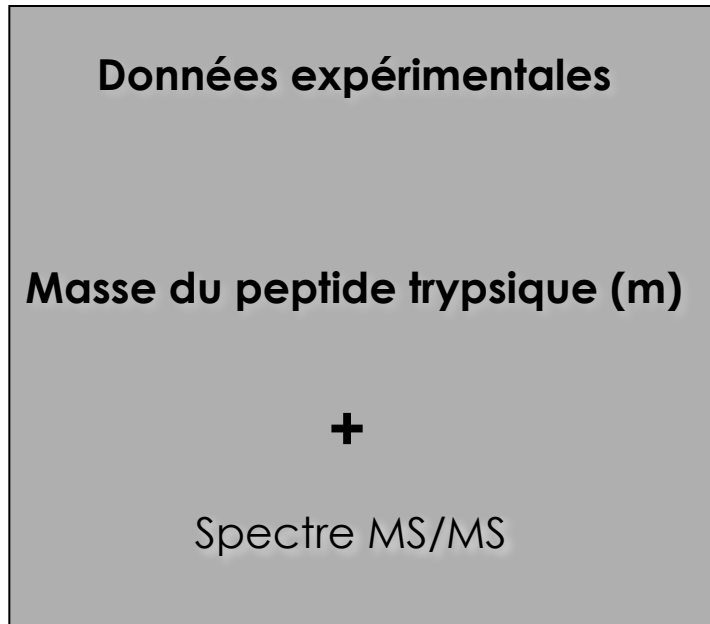
Liste de masses
expérimentale



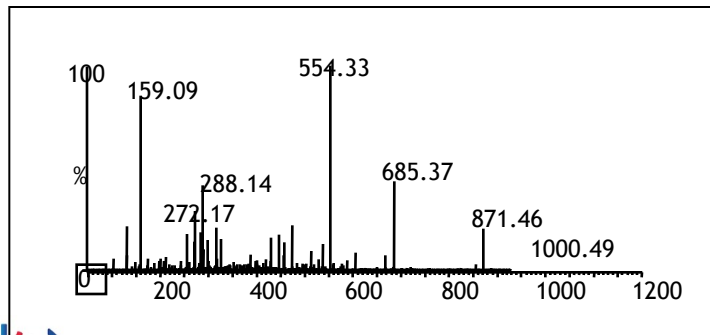
Interrogation des banques de données



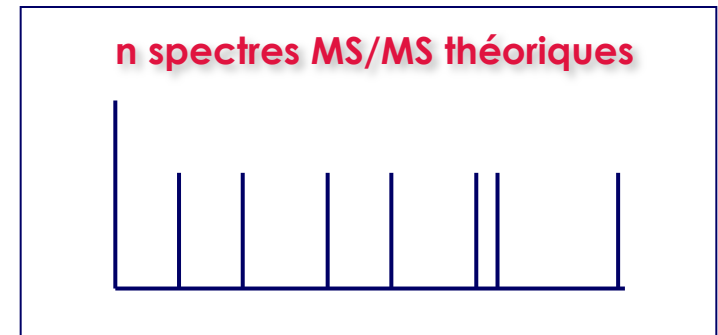
5. Les analyses protéiques



Sélection des n protéines pour lesquelles on attend un peptide tryptique de masse m



MASCOT



6. Exemple publication utilisant la bioinfo

OPEN ACCESS Freely available online



A Rapid Screening Assay to Search for Phosphorylated Proteins in Tissue Extracts

Ignazio Garaguso, Juergen Borlak*

Centre for Pharmacology and Toxicology, Hannover Medical School, Hannover, Germany

Un papier de 2012 mais qui est représentatif du cours...

Abstract

Reversible protein phosphorylation is an essential mechanism in the regulation of diverse biological processes, nonetheless is frequently altered in disease. As most phosphoproteome studies are based on optimized *in-vitro* cell culture studies new methods are in need to improve *de novo* identification and characterization of phosphoproteins in extracts from tissues. Here, we describe a rapid and reliable method for the detection of phosphoproteins in tissue extract based on an experimental strategy that employs 1D and 2D SDS PAGE, Western immunoblotting of phosphoproteins, in-gel protease digestion and enrichment of phosphopeptides using metal oxide affinity chromatography (MOAC). Subsequently, phosphoproteins are identified by MALDI-TOF-MS/MS with the CHCA-TL or DHB ML sample matrix preparation method and further characterized by various bioinformatic software tools to search for candidate kinases and phosphorylation-dependent binding motifs. The method was applied to mouse lung tissue extracts and resulted in an identification of 160 unique phosphoproteins. Notably, TiO₂ enrichment of pulmonary protein extracts resulted in an identification of additional 17 phosphoproteins and 20 phosphorylation sites. By use of MOAC, new phosphorylation sites were identified as evidenced for the advanced glycosylation end product-specific receptor. So far this protein was unknown to be phosphorylated in lung tissue of mice. Overall the developed methodology allowed efficient and rapid screening of phosphorylated proteins and can be employed as a general experimental strategy for an identification of phosphoproteins in tissue extracts.

Citation: Garaguso I, Borlak J (2012) A Rapid Screening Assay to Search for Phosphorylated Proteins in Tissue Extracts. PLoS ONE 7(11): e50025. doi:10.1371/journal.pone.0050025

Editor: Christina Lynn Addison, Ottawa Hospital Research Institute, Canada

Received: August 30, 2012; **Accepted:** October 19, 2012; **Published:** November 15, 2012

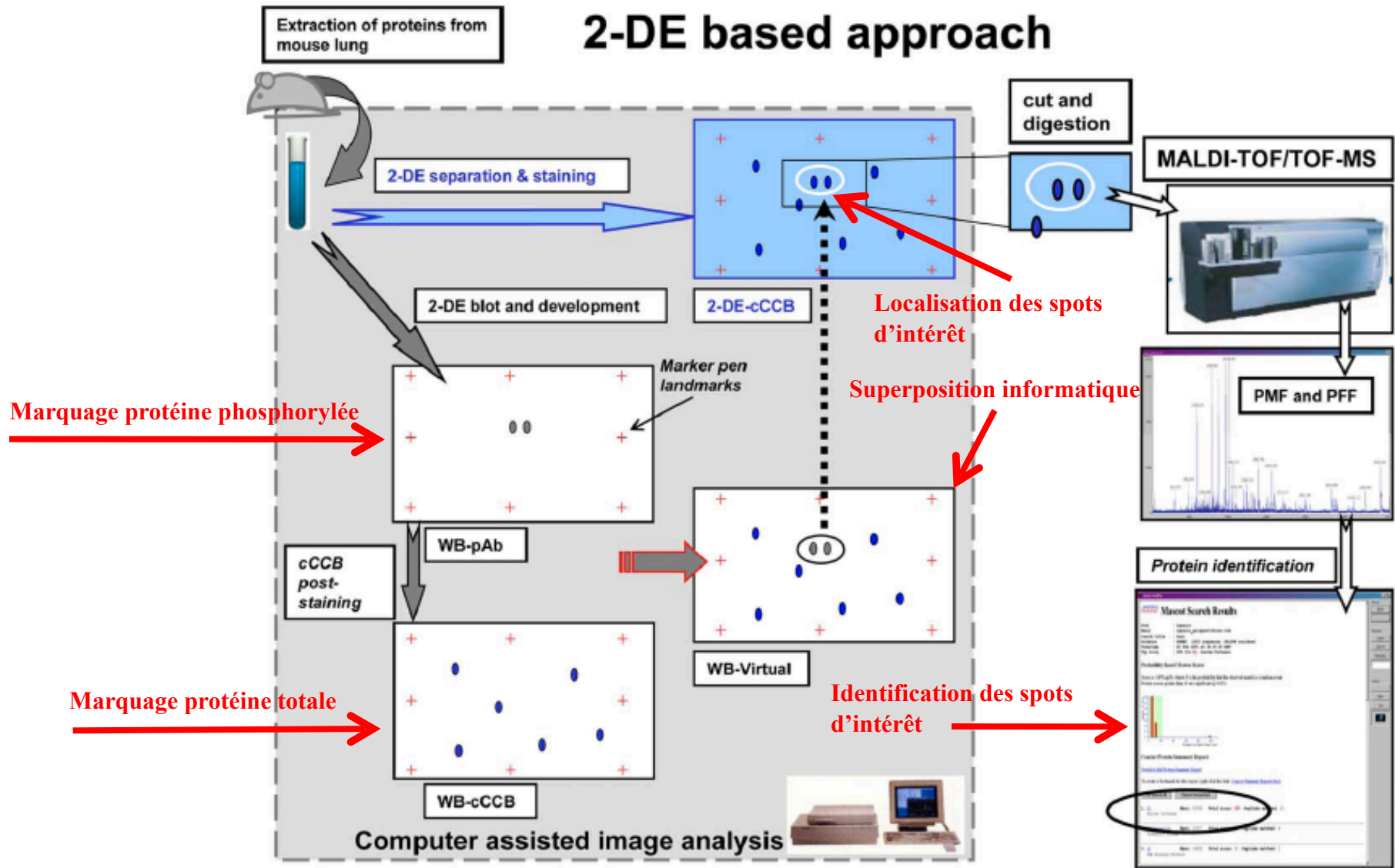
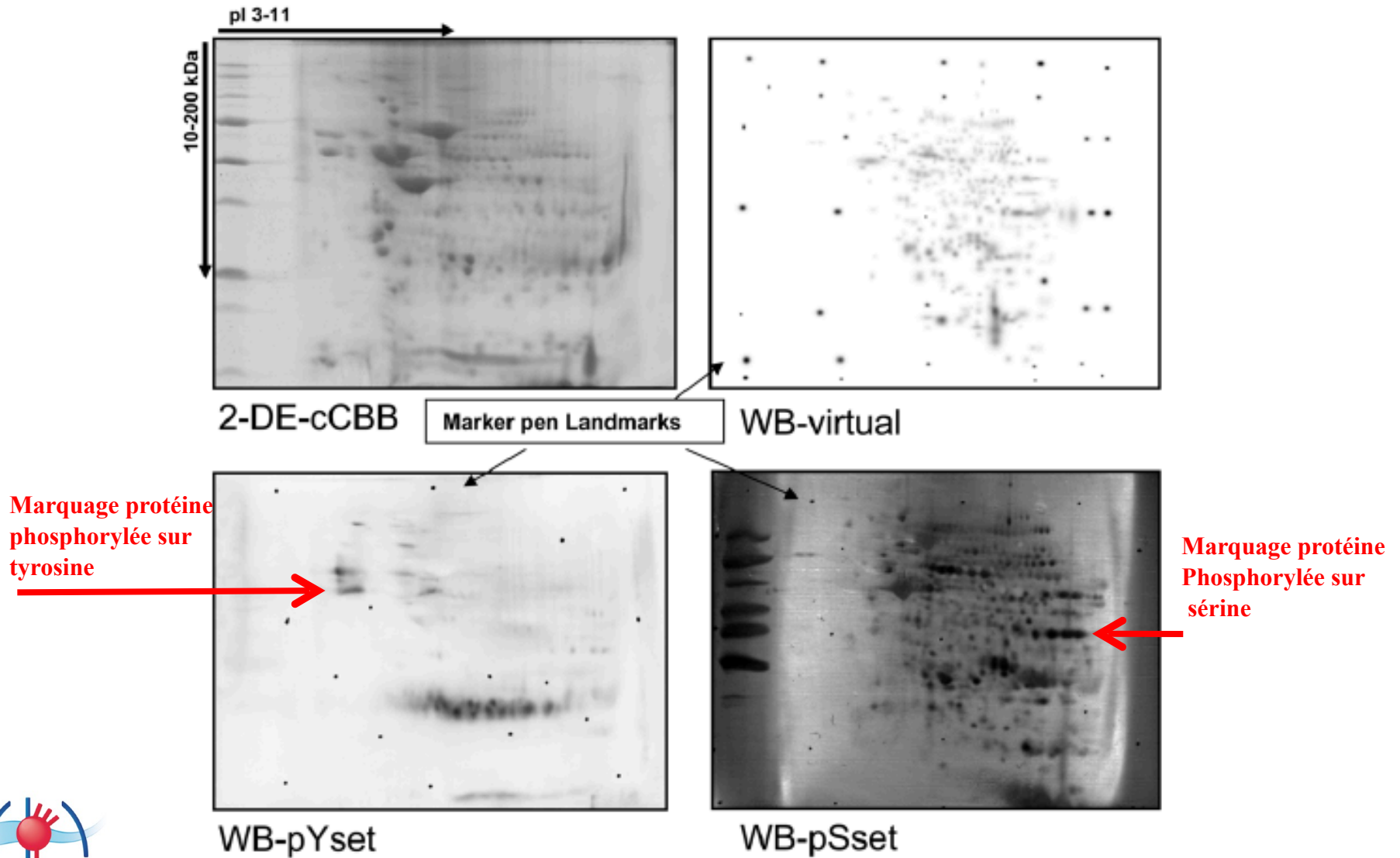
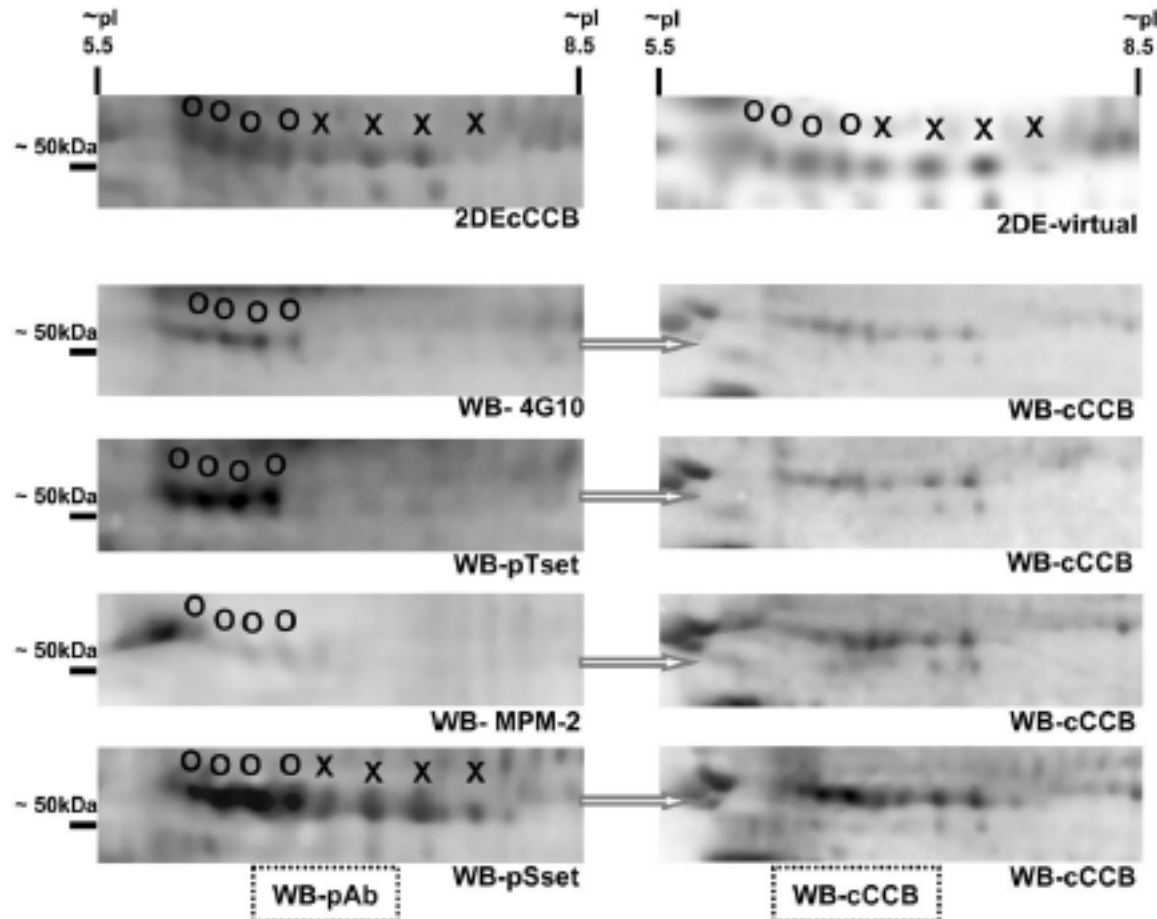


Figure 1. Description of the combined 2-DE-WB approach. 200 µg of tissue lysate protein extracts were separated on 2-DE, stained with Colloidal Coomassie G-250 and acquired as an image (2-DE-cCCB). In parallel 40 µg of total protein extract was separated by 2-DE and subsequently transferred onto PVDF membrane for incubation with antibodies directed against phosphorylated proteins. With a marker pen, landmarks points (crosses in Figure) were set around the membrane and the image of phosphorylated proteins was acquired (WB-pAb). Subsequently, the total proteins on the same membrane were revealed by cCCB-post staining and the image was recorded (WB-cCCB). Using the marker added landmarks the two images were superimposed and combined by the image analysis software to create a virtual image showing the phosphoproteins and the total proteins together (WB-virtual). Several protein spots from this image, which are in common with the cCCB-2-DE image, were selected as additional landmarks and used to superimpose the WB-CBB image to the 2-DE-cCCB image. This allowed deciphering of phosphorylated proteins on the gel. Highlighted spots were then excised from the gel using a spot cutter, followed by in-gel digestion using trypsin. The proteins were identified using MALDI-TOF MS.

6. Exemple publication utilisant la bioinfo

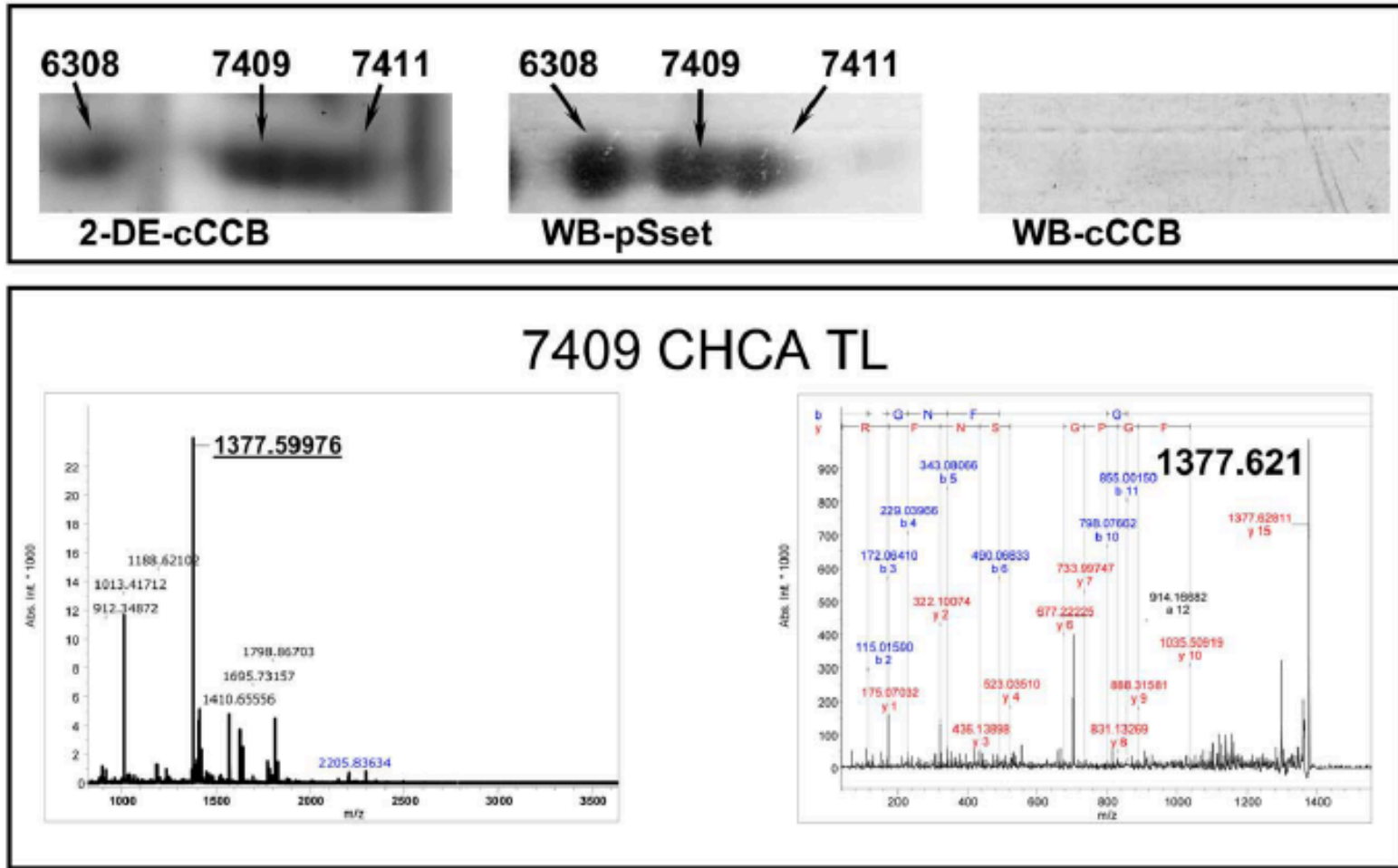


6. Exemple publication utilisant la bioinfo



Une phosphorylation modifie une immunoréactivité: notion de comètes:

6. Exemple publication utilisant la bioinfo



Analyse jusqu'à l'identification

6. Exemple publication utilisant la bioinfo

Table 1. Identified phosphopeptide by MALDI tandem MS using DHB ML sample preparation.

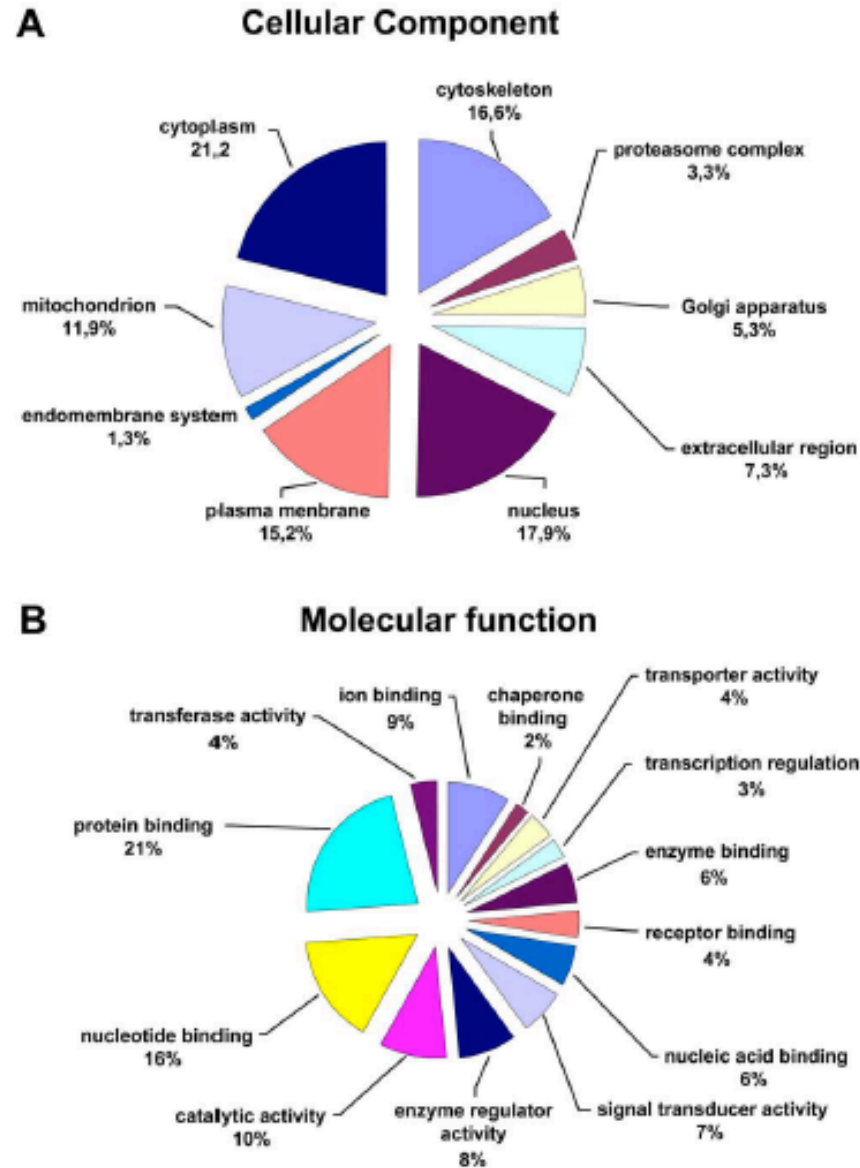
Protein Entry Name	Accession	Sequence	Start end	Meas. mass	Ion Score	Miss	MW
Angiotensin-converting enzyme	P09470	R.GPQFG <u>S</u> EVLR.H	1300–1310	1298.57765	63	0	151.888
Calnexin precursor	P35564	K.AEEDEILNR <u>S</u> PR.N	573–584	1508.67402	39	1	67.733
Advanced glycosylation end product-specific receptor	Q62151	R.KAPES <u>S</u> QEDEEERA	373–384	1526.60058	60	1	43.068
Nascent polypeptide-associated complex alpha subunit	P70670	R. <u>S</u> VTDPAMAPRTAK.N	588–600	1600.58786	20	1	221.603
Matrix-remodeling-associated protein 7	Q9CZH7	R.VAEPEE <u>S</u> EAEPPAAEGR.Q	73–89	1879.75921	82	0	19.516
Tensin	gil226437589	R. <u>S</u> QSFPDVERQLPQAPTR.G	790–806	1976.91134	56	0	203.317
Arginase-1	Q61176	- <u>M</u> SSKPK <u>S</u> LEIIGAPFSK.G	1–17	2075.89248	35	0	34.999
60S acidic ribosomal protein	P99027	K.KEE <u>S</u> EE <u>S</u> DDDMGFGFLD.-	99–115	2125.68687	40	1	11.651
60S acidic ribosomal protein P1	P47955	K.KEE <u>S</u> EE <u>S</u> EDDMGFGFLD.-	98–114	2139.70251	40	1	11.610
Myosin phosphatase Rho-interacting protein	P97434	R.AEEQLPPLLSP <u>S</u> PTPHSR.R	280–299	2220.06959	27	0	117.357
Alpha-1 catenin	P26231	R.TPEELDD <u>S</u> DFETEDFVRS.S	634–651	2238.85983	127	0	100.896
Membrane-associated progesterone receptor component	O55022	K.EGEEPTVY <u>S</u> DDDEPKDETAR.K	173–192	2375.93983	112	1	21.692
60S acidic ribosomal protein P0	P14869	K.AEAKEE <u>S</u> EE <u>S</u> EDDMGFGFLD.-	298–317	2410.81924	45	1	34.408
Septin-2	P42208	K.IYHLPDAE <u>S</u> DEDEDFKEQTRL.L	210–229	2517.04527	115	0	41.783
EH domain-containing protein	Q8BH64	R.GPDEAIEDGEE <u>S</u> EDDAEWVVK.D	426–448	2557.01375	112	1	50.135
Elongation factor 1-delta	P57776	K.GATPAEDDEDKIDILFG <u>S</u> DEEEEDKEAARL	145–173	3276.32225	144	2	31.916
Serum deprivation-response protein	Q63918	R.GNNSAVG <u>S</u> NADLTIEDEEEEPVALQQAQ QVR.Y	356–387	3520.57109	135	0	46.806
		R.RGNNSAVG <u>S</u> NADLTIEDEEEEPVALQQAQ QVR.Y	355–387	3676.67219	105	1	
		K.SSPFKV <u>S</u> PLSFRGK	287–299	1488.72465	53	1	

Phosphopeptides identified by MALDI-TOF-MS/MS from 50 µg of protein extracted from mouse lung and separated by SDS-PAGE.

S = phosphorylated serine determined by MALDI TOF-MS/MS. M = oxidized methionine.

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