

# La biologie a changé: comment enrichir mes cours?

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## Protéomique et marqueurs de l'AVC

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*1211 Geneva 4*

# Protéomique et marqueurs de l'AVC

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- **POURQUOI LA PROTEOMIQUE?**
- **ASPECTS METHODOLOGIQUES.**
  - L'EXEMPLE D'*E. COLI*.
- **APPLICATION BIOMEDICALE.**
  - Accident Vasculaire Cérébral (AVC).
- **CONCLUSION**

# DEFINITIONS

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**PROTEOME**

=

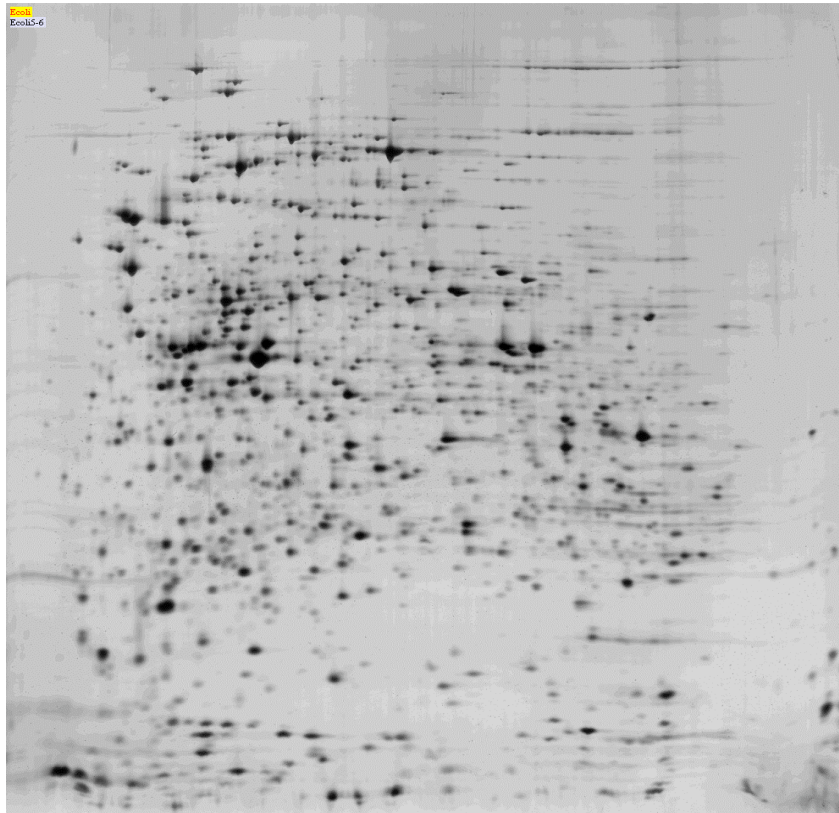
Le complément **PROTE**ique d'un gén**OME**

**PROTEOMIQUE**

=

La comparaison qualitative et quantitative de protéomes similaires sous des conditions différentes afin d'investiguer des processus biologiques

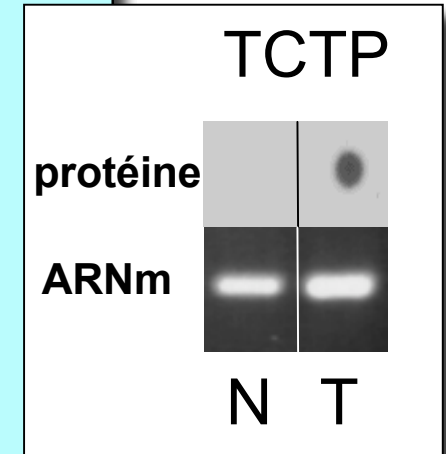
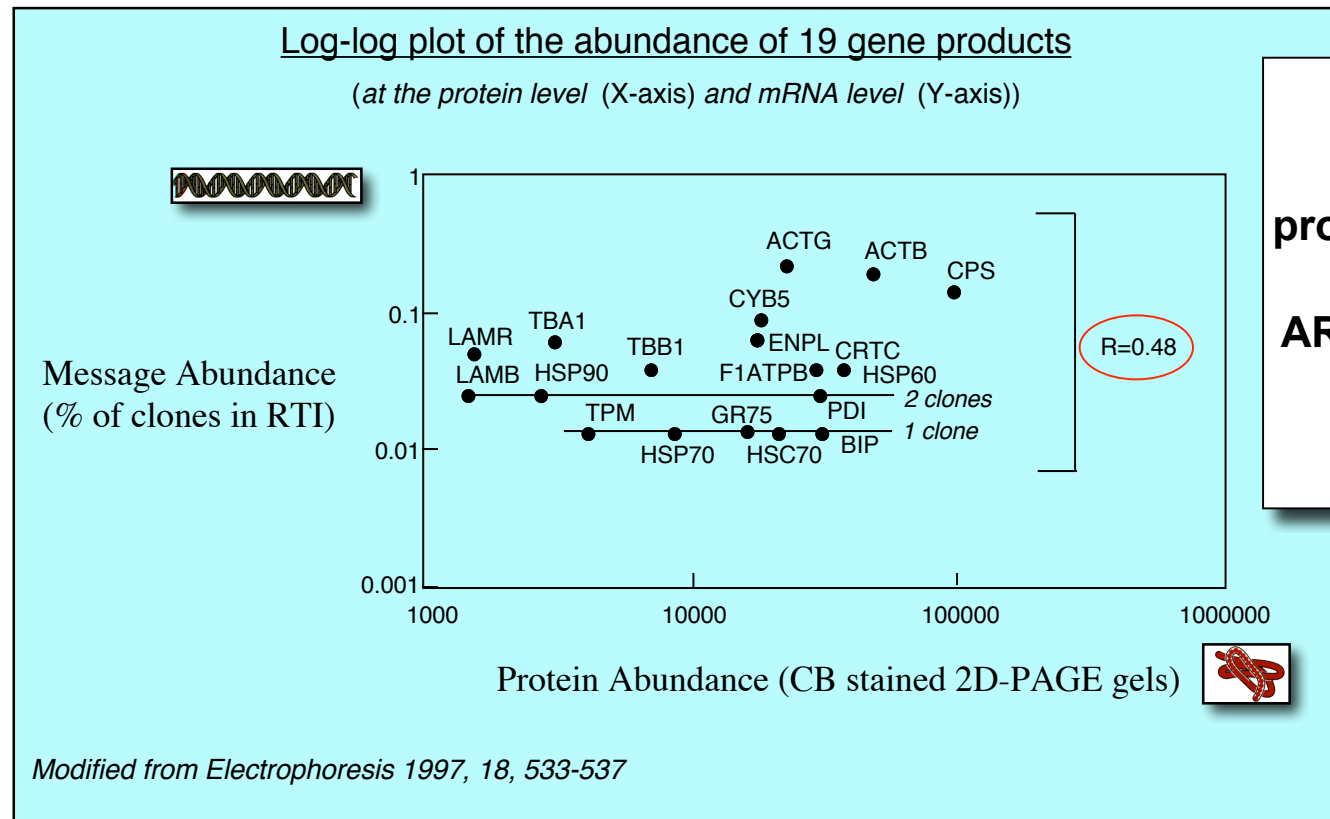
# POURQUOI LA PROTEOMIQUE ?



<b>Espèce:</b>	<b><i>E.coli</i></b>
<b>Quantité:</b>	<b>100 µg</b>
<b>Coloration:</b>	<b>Argent</b>
<b>IEF:</b>	<b>3.5-10</b>
<b>SDS PAGE:</b>	<b>9-16%T</b>
<b>Taches:</b>	<b>2500</b>

**Plusieurs milliers de produits de gènes fonctionnels sont visualisés**

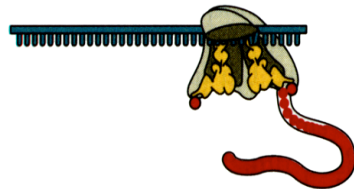
# POURQUOI LA PROTEOMIQUE ?



**La quantité d'ARNm ne corréle pas avec le niveau d'expression de sa protéine correspondante**

# POURQUOI LA PROTEOMIQUE ?

ATTTTATTAATATAATTCTTAATAATTATAAAAAAAAAAAAAAAAAAAAAACAACCAAATATTATATTATTTTTG  
 TAAATATAAATTAATAAAATGAAATTCCAACATACATTTATTGCATTATTATCACTATTAACATATGCAAAATGC  
 ATATGATTATTTACAACAACATTGGCCAATCAAATCCAGTTTGTGCTTCAGTAGATGTCATACAAATGTTT  
 GTACTGAGGTTTGTGGTAGATTTGTCCGTTACATTCCTGATGCTACCAATACAAATCAATTCACTTTTGCCGAA



Traduction pré-déterminée  
du produit d'un gène

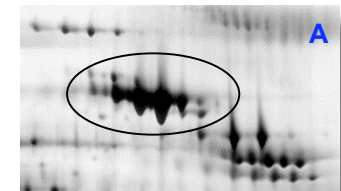
MetLysPheGlnHisThrPhelleAlaLeuLeuSerLeuLeuThrTyrAlaAsnAla  
 TyrAspTyrPheThrThrThrLeuAlaAsnGlnAsnProValCysAlaSerValAsp  
 VallieGlnAsnValCysThrGluValCysGlyArgPheValArgTyrilleProAsp



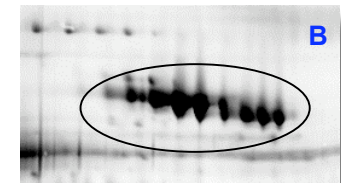
Modifications  
post-traductionnelles  
des protéines

- Coupures
- Phosphorylation
- Glycosylation
- Méthylation
- Beaucoup d'autres

Transferrine



Plasma



LCR

Les modifications post-traductionnelles ne peuvent pas être pré-déterminées à partir de la séquence des gènes

# TECHNOLOGIES UTILISEES

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- **SEPARATION DES PROTEINES**

- ELECTROPHORESE
- CHROMATOGRAPHIE LIQUIDE

- **IDENTIFICATION DES PROTEINES**

- SPECTROMETRIE DE MASSE
- ANTICORPS
- SEQUENCAGE D'EDMAN
- COMPOSITION EN ACIDES AMINES

- **BIOINFORMATIQUE**

- OUTILS D'INTERPRETATION DES DONNEES
- OUTILS DE GESTION DES DONNEES
- BASE DE DONNEES

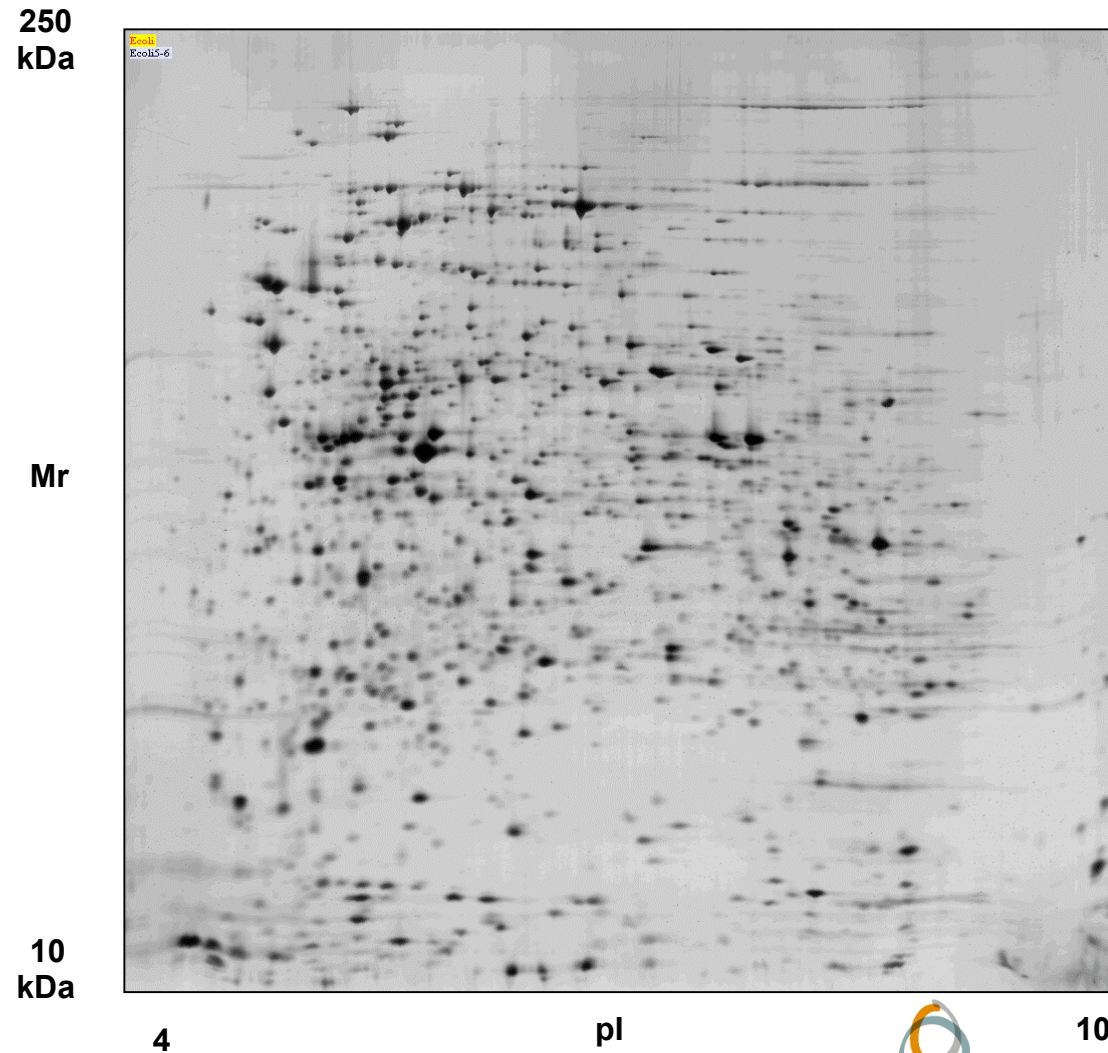
# SEPARATION D'E.COLI PAR 2-D PAGE

**Espèce:**  
E.coli

**Quantité:**  
100 µg

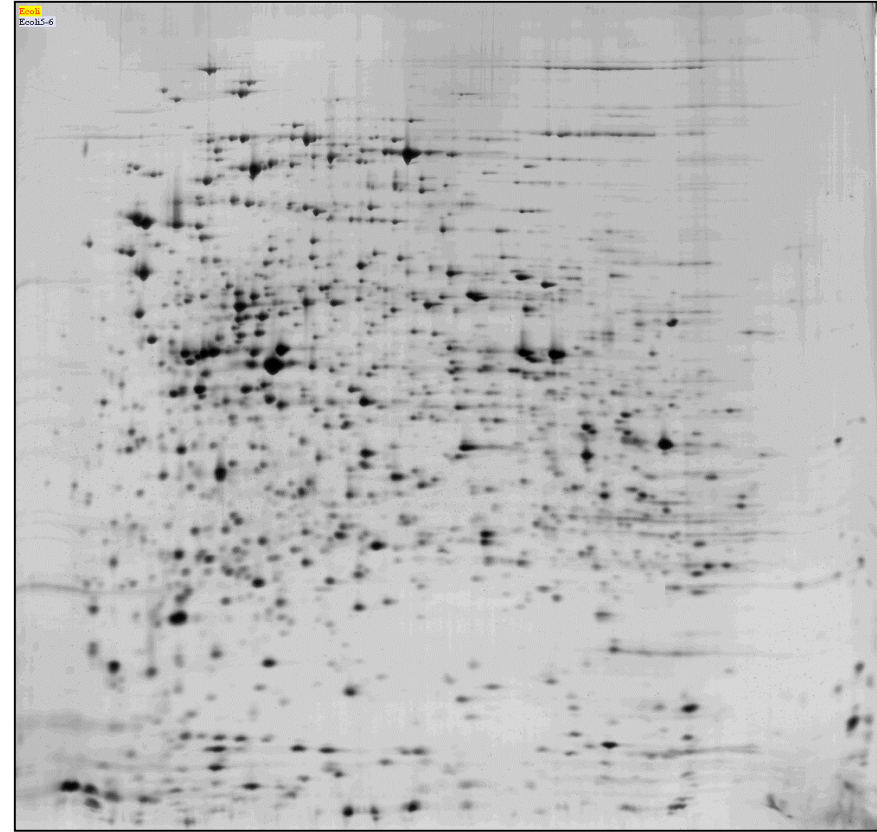
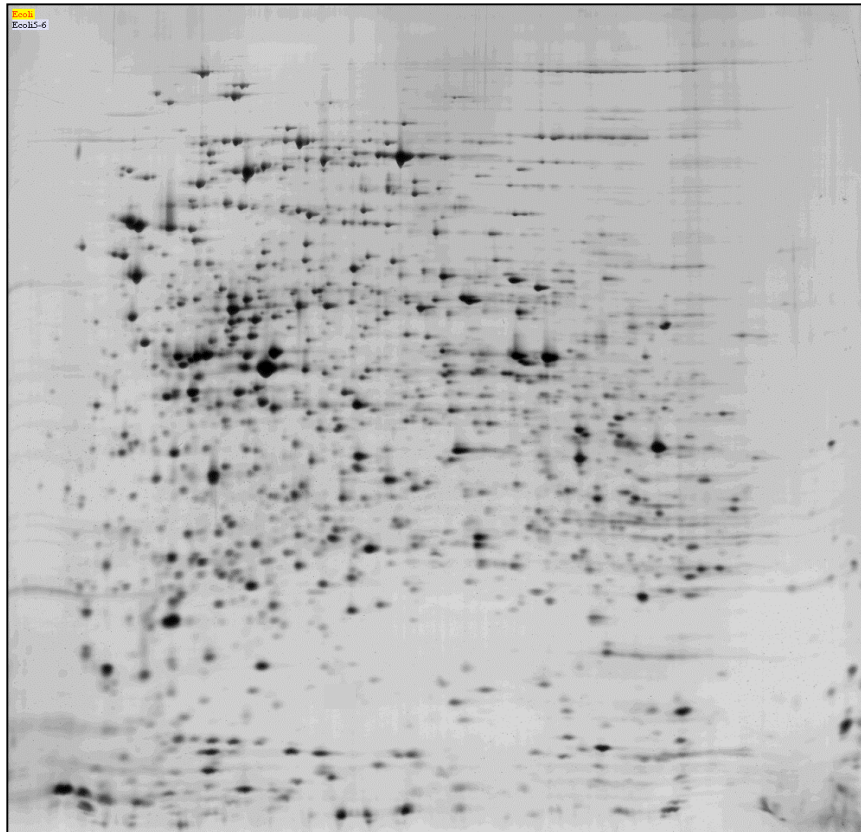
**Coloration:**  
Argent

**Spots:**  
2364

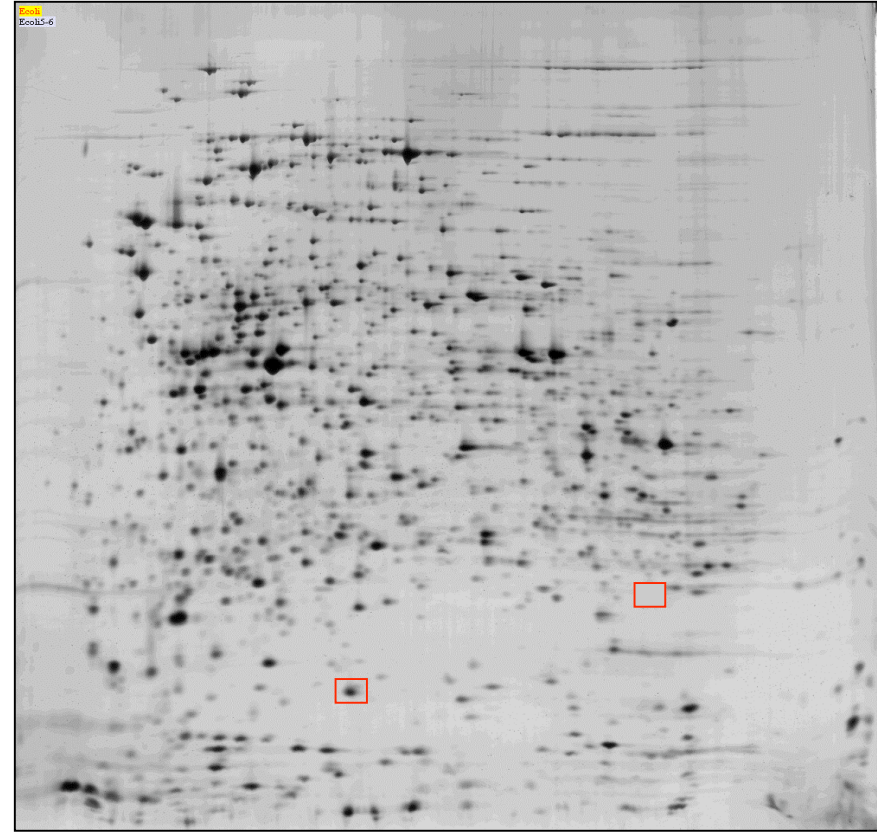
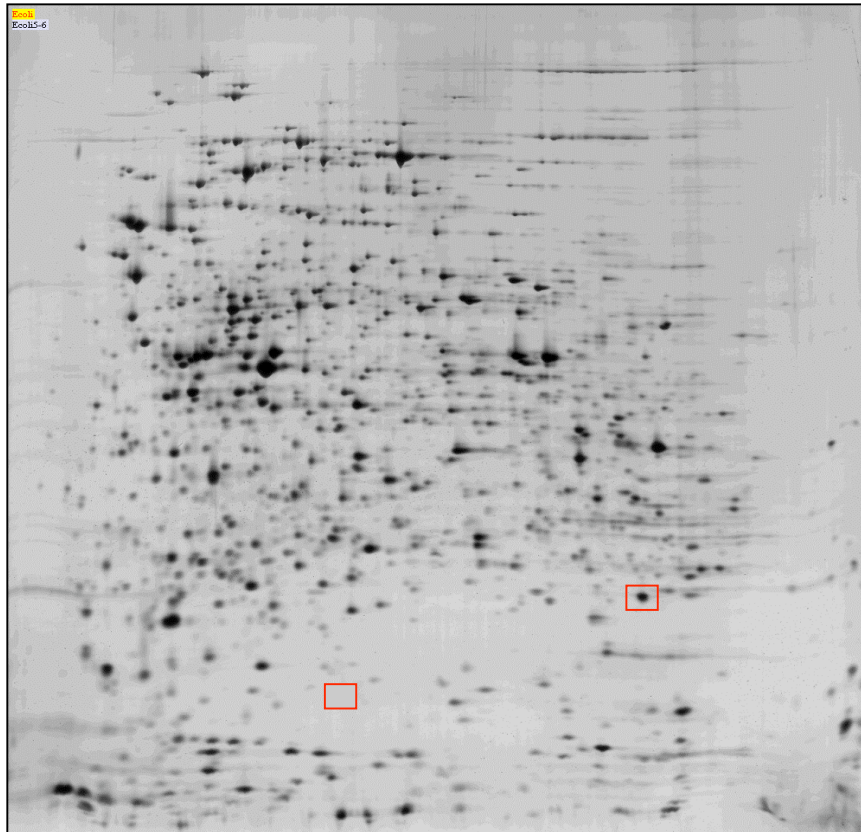




# Comparaison d'*E. COLI* sauvage vs. resistant



# Comparaison d'*E. COLI* sauvage vs. resistant



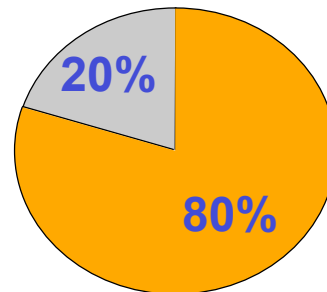
# Qu'est-ce qu'un AVC ?

Accident Vasculaire Cérébral : interruption du flux sanguin vers le cerveau

- 1<sup>ère</sup> cause de déficience neurologique
- 3<sup>ème</sup> cause de décès dans les pays développés

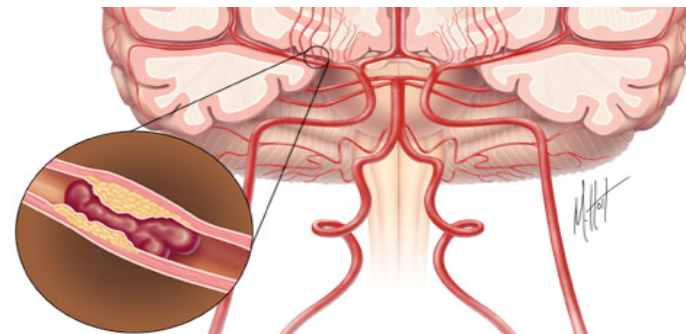
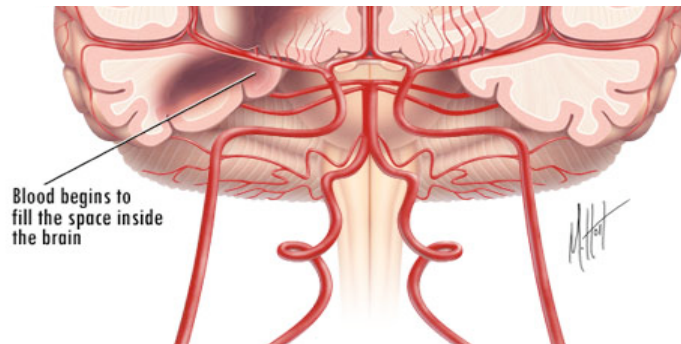
## ✓ **AVC Hémorragique** Rupture d'un vaisseau

- ✓ Défaut de la coagulation
- ✓ Hypertension artérielle
- ✓ Anévrisme



## ✓ **AVC Ischemic** Occlusion artérielle

- ✓ Athérosclérose
- ✓ Embole



# Diagnostic de l'AVC

A l'admission



Evaluation des symptômes

Suspicion d'AVC



0 - 3 h



0 - 3 h

Marqueur plasmatique  
de l'AVC **Ischémique**

Traîtement Anti-thrombotique  
(0 - 3 h)

~~> 24 h : MRI  
3 jours : CT-scan~~

AVC **Haemorrhagique**

Diagnostiqué avec grande sensibilité

~~Traîtement Anti-thrombotique~~

Besoin d'un test qui **inclue les AVC** ischémiques

# Phase de découverte

HAUT

Spécificité

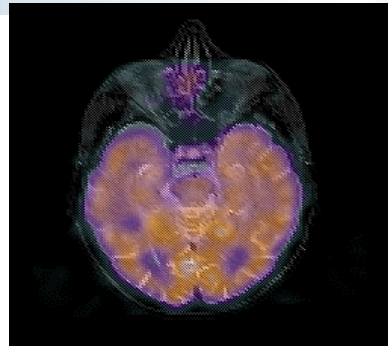
Facilité

Contexte Biologique

Abondance

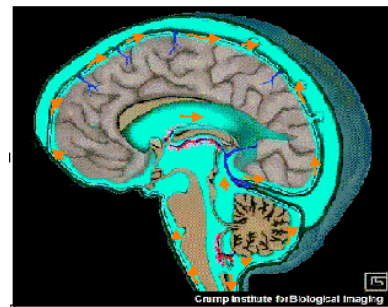
Invasif

BAS



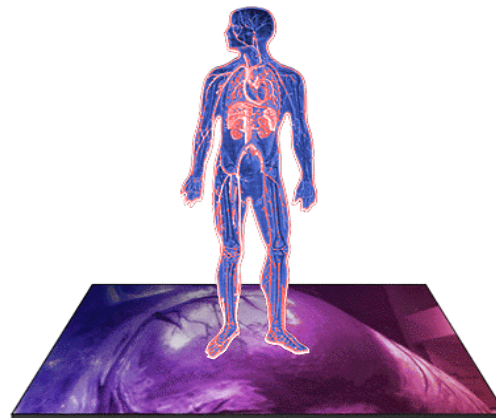
Tissu cérébral

Pathologie



LCR

Fluide avoisinant



Plasma

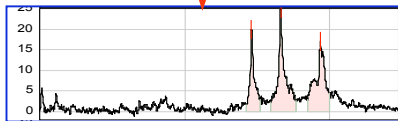
Diagnostique

# Phase de découverte

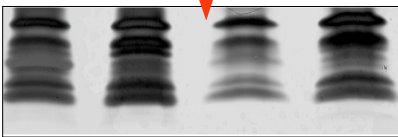
## A) Stratégie de separation

### Approche 1

Stroke plasma  
vs.  
Control plasma

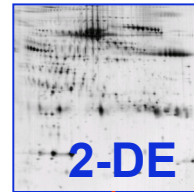


SELDI



1-DE

### Approche 2



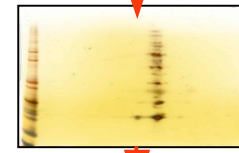
2-DE

Post-mortem CSF  
vs.  
Ante-mortem CSF

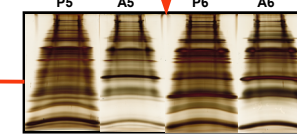
### Approche 3



Déplétion



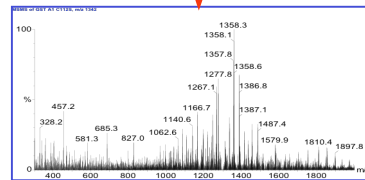
Off-gel elec.



1-DE

## B) Stratégie d'identification

MS/MS



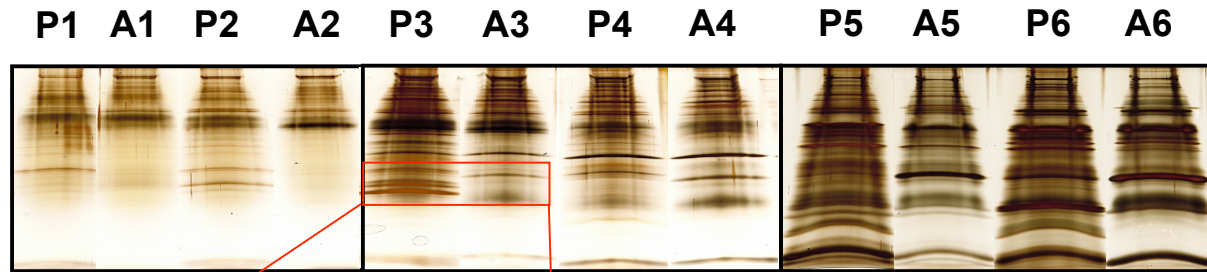
## C) Stratégie de validation

Immunoessais

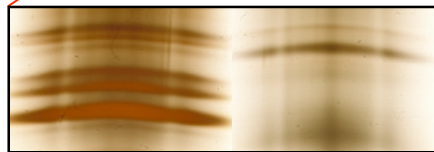


Plasma AVC  
vs.  
Plasma control  
(Patients hospitalisés)

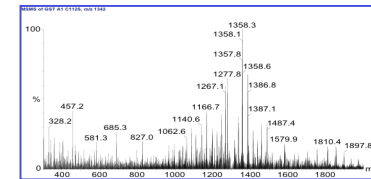
# Fractionnement par électrophorèse Off-gel



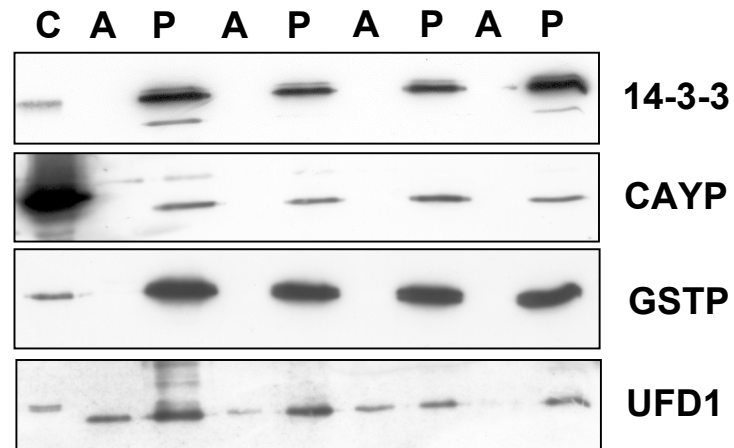
Gel 1DE coloré à l'argent  
LCR *post-mortem* et *ante-mortem*



MS/MS

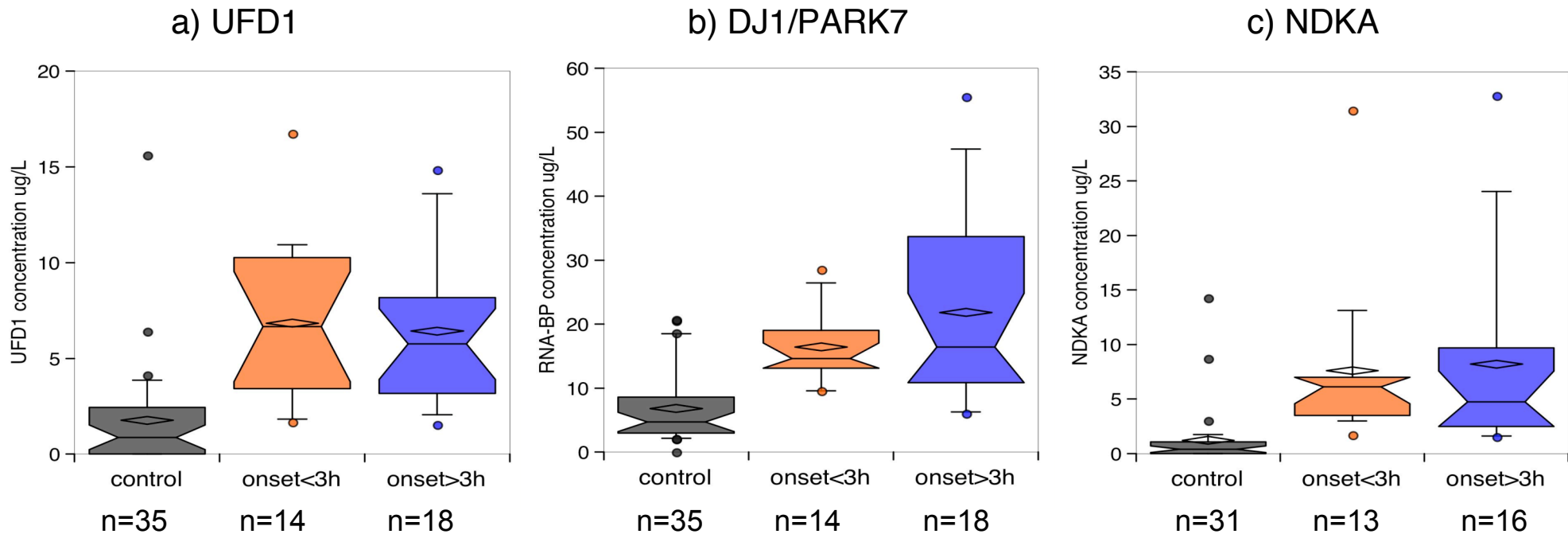


>200 protéines  
uniquement dans  
le LCR *post-mortem*



Approche 3

# Concentration des marqueurs en fonction du temps après l'apparition des symptômes



control

vs.

0-3 h

p < 0.01



# Autres utilisations possibles

A l'admission



Evaluation des symptômes

Suspicion d'AVC



0 - 3 h



0 - 3 h

1

Marqueur Plasmaticque de l'AVC **Ischémique**

Traîtement Anti-thrombotique (0 - 3 h)

~~> 24 h : MRI  
3 jours : CT-scan~~

2

0 - 24 h

Marqueurs distinguant different types d'AVC

Marqueurs pronostic

AVC **Haemorrhagique**

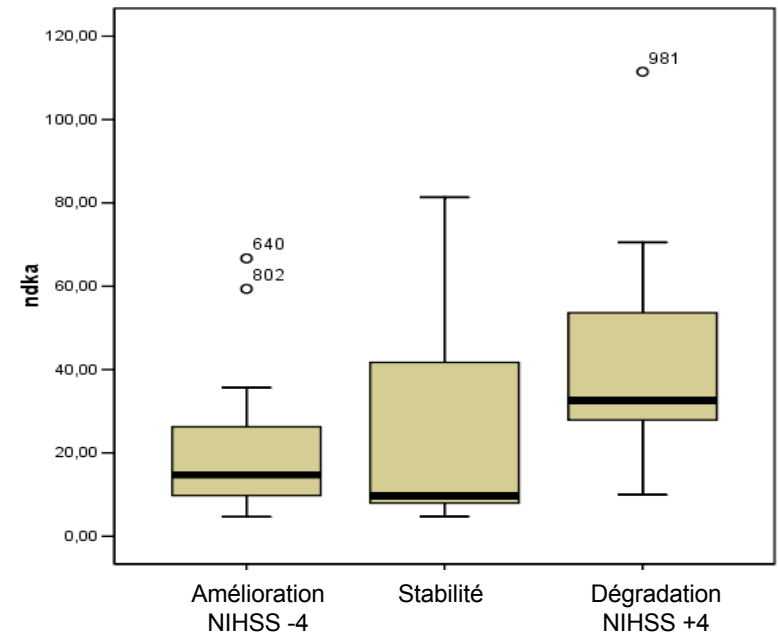
Diagnostiqué avec grande sensibilité

~~Traîtement Anti-thrombotique~~

# NDKA : corrélation avec la dégradation neurologique et la mortalité

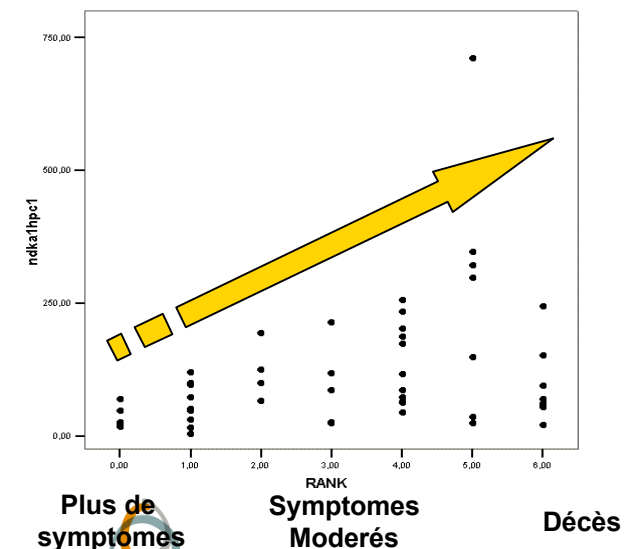
## • Dégradation Neurologique

	DJ-1	UFD1	NDKA	GSTP-1
Mann-Whitney U	92,000	67,000	<b>48,000</b>	79,000
Wilcoxon W	588,000	563,000	<b>544,000</b>	575,000
Z	-,621	-1,563	<b>-2,278</b>	-1,111
Asymp. Sig (2-tailed)	,534	,118	<b>0,023</b>	,267
Exact Sig. (1-tailed Sig.)	,555	,125	<b>0,021</b>	,282



## • Mortalité (jusqu'à 3 mois)

	DJ-1	UFD1	NDKA	GSTP-1
Mann-Whitney U	73,000	43,000	<b>42,000</b>	58,000
Wilcoxon W	634,000	604,000	<b>603,000</b>	619,000
Z	-1,012	-2,180	<b>-2,219</b>	-1,596
Asymp. Sig (2-tailed)	,312	,029	<b>0,027</b>	,111
Exact Sig. (1-tailed Sig.)	,330	,028	<b>0,025</b>	,117



# Autres utilisations possibles

A l'admission



Evaluation des symptômes

Suspicion d'AVC



0 - 3 h



0 - 3 h

①

Marqueur Plasmaticque de l'AVC **Ischémique**



Traîtement Curatif (3 - 72 h)



③

Marqueurs du suivi thérapeutique

②

0 - 24 h

Marqueurs distinguant different types d'AVC



Marqueurs pronostic

AVC **Haemorrhagique**  
Diagnostiqué avec grande sensibilité



~~Traîtement Anti-thrombotique~~

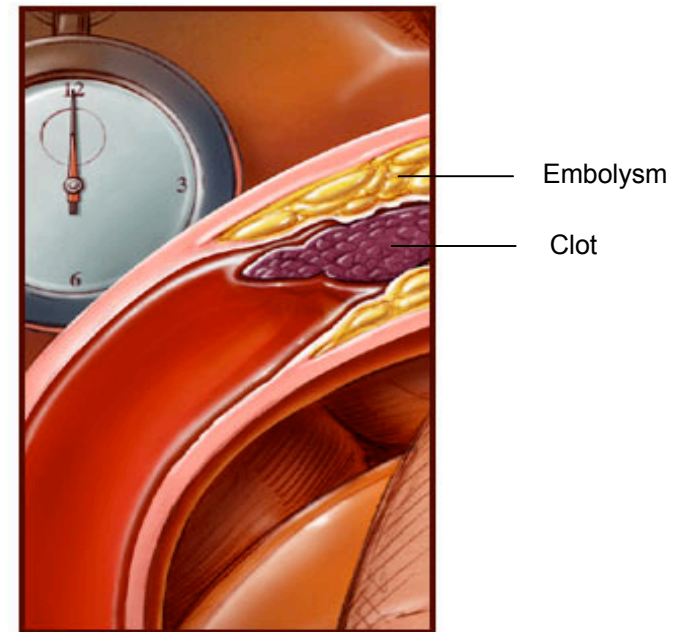
# Marqueurs du suivi thérapeutique

**tPA (tissu plasminogen activator)** = Traitement thrombolytique

- Seul traitement accepté pour l'AVC ischémique
- Administration rapide (<3h)
- Initie une fibrinolyse locale

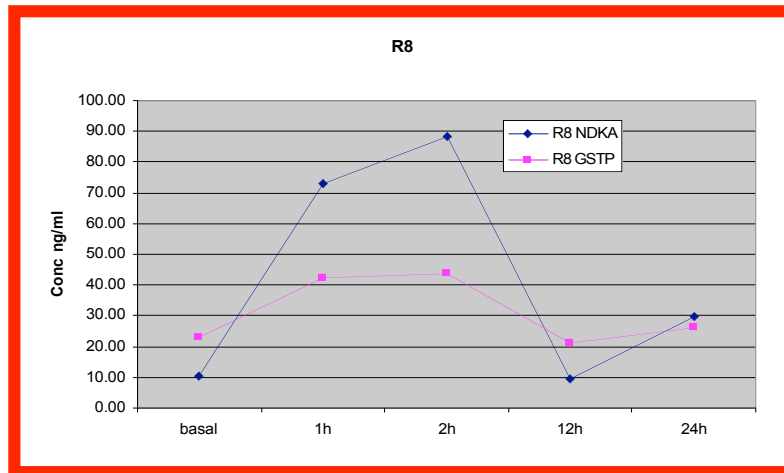
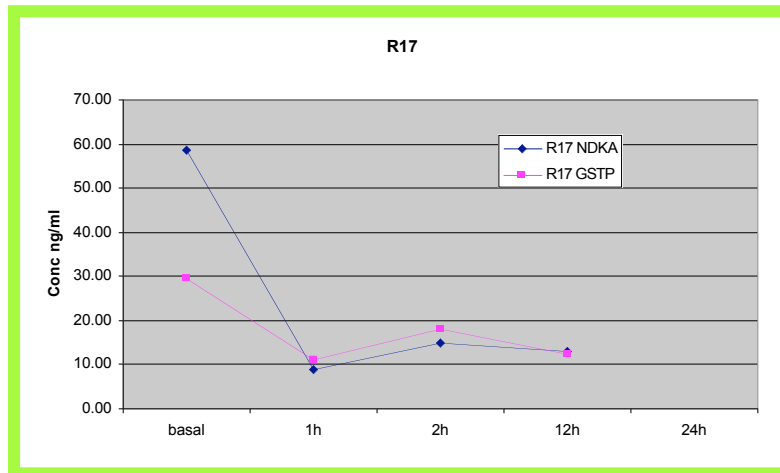
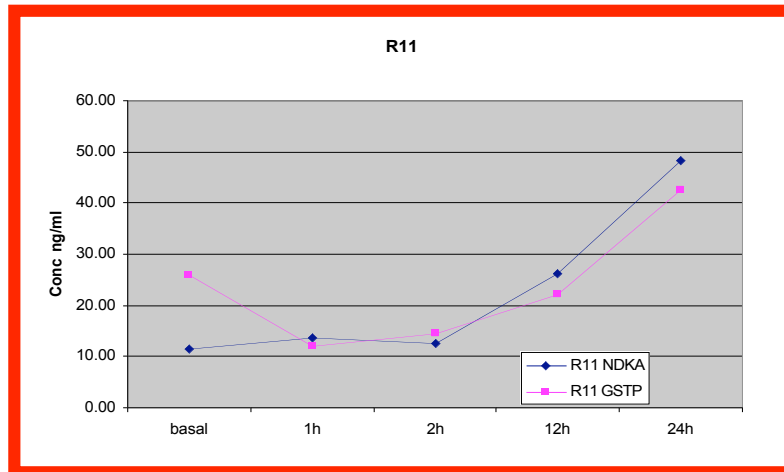
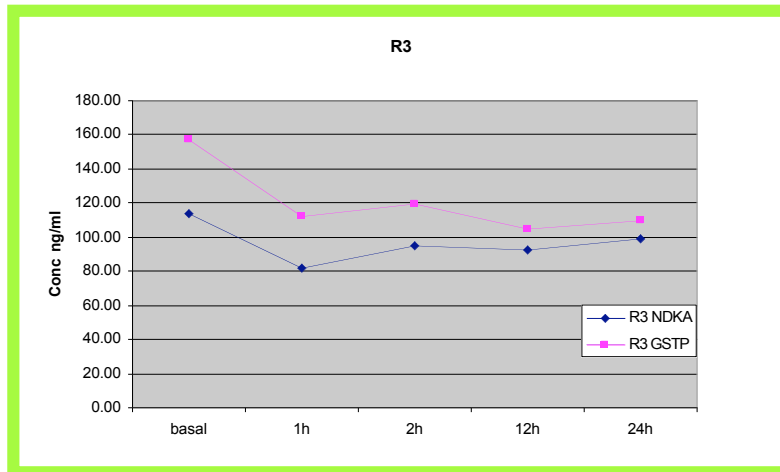
tPA a 0.9mg/kg pendant 1 heure

**Effet secondaire= Hémorragie**



# NDKA and GSTP

Cohorte tPA : 60 AVC ischémiques testés à 5 temps différents (basal, 1h, 2h, 12h and 24h)



**BON PRONOSTIQUE**  
(Rankin scale 1)

**MAUVAIS PRONOSTIQUE**  
(Rankin scale 4-5)

# LA PROTEOMIQUE: CONCLUSION

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Les technologies utilisées en protéomique sont en pleine maturation.

Besoin d'améliorer l'automatisation des analyses et l'intégration des données.

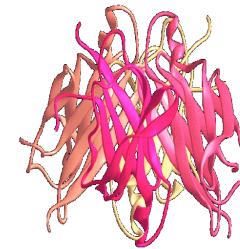
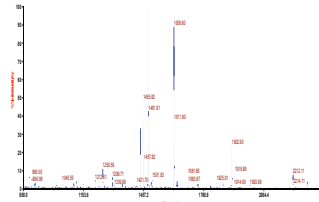
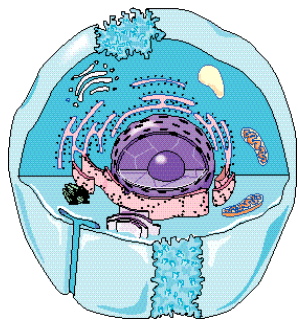
La combinaison de la génomique et de la protéomique va devenir la norme.

La protéomique et la génomique vont accélérer les processus décisionnels.

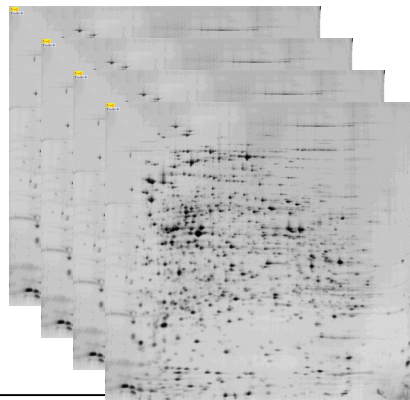
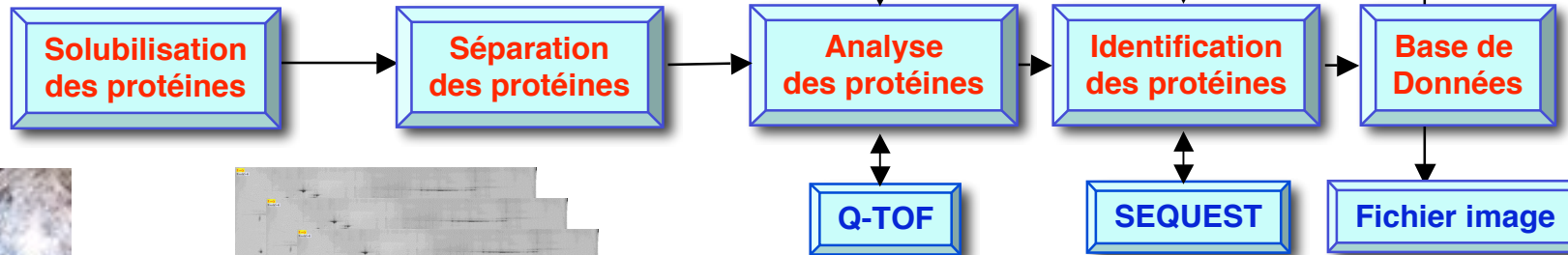
La valeur ajoutée des bases de données protéomiques a augmenté de manière exponentielle (SWISS-PROT).

Les outils bioinformatiques sont incontournables dans notre recherche.

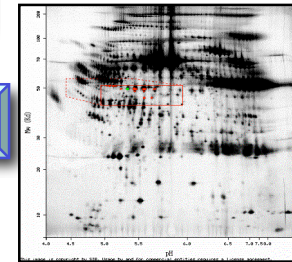
# De l'échantillon à la base de données



MAP LOCATIONS	PROT ID	PROT NAME	PROT MW (kDa)	PROT PI
+	IPROT_01000101	p14-45	45	4.5
+	IPROT_01000102	p14-50	50	4.5
+	IPROT_01000103	p14-55	55	4.5
+	IPROT_01000104	p14-60	60	4.5
+	IPROT_01000105	p14-65	65	4.5
+	IPROT_01000106	p14-70	70	4.5
+	IPROT_01000107	p14-75	75	4.5
+	IPROT_01000108	p14-80	80	4.5
+	IPROT_01000109	p14-85	85	4.5
+	IPROT_01000110	p14-90	90	4.5
+	IPROT_01000111	p14-95	95	4.5
+	IPROT_01000112	p14-100	100	4.5

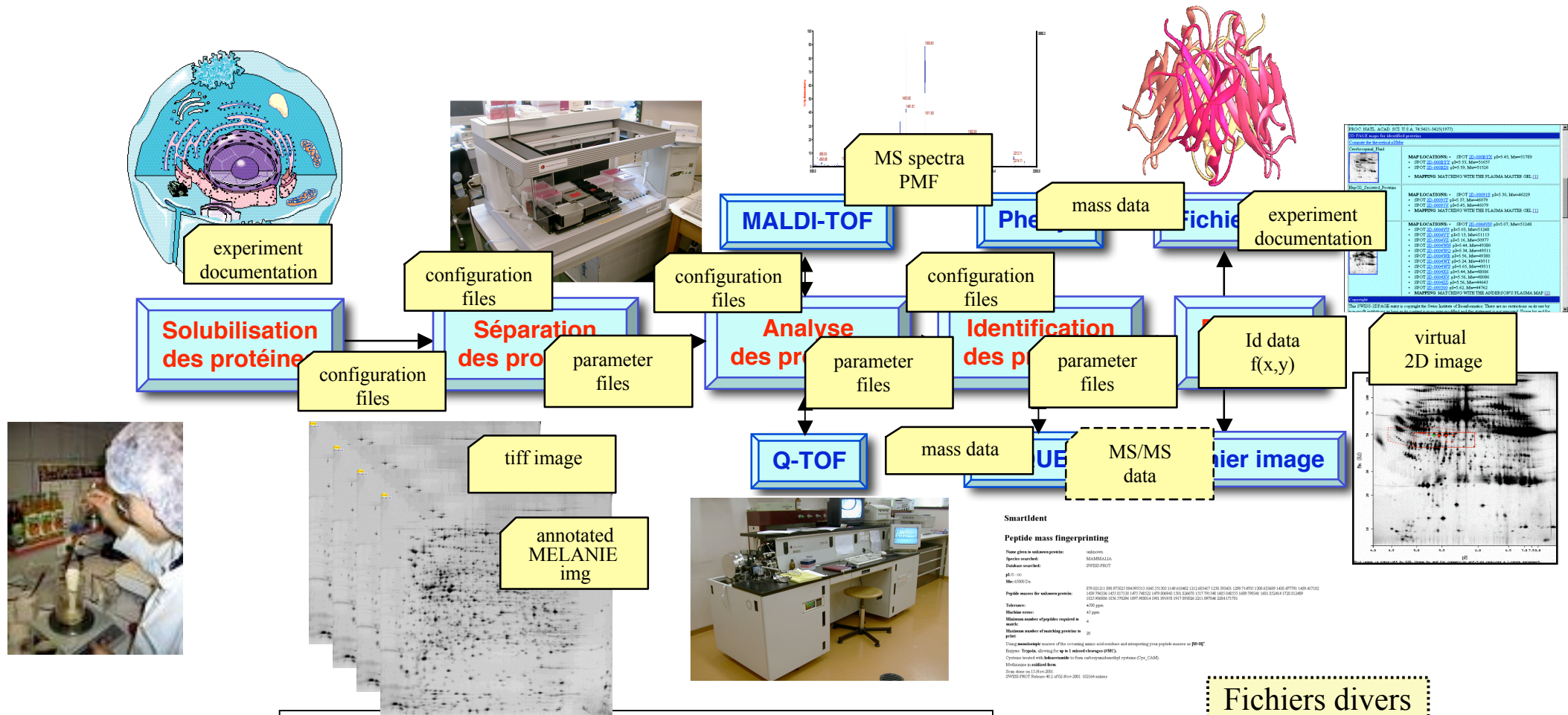


**SmartIdent**  
**Peptide mass fingerprinting**  
 Name gene in volcano protein: volcano  
 Species identifier: MAMMILLA  
 Database searched: proteo:PROT  
 pI: 00  
 Mw: 0000 Da  
**Peptide masses for volcano protein:**  
 149796130 143 87118 145 146202 147 1493684 150 124078 157 174 146 146 146153 149 79934 1461 15244 153 132489  
 155 14998 156 15266 157 16261 148 16191 161 17689 161 13766 164 11791  
**Database:**  
 430 ppm  
**Database error:**  
 40 ppm  
**Maximum number of peptides required to match:**  
 10  
**Maximum number of matching protein in ppm:**  
 10  
 Using **swapsort** method of file opening, sorting and merging (your protein source is **PROT**)  
 Output: Triplet: identical to q in 1 missed cleavage (MCS)  
 Output: Triplet: identical to q in 1 missed cleavage (MCS)  
 Output: Triplet: identical to q in 1 missed cleavage (MCS)  
**Method name:** volcano  
 Date: Mon Jul 12 16:10:2010  
 201007 PROT Release 41.2 of 010100-2001 102164 entries



**Le laboratoire mouillé**

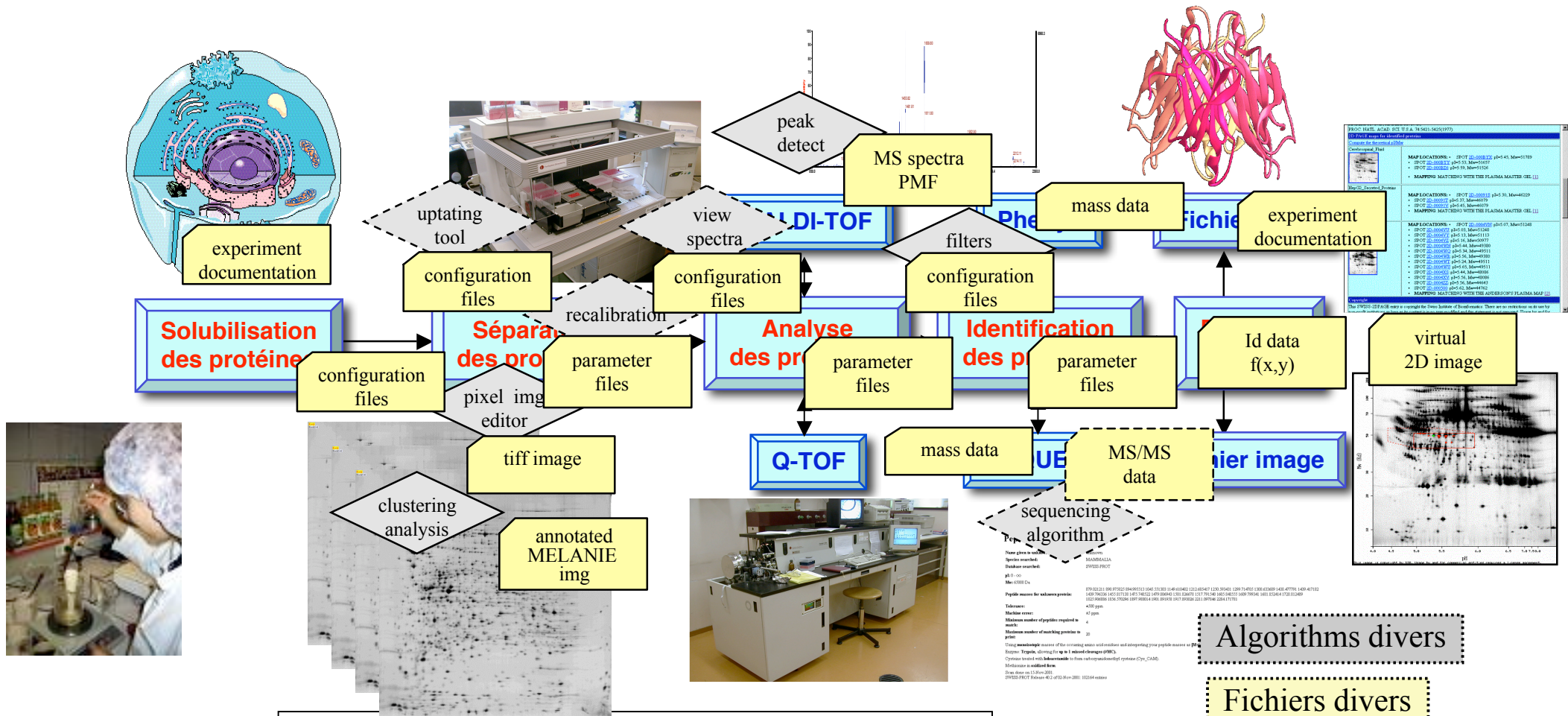
# De l'échantillon à la base de données



**Le laboratoire mouillé**

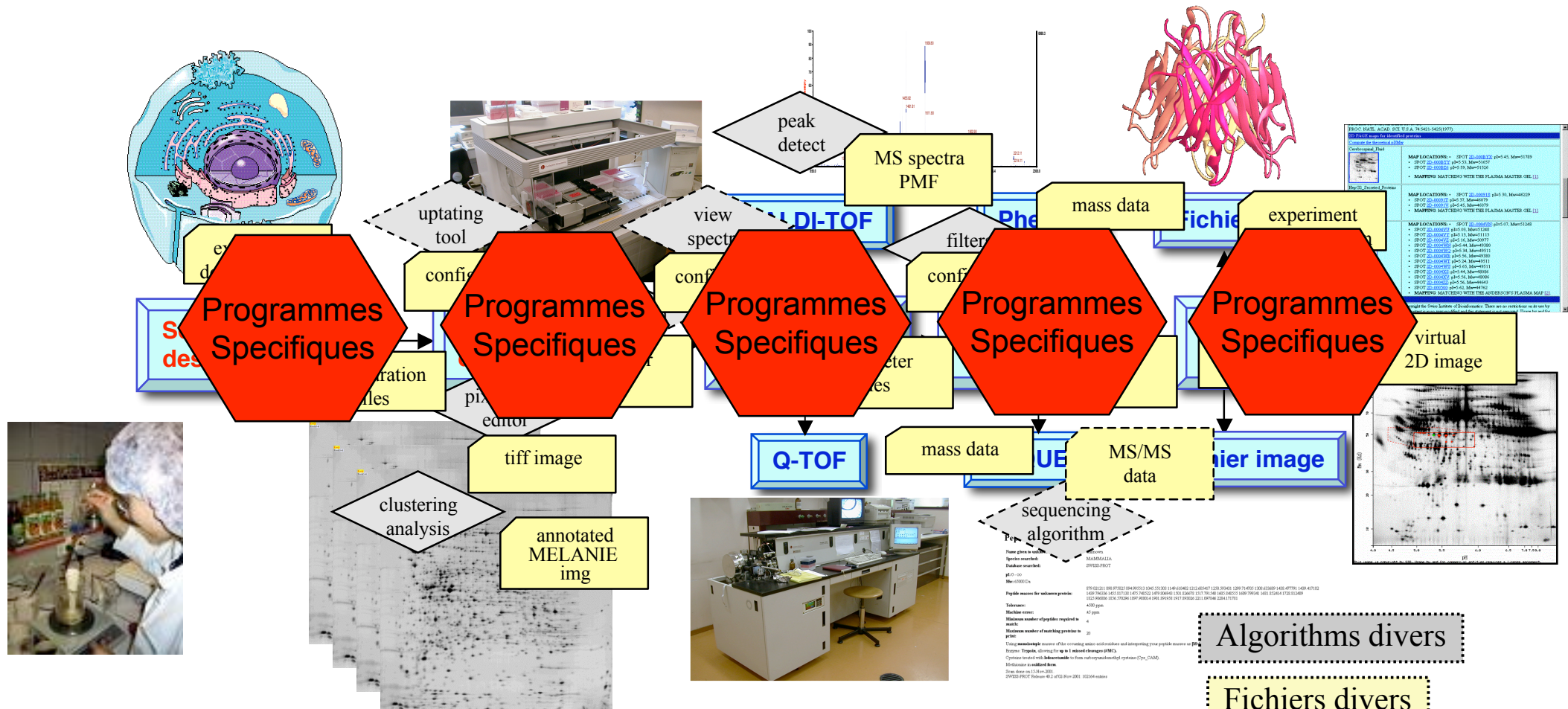


# De l'échantillon à la base de données



**Le laboratoire mouillé**

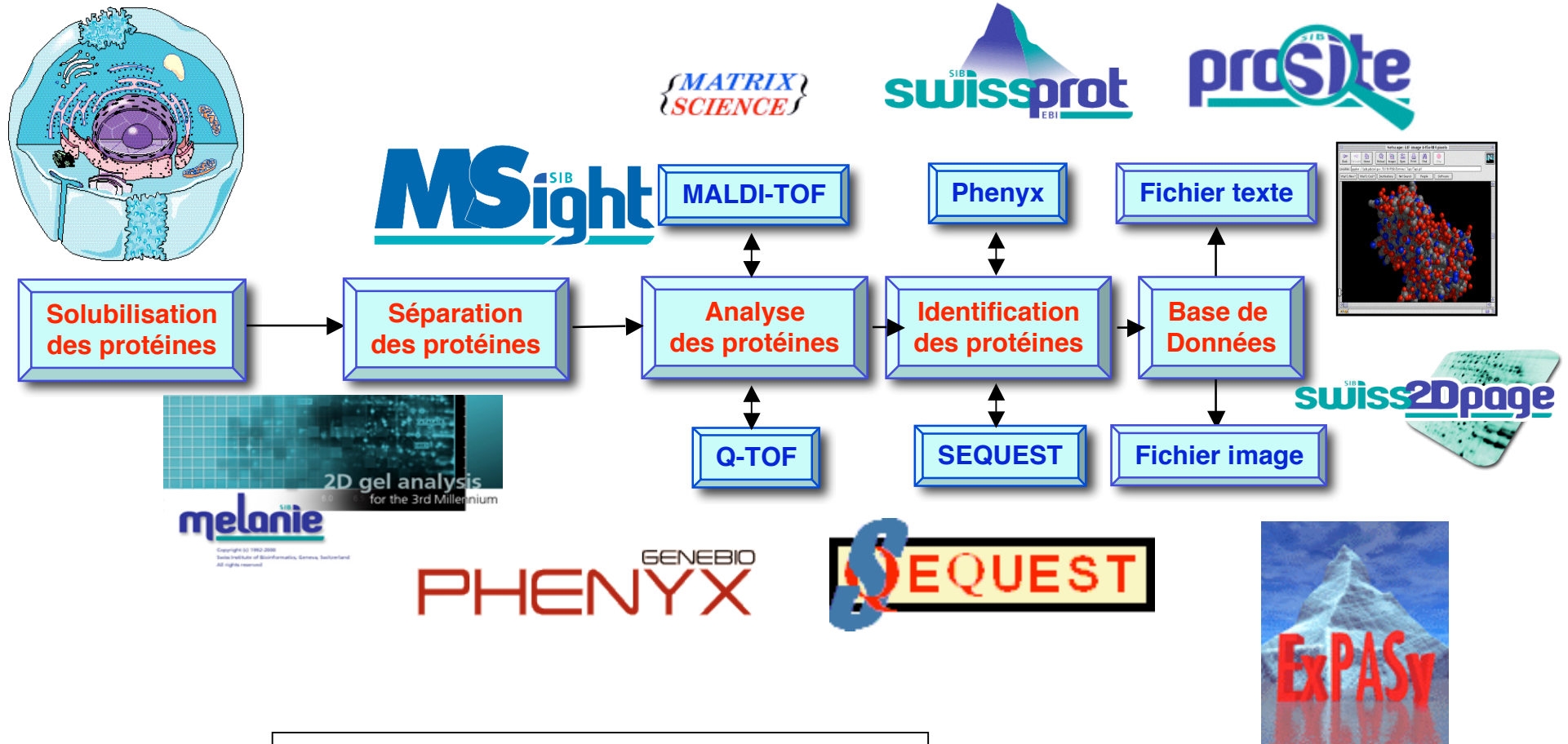
# De l'échantillon à la base de données



**Le laboratoire mouillé**

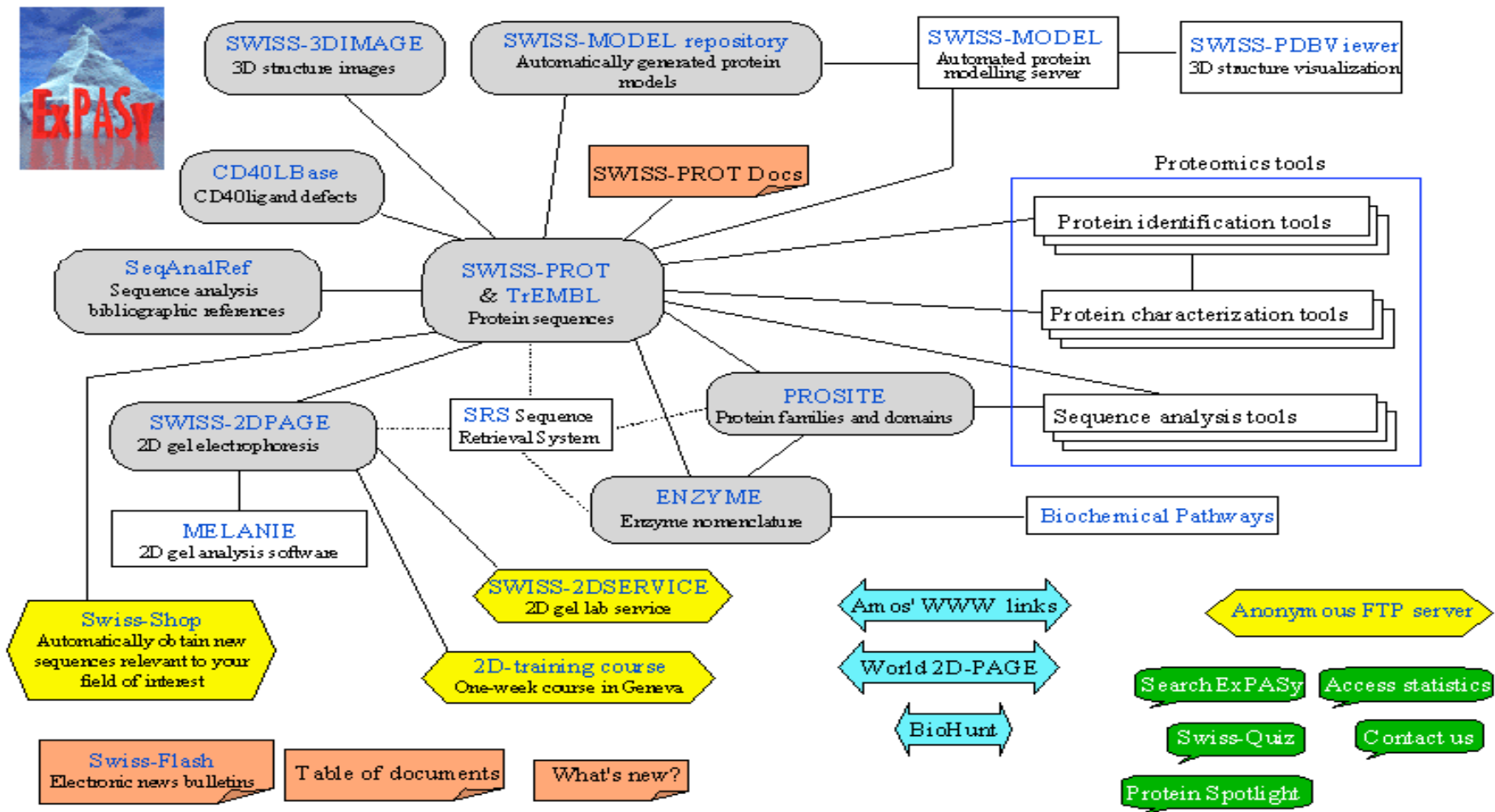


# De l'échantillon à la base de données



**Le laboratoire sec**

# ExpASY site map



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[Site Map](#)

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Search  for



# ExpASY Life Science Directory

(formerly known as [Amos'](#) WWW links page)

## Notes:

- 1) The URL for this page is <http://www.expasy.org/links.html>
- 2) If you would like to submit a specific link or to notify us of a modified link, please [send us an email](#), but remember that we reserve the right to choose the links we want to include !
- 3) Links to protein sequence, 3D structure and 2D-gel analytical tools are provided on ExpASY's [Proteomics tools](#) page.

## Quick jump to the following topics:

[Protein db](#) | [3D structure db](#) | [2D-PAGE & MS db](#) | [DNA/RNA db](#) | [Carbohydrates db](#) | [Organisms specific db](#) | [Human mutation db](#) | [Genes/proteins specific db](#) | [PTM db](#) | [Phylogenetics db](#) | [Microarrays db](#) | [Patents](#) | [References](#) | [Dict., protocols & nomenclat.](#) | [Biol. soft. & db catalogs](#) | [Gateways](#) | [Biol. journals & publishers](#) | [Biol. societies](#) | [Biocomputing servers](#) | [Biotech. companies](#) | [Bioinformatics companies](#) | [Misc. medical ref. sites](#) | [Misc. scientific ref. sites](#)

## Protein related databases

- [UniProt](#) - the universal protein resource
- [UniProt Knowledgebase](#) - consists of UniProtKB/Swiss-Prot (high-level annotation) and UniProtKB/TrEMBL (computer-annotated)
- [PMD](#) - Protein Mutant db
  
- [InterPro](#) - Integrated Resources of Proteins Domains and Functional Sites
- [PROSITE](#) - Database of protein families and domains
- [BLOCKS](#) - BLOCKS db
- [Gene3D](#) - Structural and Functional Annotation of Protein Families
- [Panther](#) - Functional classification system
- [Pfam](#) - Protein families db (HMM derived) [Mirrors at [St. Louis \(USA\)](#), [Sanger Institute, UK](#), [Karolinska Institutet \(Sweden\)](#)]
- [PIRSF](#) - Protein classification system
- [PRINTS](#) - Protein Motif fingerprint db

- [PRINTS](#) - Protein Motif fingerprint db
- [ProDom](#) - Protein domain db (Automatically generated)
- [PROTOMAP](#) - An automatic hierarchical classification of UniProtKB/Swiss-Prot proteins
- [SBASE](#) - SBASE domain db
- [SMART](#) - Simple Modular Architecture Research Tool
- [Superfamily](#) - Library of profile HMMs representing all proteins of known structure
- [STRING](#) - Search Tool for the Retrieval of Interacting Genes/Proteins
- [TIGRFAMs](#) - TIGR protein families db
  
- [BIND](#) - Biomolecular Interaction Network Database
- [DIP](#) - Database of Interacting Proteins
- [MINT](#) - Molecular INTERaction database
- [HPRD](#) - Human Protein Reference Database
- [IntAct](#)
- [BioGRID](#) - General Repository for Interaction Dataset
- [PPI](#) - JCB Protein-Protein Interaction Website

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### Protein 3D structure related databases

- [PDB](#) - Protein Data Bank
- [BioMagResBank](#) - Repository for data on proteins, peptides, and nucleic acids from NMR spectroscopy
- [SWISS-MODEL Repository](#) - Automatically generated protein models db
- [ModBase](#) - Db of comparative protein structure models
- [CATH](#) - UCL BSM structural classification of proteins
- [SCOP](#) - Structural classification of proteins [Mirror at [USA](#) | [Israel](#) | [Singapore](#) | [Australia](#)]
- [Molecules To Go](#) - Molecules To Go (formerly known as Molecules R Us), browser for PDB
- [BMM Domain Server](#) - Biomolecular Modelling Laboratory (ICRF) protein domain server
- [ReLiBase](#) - Receptor/ligand complexes db [Mirror in [USA](#)]
- [TOPS](#) - Protein topology atlas
- [CCDC](#) - Cambridge Crystallographic Data Center (Cambridge Structural Db (CSD))
- [HSSP](#) - Homology-derived secondary structure of proteins db
- [MutaProt](#) - Comparison of PDB files which differ by point mutations
  
- [SWISS-3DIMAGE](#) - 3D images of proteins and other biological macromolecules
- [BioImage](#) - Biological image db (contains imaging data on macromolecules)

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### Proteomics databases and links

- [Links to known 2-D PAGE database servers, as well as to 2-D PAGE related servers and services](#)
- [Proteomics Links page](#)

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# @-PROXEMIS

BIOINFORMATICS LEARNING PORTAL  
FOR PROTEOMICS

**RESOURCES****CASE STUDIES****SCENARIOS****PRACTICE**

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e-proxemis@expasy.org

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## NEWS [October 2006]

**E-PROXEMIS WEBSITE NEWS****Server migration**

e-Proxemis is on its new server !! From now on, you need to use your new password to navigate through e-Proxemis. This password can be modified in Personal Space -> My Profile. Thank you for understanding.

**Important notice**

Geneva Bioinformatics (GeneBio) SA and the Swiss Institute of Bioinformatics (SIB) announce a strategic partnership involving GeneBio's e-Proxemis (see the **press release**).

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- SCENARIOS
- PRACTICE

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- FUNCTIONAL INFORMATION
- STRUCTURAL INFORMATION
- PTM
- VARIATION & MUTATION
- INTEGRATED GENOMICS
- NUCLEOTIDE SEQUENCE
- TAXONOMY
- REFERENCE & ONTOLOGY
- GENE FINDING & TRANSLATING TOOLS
- SUBCELLULAR LOCATION PREDICTION
- PTM PREDICTION
- STRUCTURE & TOPOLOGY PREDICTION
- SEQUENCE ALIGNMENT
- SIMILARITY SEARCH
- PROTEIN SEPARATION, IDENTIFICATION & CHARACTERISATION



- RESOURCES
- SCENARIOS
- PRACTICE

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**ALPHABETICAL ORDER** **MODIFICATION ORDER (INVERSE)** **CREATION ORDER (INVERSE)**

**A DATA UPDATE EQUALS A KNOWLEDGE EXTENSION FOR E.COLI ENTRY P36679, ALIAS COAE\_ECOLI**

Creation: November 2004 / Last verification: October 2006 /

**A DATA UPDATE EQUALS A KNOWLEDGE REVISION FOR E.COLI ENTRY P36679**

Creation: November 2004 / Last verification: October 2006 /

**A PROTEIN OF KNOWN FUNCTION**

Creation: October 2004 / Last verification: October 2006 /

**A PROTEIN OF UNEXPECTED FUNCTION**

Creation: October 2004 / Last verification: October 2006 /

**A PROTEIN OF UNKNOWN FUNCTION**

Creation: October 2004 / Last verification: October 2006 /

**A PROTEOMICS STUDY OF E.COLI**

Creation: November 2004 / Last verification: October 2006 /

**A VERY SMALL PROTEIN FAMILY**

Creation: January 2005 / Last verification: November 2006 /

**ALTERNATIVELY SPLICED GENES AND ISOFORMS OF CATENIN**

Creation: November 2004 / Last verification: October 2006 /

**AN ESCHERICHIA COLI ENDOPEPTIDASE**

Creation: December 2004 / Last verification: October 2006 /

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RESOURCES CASE STUDIES SCENARIOS

SIMPLE INTERMEDIARY COMPLEX

**PROTEIN SEQUENCE DATABASES**

**INFORMATION IN UNIPROT KNOWLEDGBASE (UNIPROTKB)**  
Creation: April 2005 / Last verification: October 2006 /

**PROTEIN SEQUENCE DATABASES**  
Creation: April 2005 / Last verification: October 2006 /

**SECTIONS OF UNIPROT KNOWLEDGBASE:TREMBL VS SWISS-PROT**  
Creation: April 2005 / Last verification: October 2006 /

**GENOMIC & SPECIES RESOURCES, POLYMORPHISM & MUTATIONS**

**REFERENCE FOR DROSOPHILA**  
Creation: April 2005 / Last verification: October 2006 /

**RETRIEVE GENES OF A CHROMOSOME**  
Creation: April 2005 / Last verification: October 2006 /

**SEQUENCE SIMILARITY & ALIGNMENT**

**SEQUENCE COMPARISON**  
Creation: April 2005 / Last verification: October 2006 /

**MULTIPLE SEQUENCE ALIGNMENT (MSA)**  
Creation: April 2005 / Last verification: October 2006 /

**BLAST**  
Creation: April 2005 / Last verification: October 2006 /

**STRUCTURE, DOMAIN & FAMILY**

**PTM DATABASES**  
Creation: April 2005 / Last verification: October 2006 /

**ABOUT DOMAINS**

# Un exemple pratique

---

De l'identification de protéines par empreinte  
peptidique jusqu'aux bases de données

# PROBLEME

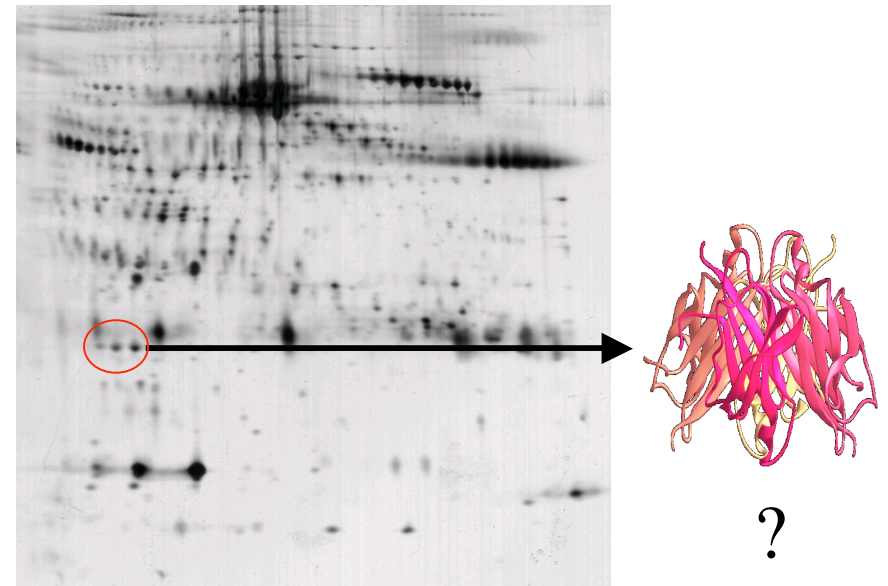
Directeur de la banque OUBS

Qui a volé la banque?



Biologiste

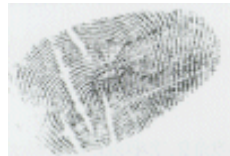
Quelle protéine ai-je isolé ?



# RASSEMBLER DES EVIDENCES

## Officier de Police

1. Interview les témoins
2. Mesure les empreintes

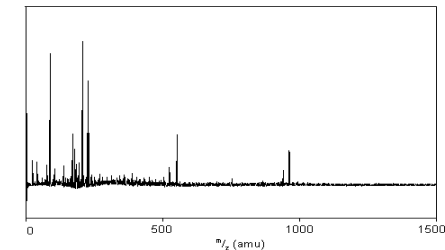


## Spectrométriste de masse

1. Interview le biologiste qui a isolé la protéine
2. Clive la protéine pour obtenir des peptides



3. Analyse les peptides par spectrométrie de masse afin d'obtenir la **masse moléculaire précise des peptides!**



# RECHERCHE DANS LA BASE DE DONNEES

## Officier de Police

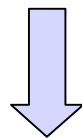
Hauteur: 1m 79cm

Poid: 80 kg

Sex: mâle

Age: 35-40

Empreintes



*recherche*

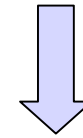
**BASE DE DONNEES DES  
CRIMINELS CONNUS**

## Spectrométriste de masse

Approx. poid moléculaire weight: 30,000 Da

Origine: Plasma humain

Liste des masses peptidiques par analyse MS:  
975.4832, 1112.5368, 632.3147, 803.4134,  
764.3892



*recherche*

**BASE DE DONNEES DES  
MASSES PEPTIDIQUES  
DES PROTEINES CONNUES**



# RESULTATS DE LA RECHERCHE

Officier de Police

Identifie le voleur

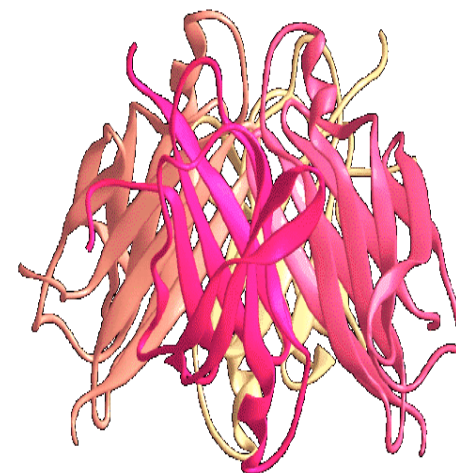
J.-C Criminel



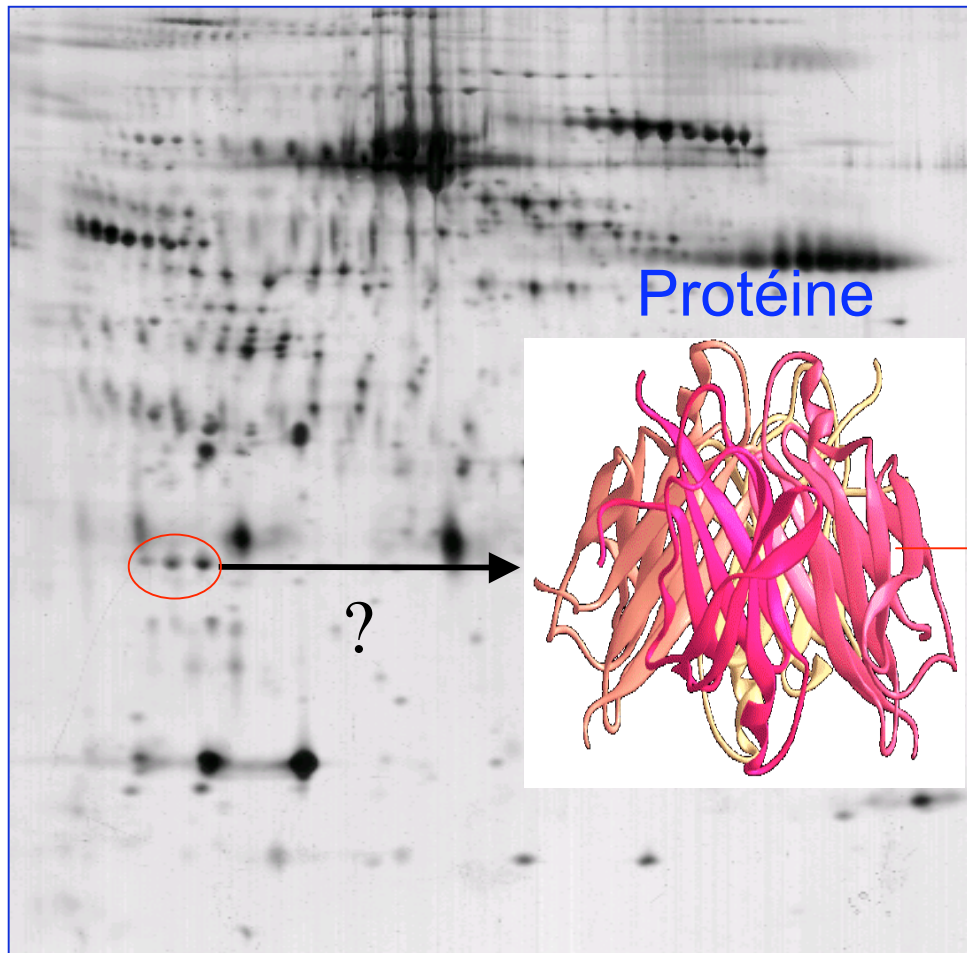
Spectrométriste de masse

Identifie la protéine

Apolipoprotéine A1



# Digestion Tryptique



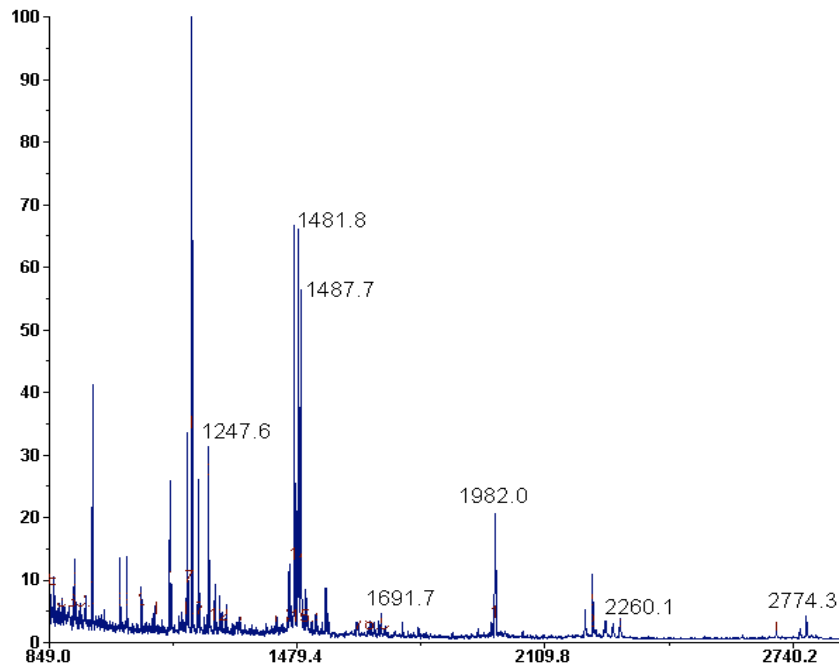
Digestion

## Peptides

NVLIFDLGGGTFDVSILTIE DGIFEVK  
QTQTFTTYSNQPGLVLIQVY EGER  
GVPQIEVTFDIDANGILNVS AVDK  
SINPDEAVAYGAAVQAAILS GDK  
GPAVGIDLGTTYSCVGVFQH GK  
TVTNAVVTVPAYFNDSQR  
STAGDTHLGGEDFDNR  
NQVAMNPTNTVFDK  
SFYPEEVSSMLTK  
TTPSYVAFTDTER  
SQIHDIVLVGGSTR  
NSLESYAFNMK  
FEELNADLFR  
CNEIINWLDK  
VEIANDQGNR



# Analyse MS et détection de Pics



896.325  
1012.548  
1157.589  
1214.057  
1230.64  
1235.617  
1236.717  
1242.708  
1252.678  
1268.674  
1274.631  
1302.654  
1386.642  
1392.74  
1398.703  
1408.692

• • • • •

## MASCOT Peptide Mass Fingerprint

<b>Your name</b>	<input type="text" value="sanchez"/>	<b>Email</b>	<input type="text" value="jean-charles.sanchez@medecine."/>
<b>Search title</b>	<input type="text" value="spot1"/>		
<b>Database</b>	SwissProt <input type="button" value="v"/>		
<b>Taxonomy</b>	..... Homo sapiens (human) <input type="button" value="v"/>		
<b>Enzyme</b>	Trypsin <input type="button" value="v"/>	<b>Allow up to</b>	1 <input type="button" value="v"/> missed cleavages
<b>Fixed modifications</b>	<input type="checkbox"/> Biotin (N-term) <input checked="" type="checkbox"/> Carbamidomethyl (C) <input type="checkbox"/> Carbamyl (K) <input type="checkbox"/> Carbamyl (N-term) <input type="checkbox"/> Carboxymethyl (C)	<b>Variable modifications</b>	<input type="checkbox"/> N-Acetyl (Protein) <input type="checkbox"/> N-Formyl (Protein) <input type="checkbox"/> NIPCAM (C) <input type="checkbox"/> O18 (C-term) <input checked="" type="checkbox"/> Oxidation (M) <input type="checkbox"/> Oxidation (DM)
<b>Protein mass</b>	<input type="text"/> kDa	<b>Peptide tol. ±</b>	1 <input type="text"/> Da <input type="button" value="v"/>
<b>Mass values</b>	<input checked="" type="radio"/> MH <sup>+</sup> <input type="radio"/> M <sub>r</sub> <input type="radio"/> M-H <sup>-</sup>		
<b>Data file</b>	<input type="text"/> <input type="button" value="Parcourir..."/>		
<b>Query</b>	1484.817 NB Contents of this field are ignored if a data file is specified. 1498.782 1500.797 1514.739 1552.718 1568.868 1579.873		
<b>Overview</b>	<input type="checkbox"/>	<b>Report top</b>	20 <input type="button" value="v"/> hits
<input type="button" value="Start Search ..."/>		<input type="button" value="Reset Form"/>	

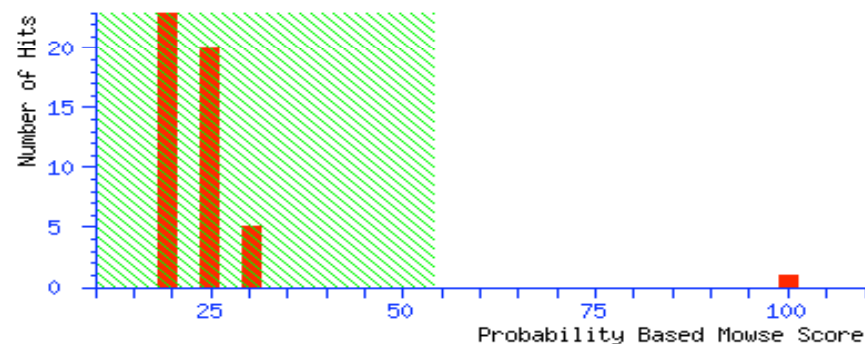


**Mascot Search Results**

**User** : sanchez  
**Email** : jean-charles.sanchez@medecine.unige.ch  
**Search title** : spot1  
**Database** : SwissProt 51.1 (241365 sequences; 88596301 residues)  
**Taxonomy** : Homo sapiens (human) (15069 sequences)  
**Timestamp** : 22 Nov 2006 at 15:47:26 GMT  
**Top Score** : 100 for **APOA1\_HUMAN**, Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)]

**Probability Based Mowse Score**

Protein score is  $-10 \cdot \log(P)$ , where P is the probability that the observed match is a random event. Protein scores greater than 54 are significant ( $p < 0.05$ ).


**Concise Protein Summary Report**

Format As	Concise Protein Summary	<a href="#">Help</a>
Significance threshold p<	0.05	Max. number of hits 20
Re-Search All	Search Unmatched	

- [APOA1\\_HUMAN](#)    **Mass:** 30759    **Score:** 100    **Expect:** 1.5e-06    **Queries matched:** 18  
 Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)] - Homo sapiens (Human)

## Concise Protein Summary Report

Format As

Concise Protein Summary

[Help](#)

Significance threshold p&lt; 0.05

Max. number of hits 20

Re-Search All

Search Unmatched

1. [APOA1\\_HUMAN](#)      **Mass:** 30759      **Score:** 100      **Expect:** 1.5e-06      **Queries matched:** 18  
Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)] - Homo sapiens (Human)

---

2. [NKG2A\\_HUMAN](#)      **Mass:** 26783      **Score:** 30      **Expect:** 14      **Queries matched:** 7  
NKG2-A/NKG2-B type II integral membrane protein (NKG2-A/B-activating NK receptor) (NK cell receptor A) (CD159a a

---

3. [KGP1A\\_HUMAN](#)      **Mass:** 76812      **Score:** 29      **Expect:** 19      **Queries matched:** 14  
cGMP-dependent protein kinase 1, alpha isozyme (EC 2.7.11.12) (CGK 1 alpha) (cGKI-alpha) - Homo sapiens (Human)
- [KGP1B\\_HUMAN](#)      **Mass:** 78325      **Score:** 23      **Expect:** 77      **Queries matched:** 14  
cGMP-dependent protein kinase 1, beta isozyme (EC 2.7.11.12) (CGK 1 beta) (cGKI-beta) - Homo sapiens (Human)

---

4. [TCF20\\_HUMAN](#)      **Mass:** 213123      **Score:** 28      **Expect:** 21      **Queries matched:** 18  
Transcription factor 20 (Stromelysin 1 PDGF-responsive element-binding protein) (SPRE-binding protein) (Nuclear

---

5. [RUNX3\\_HUMAN](#)      **Mass:** 44556      **Score:** 28      **Expect:** 24      **Queries matched:** 6  
Runt-related transcription factor 3 (Core-binding factor, alpha 3 subunit) (CBF-alpha 3) (Acute myeloid leukemia

---

6. [CO7A1\\_HUMAN](#)      **Mass:** 296010      **Score:** 28      **Expect:** 24      **Queries matched:** 19  
Collagen alpha-1(VII) chain precursor (Long-chain collagen) (LC collagen) - Homo sapiens (Human)

---

7. [DCMC\\_HUMAN](#)      **Mass:** 55368      **Score:** 25      **Expect:** 44      **Queries matched:** 11  
Malonyl-CoA decarboxylase, mitochondrial precursor (EC 4.1.1.9) (MCD) - Homo sapiens (Human)

---

8. [GNA12\\_HUMAN](#)      **Mass:** 44291      **Score:** 25      **Expect:** 47      **Queries matched:** 8  
Guanine nucleotide-binding protein alpha-12 subunit (G alpha-12) - Homo sapiens (Human)

---

9. [RBM7\\_HUMAN](#)      **Mass:** 30485      **Score:** 25      **Expect:** 50      **Queries matched:** 7  
RNA-binding protein 7 (RNA-binding motif protein 7) - Homo sapiens (Human)

# *MATRIX* SCIENCE Mascot Search Results

## Protein View

Match to: **APOA1\_HUMAN** Score: 100 Expect: 1.5e-06

**Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)] - Homo sapiens (Human)**

Nominal mass ( $M_r$ ): 30759; Calculated pI value: 5.56

NCBI BLAST search of [APOA1\\_HUMAN](#) against nr

Unformatted [sequence string](#) for pasting into other applications

Taxonomy: [Homo sapiens](#)

Fixed modifications: Carbamidomethyl (C)

Variable modifications: Oxidation (M)

Cleavage by Trypsin: cuts C-term side of KR unless next residue is P

Number of mass values searched: 55

Number of mass values matched: 18

Sequence Coverage: 53%

Matched peptides shown in **Bold Red**

```

1 MKA AVLTLAV LFLTGSQARH FWQQDEPPQS PWDRVKDLAT VYVDVLKDSG
51 RDYVSQFEGS ALGKQLNLKL LDNWDSVTST FSKLREQLGP VTQEFWDNLE
101 KETEGLRQEM SKDLEEVKAK VQPYLDDFQK KWQEEMELYS QKVEPLRAEL
151 QEGARQKLHE LQEKLSPLGE EMRDRARAHV DALRTHLAPY SDELRQRLAA
201 RLEALKENGG ARLAEYHAKA TEHLSTLSEK AKPALEDLRQ GLLPVLESFK
251 VSFLSALEEY TKKLNTQ

```

Show predicted peptides also

Sort Peptides By  Residue Number  Increasing Mass  Decreasing Mass

Start - End	Observed	Mr (expt)	Mr (calc)	Delta	Miss	Sequence
35 - 47	1462.7750	1461.7677	1461.8442	-0.0765	1	<b>R.VKDLATVYVDVLK.D</b>
37 - 47	1235.6170	1234.6097	1234.6809	-0.0711	0	<b>K.DLATVYVDVLK.D</b>
37 - 51	1650.7810	1649.7737	1649.8624	-0.0887	1	<b>K.DLATVYVDVLKDSGR.D</b>
65 - 83	2209.0730	2208.0657	2208.1426	-0.0769	1	<b>K.QLNLKLLDNWDSVTSTFSK.L</b>
70 - 83	1612.6910	1611.6837	1611.7780	-0.0943	0	<b>K.LLDNWDSVTSTFSK.L</b>
70 - 85	1882.9390	1881.9317	1880.9632	0.9685	1	<b>K.LLDNWDSVTSTFSKLR.E</b>
84 - 101	2202.0970	2201.0897	2201.1116	-0.0219	1	<b>K.LREQLGPVTQEFWDNLEK.E</b>
121 - 129	1252.6290	1251.6207	1251.6125	0.0572	0	<b>K.VQPYLDDFQK.K</b>

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# SWISS-2DPAGE

## Two-dimensional polyacrylamide gel electrophoresis database

**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 18.0, September 2006 and updates up to 02-Oct-2006 (contains 1265 entries in 36 reference maps from human, mouse, *Arabidopsis thaliana*, *Dictyostelium discoideum*, *Escherichia coli*, *Saccharomyces cerevisiae*, and *Staphylococcus aureus* (N315)).**

[\[Search\]](#)[\[Documents\]](#)[\[Services\]](#)[\[Software\]](#)[\[Related servers\]](#)[\[Other databases\]](#)[\[Job openings\]](#)

### 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](#)

### SWISS-2DPAGE documents

- [User manual](#)
- [Release notes](#) (September 26, 2006) **new**
- [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](#),

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## SWISS-2DPAGE Viewer

CSF\_HUMAN { Cerebrospinal Fluid } (All identified proteins)

[Back to the](#)

[search engine](#)

Switch to Gel:

Re-scale Gel from 100 % to:

View:

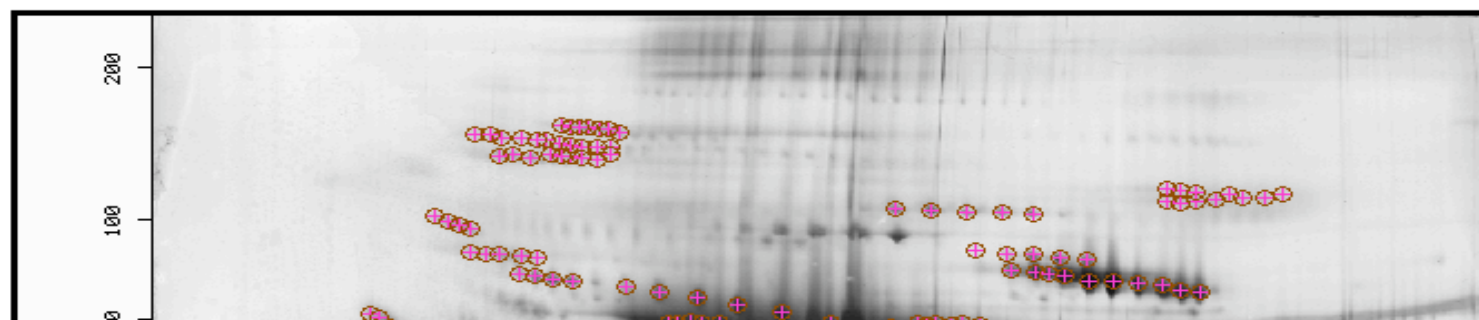
Display:  + Identified spots

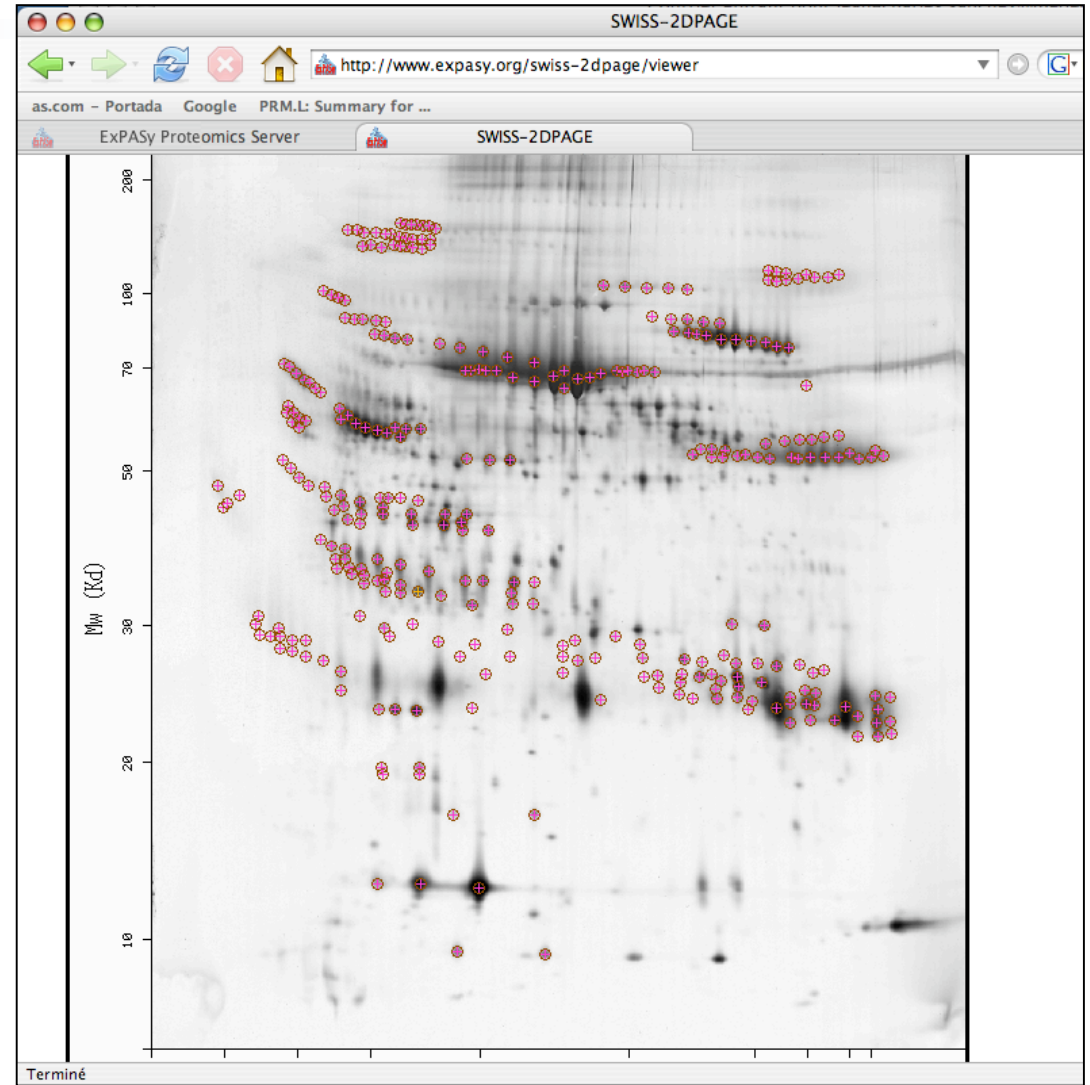
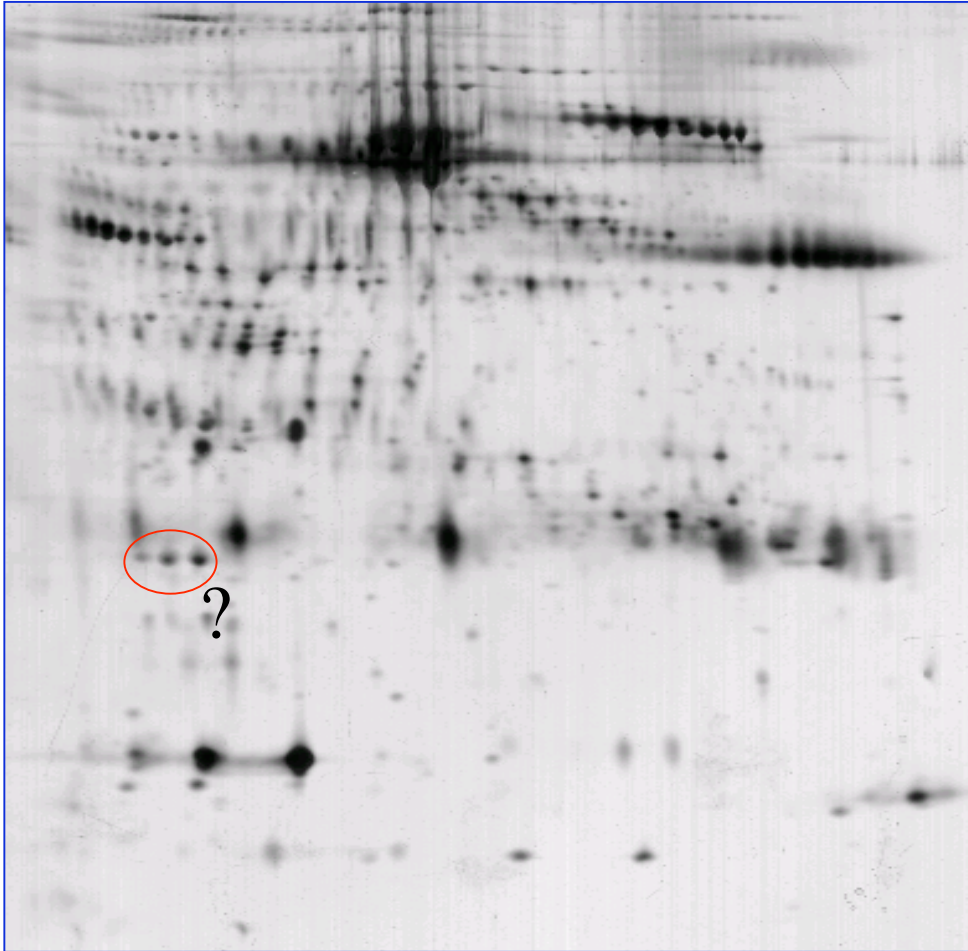
Identified by:  show  hide

(   PMF   Tandem MS (Peptide Sequencing)  + AA Composition

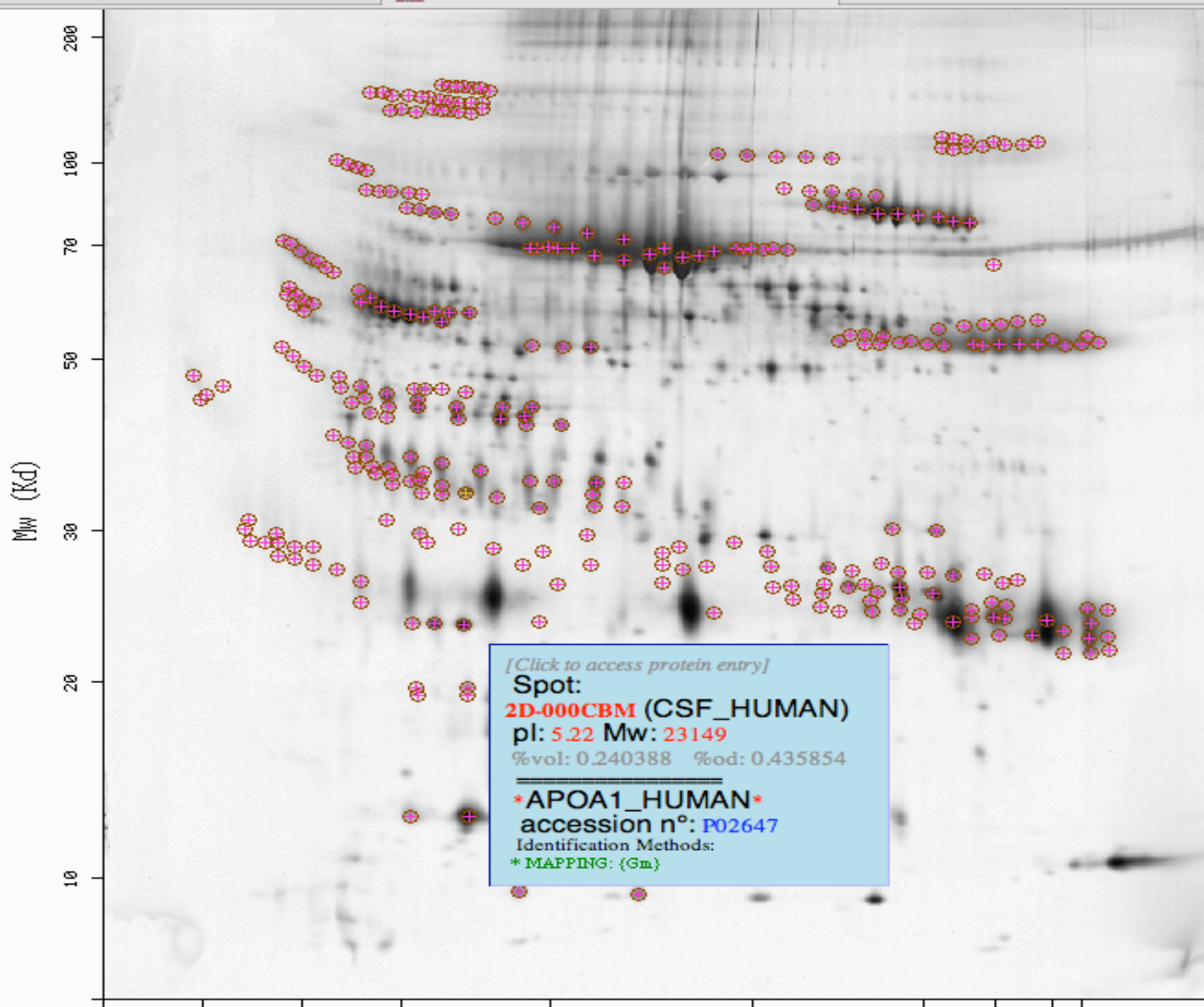
Micro-Sequencing / Tagging   Gel Matching   Comigration   Immunoblotting )

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









**Home (search engine)****Search by**

- [\[accession number\]](#)
- [\[description, ID or gene\]](#)
- [\[author's name\]](#)
- [\[spot ID / serial number\]](#) ▶
- [\[identification methods\]](#)
- [\[pI / Mw range\]](#)
- [\[combined fields\]](#)

**Maps**

- [\[experimental info\]](#)
- [\[protein list\]](#)
- [\[graphical interface\]](#)

**Query Remote Interfaces:**World-2DPAGE 
 Exclude local DBs  
*has only effect if a remote interface is selected*

## Sample Preparation and Post-separation Analysis

Searching in 'SWISS-2DPAGE' for entry matching: **P02647****SWISS-2DPAGE:** P02647**P02647****General information about the entry**[View entry in simple text format](#)

Entry name	<b>APOA1_HUMAN</b>
Primary accession number	<b>P02647</b>
integrated into SWISS-2DPAGE on	August 1, 1993 (release 0)
2D Annotations were last modified on	March 31, 2004 (version 2)
General Annotations were last modified on	September 26, 2006 (version 14)

**Name and origin of the protein**

Description	<b>Apolipoprotein A-I (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)].</b>
Gene name	<b>Name=APOA1</b>
Annotated species	Homo sapiens (Human) [TaxID: 9606]
Taxonomy	Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.

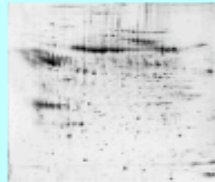
**References**

- [1] MAPPING ON GEL  
MEDLINE=93162045; PubMed=1286669; [NCBI, ExpASy, EBI, Israel, Japan]  
Hochstrasser D.F., Frutiger S., Paquet N., Bairoch A., Ravier F., Pasquali C., Sanchez J.-C., Tissot J.-D., Bjellqvist B., Vargas R., Appel R.D., Hughes G.J.  
"Human liver protein map: a reference database established by microsequencing and gel comparison"  
Electrophoresis 13:992-1001(1992)
- [2] MAPPING ON GEL  
MEDLINE=96007934; PubMed=7498157; [NCBI, ExpASy, EBI, Israel, Japan]  
Sanchez J.-C., Appel R.D., Golaz O.G., Pasquali C., Ravier F., Bairoch A., Hochstrasser D.F.  
"Inside SWISS-2DPAGE database"  
Electrophoresis 16:1131-1151(1995)
- [3] MAPPING ON GEL  
MEDLINE=78094420; PubMed=271964; [NCBI, ExpASy, EBI, Israel, Japan]

map experimental info  
protein estimated location

#### HEPG2SP\_HUMAN {HepG2 Secreted Proteins}

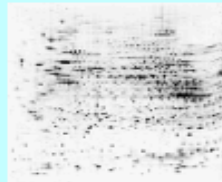
*Homo sapiens (Human)*  
Tissue: Hepatoblastoma



map experimental info  
protein estimated location

#### HEPG2\_HUMAN {HepG2}

*Homo sapiens (Human)*  
Tissue: Hepatoblastoma



map experimental info  
protein estimated location

#### LIVER\_HUMAN {Liver}

*Homo sapiens (Human)*  
Tissue: Liver



map experimental info  
protein estimated location

#### LYMPHOMA\_HUMAN {Lymphoma}

#### HEPG2SP\_HUMAN

##### MAP LOCATIONS:

- SPOT 2D-0009HS: pl=5.42; Mw=21307
- SPOT 2D-0009HW: pl=5.34; Mw=21307
- SPOT 2D-0009I3: pl=5.24; Mw=21062
- SPOT 2D-0009I8: pl=5.10; Mw=21062

##### MAPPING (identification):

MATCHING WITH THE PLASMA MASTER GEL [2].

#### HEPG2\_HUMAN

##### MAP LOCATIONS:

- SPOT 2D-0003Q0: pl=5.22; Mw=23900

##### MAPPING (identification):

MATCHING WITH THE LIVER MASTER GEL [2].

#### LIVER\_HUMAN

##### MAP LOCATIONS:

- SPOT 2D-0001E9: pl=5.21; Mw=23862

##### POSITIONAL VARIANTS:

MILANO, MARBURG, FUKUOKA, NORWAY, GIESSEN, MUNSTER AND IOWA A-1 VARIANTS.

##### MAPPING (identification):

MICROSEQUENCING [1].

# UniProtKB/Swiss-Prot entry **P02647**


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*Note: most headings are clickable, even if they don't appear as links. They link to the user manual or other documents.*

## Entry information

Entry name	<b>APOA1_HUMAN</b>
Primary accession number	<b>P02647</b>
Secondary accession numbers	Q6LDN9 Q6Q785
Integrated into Swiss-Prot on	July 21, 1986
Sequence was last modified on	July 21, 1986 (Sequence version 1)
Annotations were last modified on	November 14, 2006 (Entry version 98)

## Name and origin of the protein

Protein name	<b>Apolipoprotein A-I [Precursor]</b>
Synonyms	<b>Apo-AI ApoA-I</b>
Contains	<b>Apolipoprotein A-I(1-242)</b>
Gene name	<b>Name: APOA1</b>
From	<b>Homo sapiens (Human) [TaxID: 9606]</b>
Taxonomy	<b>Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi; Mammalia; Eutheria; Euarchontoglires; Primates; Haplorrhini; Catarrhini; Hominidae; Homo.</b>

## References

- [1] NUCLEOTIDE SEQUENCE [GENOMIC DNA].  
PubMed=6406984 [NCBI, ExPASy, EBI, Israel, Japan]  
Shoulders C.C., Kornblihtt A.R., Munro B.S., Baralle F.E.;  
"Gene structure of human apolipoprotein A1."  
*Nucleic Acids Res.* 11:2827-2837(1983).
- [2] NUCLEOTIDE SEQUENCE [GENOMIC DNA].  
PubMed=6304641 [NCBI, ExPASy, EBI, Israel, Japan]  
Cheung P., Chan L.;  
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*Nucleic Acids Res.* 11:3703-3715(1983).
- [3] NUCLEOTIDE SEQUENCE [GENOMIC DNA].

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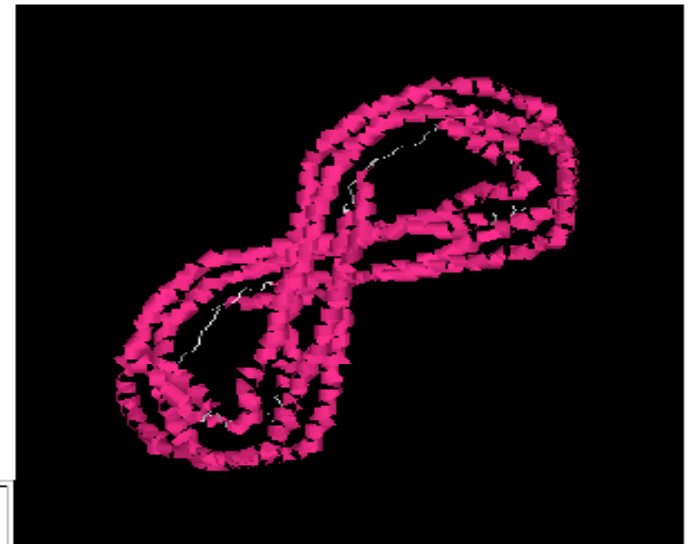
# PDB code: 1AV1

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HEADER      LIPID TRANSPORT                      23-SEP-97   1AV1
TITLE      CRYSTAL STRUCTURE OF HUMAN APOLIPOPROTEIN A-I
SOURCE     MOL_ID: 1;
SOURCE     2 ORGANISM_SCIENTIFIC: HOMO SAPIENS;
SOURCE     3 ORGANISM_COMMON: HUMAN;
SOURCE     4 TISSUE: BLOOD;
SOURCE     5 EXPRESSION_SYSTEM: ESCHERICHIA COLI;
SOURCE     6 EXPRESSION_SYSTEM_STRAIN: BL21 (DE3);
SOURCE     7 EXPRESSION_SYSTEM_VECTOR_TYPE: PLASMID;
SOURCE     8 EXPRESSION_SYSTEM_VECTOR: PGEMEX
EXPDTA     X-RAY DIFFRACTION
  
```

## Data retrieval:

<b>Coordinate file</b>	<a href="#">PDB header only [ExpASY / RCSB]</a> <a href="#">PDB complete entry [ExpASY / RCSB]</a> <a href="#">mmCIF entry [RCSB]</a>
<b>Image visualisation</b>	<a href="#">ExpASY: Still image / Chime / RasMol</a> <a href="#">RCSB: Interactive view</a> <a href="#">IMB Jena Image Library</a> <a href="#">EBI: First glance / AstexViewer™</a> <a href="#">STING: Interactive DIAMOND Image / Protein Dossier / STING Report / Sting98</a>



## Swiss-Prot entry with a cross-reference to 1AV1:

[P02647](#) (APOA1\_HUMAN) Apolipoprotein A-I precursor (Apo-AI) (ApoA-I) [Contains: Apolipoprotein A-I(1-242)] (Gene name: APOA1) [Homo sapiens (Human)]

## Other resources with information on 1AV1:

- [PDBsum](#) (Summarized PDB information)
- [CATH](#) (Protein Structure Classification)

# LIENS

**AVC:** <http://www.attaquecerebrale.org/>

**ExpASy:** <http://www.expasy.org/>

<http://www.expasy.org/sitemap.html>

<http://www.expasy.org/links.html>

**e-proxemis:** [http://e-proxemis.expasy.org/?ep\\_random=8115622](http://e-proxemis.expasy.org/?ep_random=8115622)

[http://e-proxemis.expasy.org/rubrique.php3?id\\_rubrique=1](http://e-proxemis.expasy.org/rubrique.php3?id_rubrique=1)

[http://e-proxemis.expasy.org/rubrique.php3?id\\_rubrique=4](http://e-proxemis.expasy.org/rubrique.php3?id_rubrique=4)

[http://e-proxemis.expasy.org/rubrique.php3?id\\_rubrique=46](http://e-proxemis.expasy.org/rubrique.php3?id_rubrique=46)

**Mascot et empreinte peptidique:**

[http://www.matrixscience.com/cgi/search\\_form.pl?FORMVER=2&SEARCH=PMF](http://www.matrixscience.com/cgi/search_form.pl?FORMVER=2&SEARCH=PMF)

**SWISS-2DPAGE:** <http://www.expasy.org/ch2d/>

[http://www.expasy.org/swiss2dpage/ac=P02647&map=csf\\_human&spot=2D-000CBM#spot](http://www.expasy.org/swiss2dpage/ac=P02647&map=csf_human&spot=2D-000CBM#spot)

**UNIPROT:** <http://www.expasy.org/uniprot/P02647>