Applied Medical Proteomics
issues and solutions

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Integromics SL

Reunión científica sobre proteómica clínica
17/18 de septiembre de 2009
Hospital Universitario A Coruña

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Applied Medical Proteomics issues and solutions

- Presentation outline

  - Applied Proteomics Overview
    - The biological and medical context
    - Differential proteomics applied to neurodegeneration (the case of Huntington's Disease)
    - Some issues

  - OmicsHub Proteomics
    - The solutions

  - Conclusions

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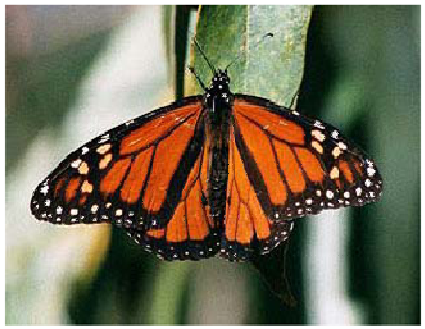
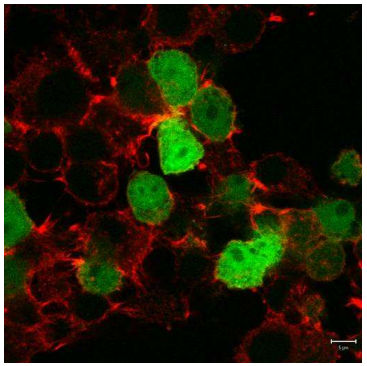
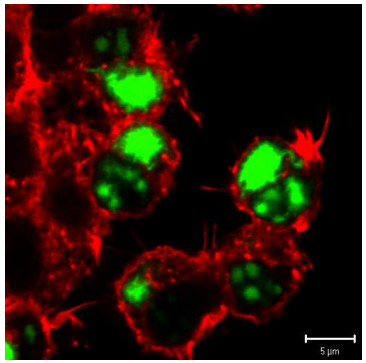
Applied Proteomics Overview

- The biological and medical context
  - The cells of an organism express the same genome but…



  - …understanding gene expression modulation is key…





  - …particularly in the context of diseases like HD

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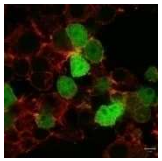
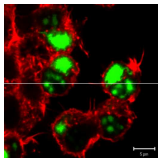
Differential proteomics applied to neurodegeneration

- Approach

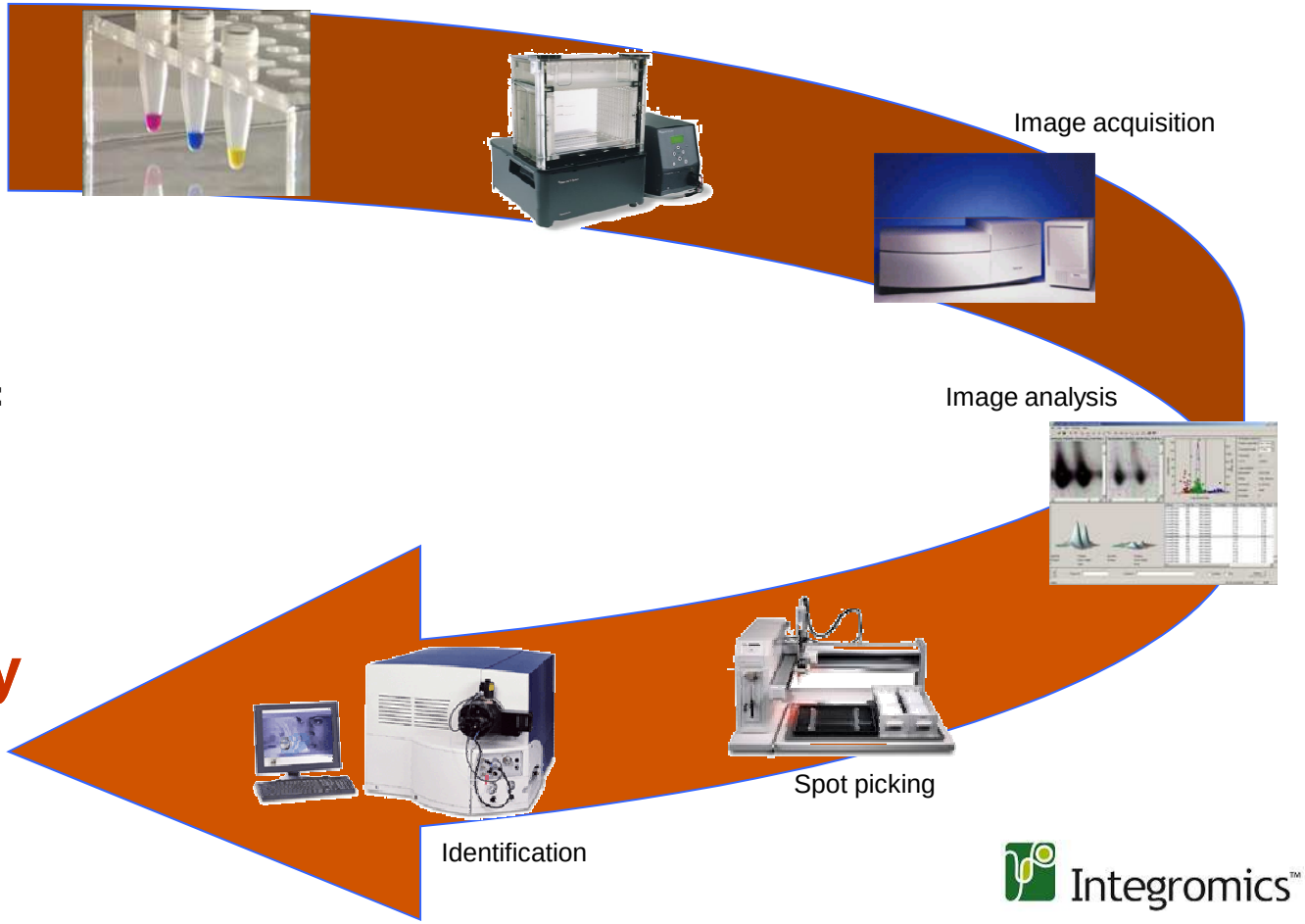
Wild type Huntingtin



Mutant Huntingtin



Cellular disease model of Huntington's Disease (HD):
Recombinant rat PC-12 cells



Differentially modulated proteins

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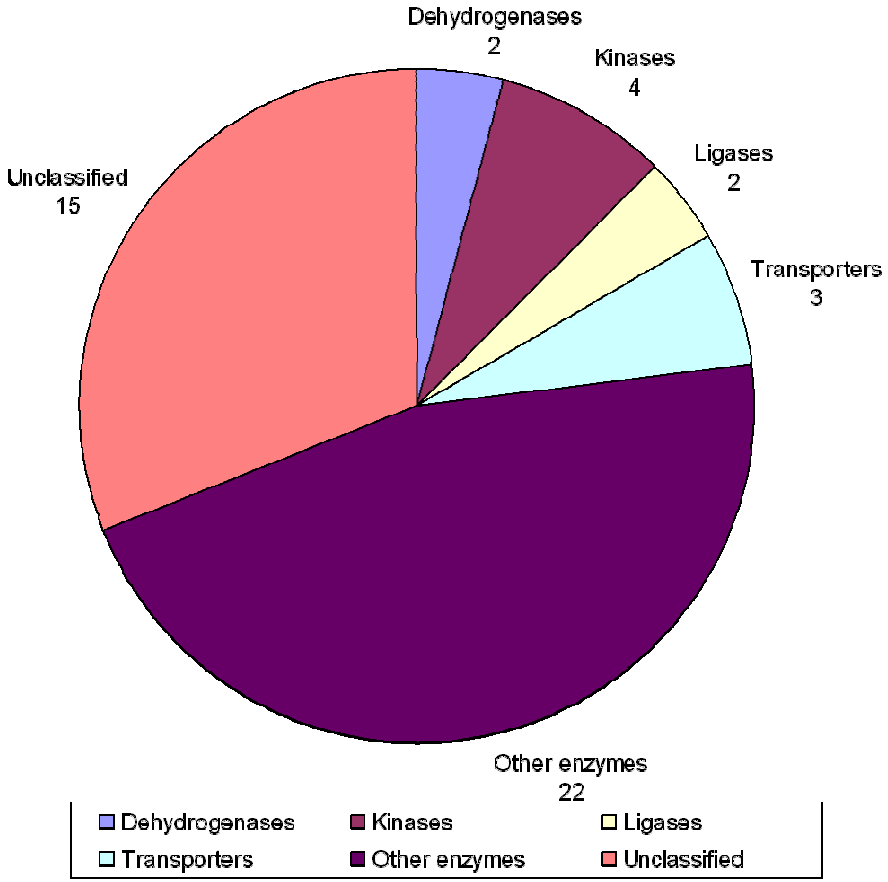
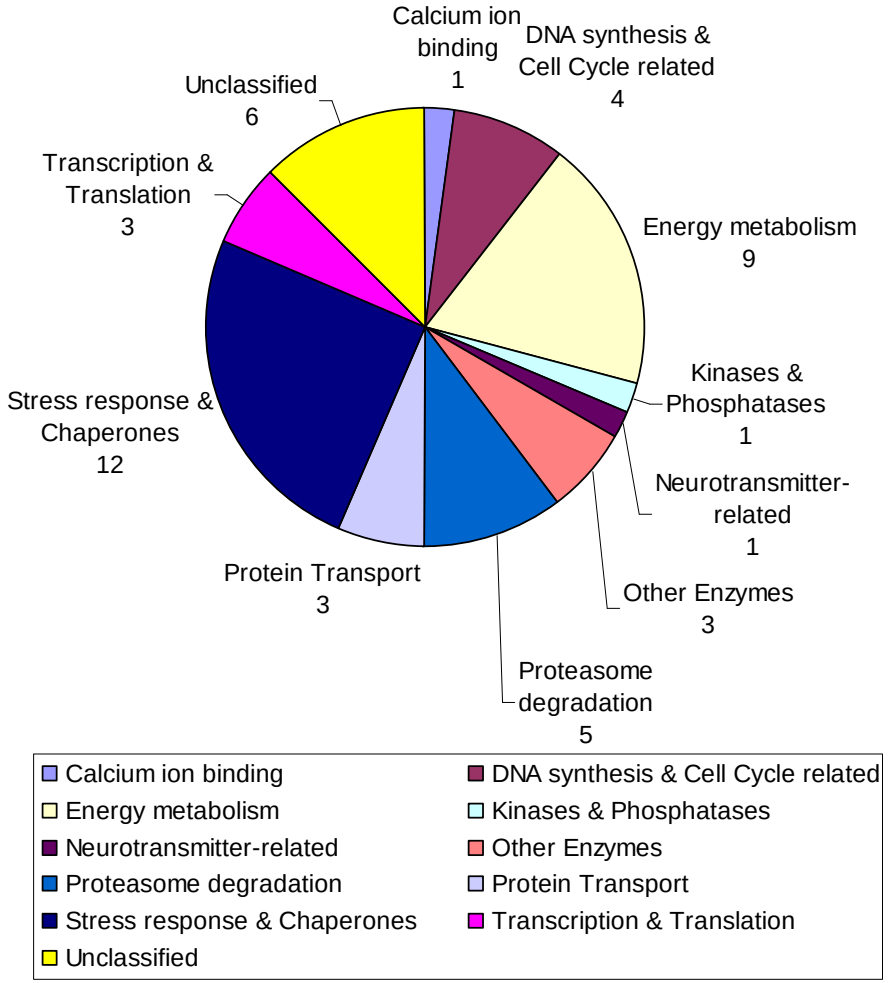
Differential proteomics applied to neurodegeneration

- Results overview
  - Tractable protein families

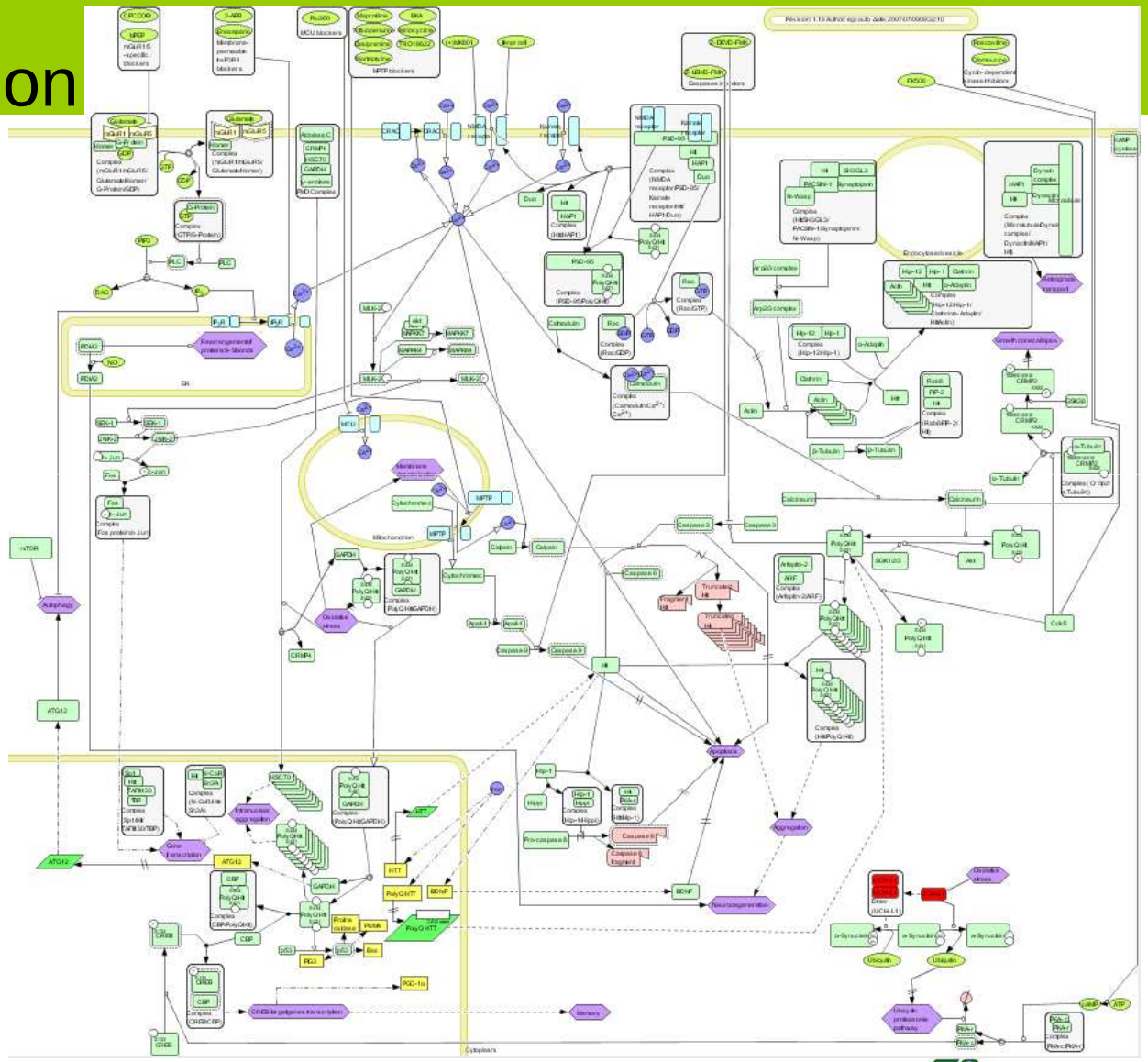


  - Functional processes



Pathways
in silico integration

- HD patho-pathway integrating
  - literature evidences
  - public & proprietary pathways and protein networks databases
  - in house experiments



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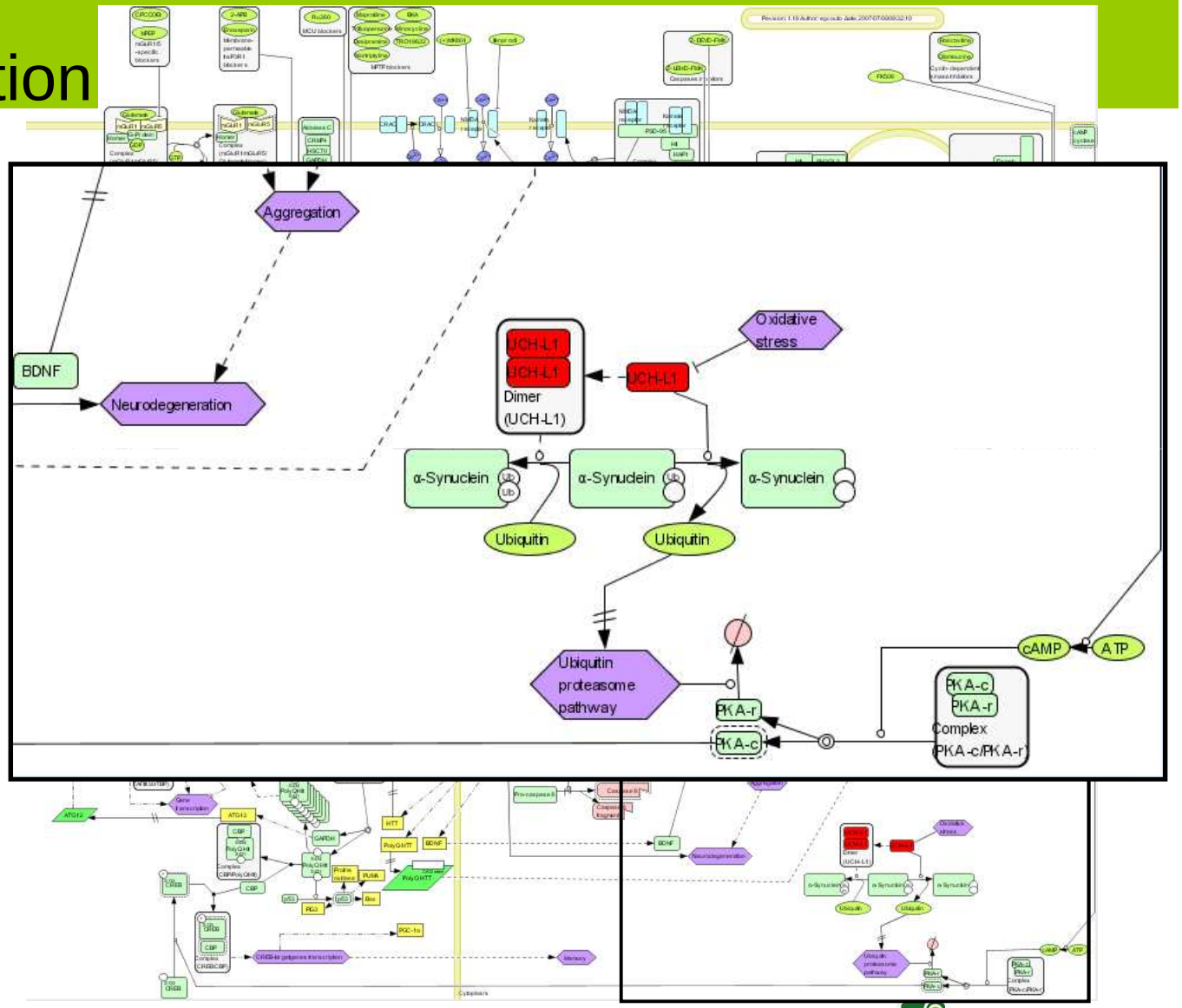
Pathways
in silico integration

- An example of a potential target
  - Based on
    - literature
    - in house evidences
  - Proteasome
    - UCHL1



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Applied Medical Proteomics issues and solutions

- Some issues
  - More than one protein per spot in 2D DIGE
  - Abundant proteins mask low abundance proteins
  - Tissue / cell type “frequent hitters”
  - Redundancy (i.e. usage of overlapping DBs)
  - Traceability of bioinformatics analysis (HUPO)
  - Few groups act in accordance with proteomics standards

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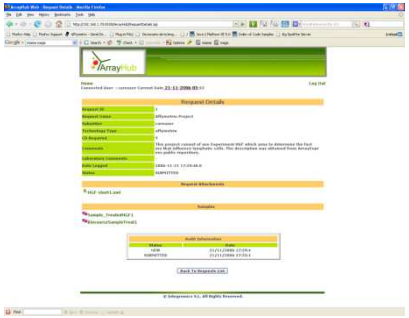
Integromics Products Overview

Microarray

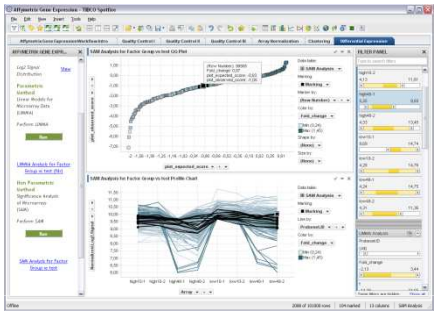
ArrayHub

GeneChip Compatible



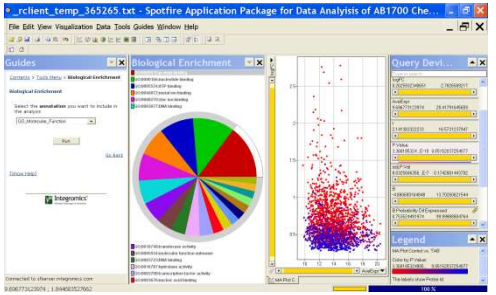
IBD

Spotfire



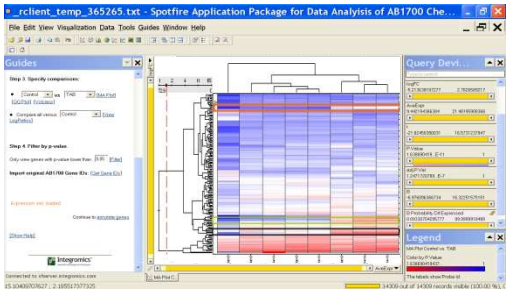
ArrayUnlock

Spotfire



RealTime StatMiner™

Spotfire



RT-PCR

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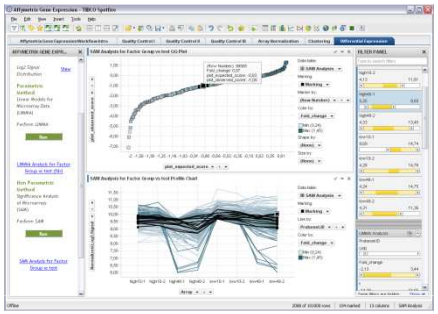
Integromics Products Overview

Microarray

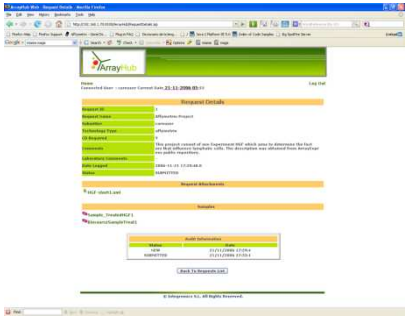
IBD

Spotfire



ArrayHub

GeneChip Compatible



ArrayUnlock

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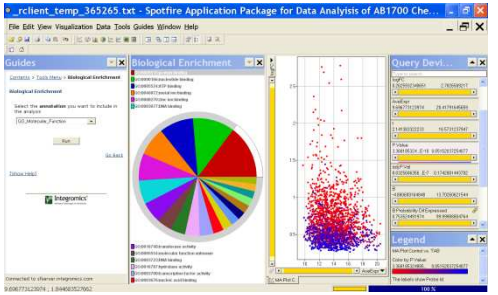
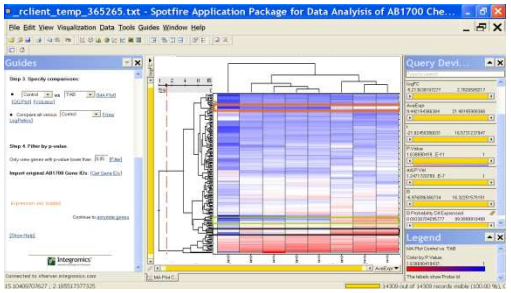


OmicsHub™

RealTime StatMiner™

Spotfire



RT-PCR

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OmicsHub Proteomics

Instrument Data Import

Ontology Annotation

Peak List Information

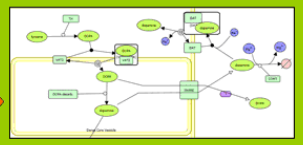
Sample Information

Protocol Information

Experiment Information

Protein Search Engines

Pathways Integration



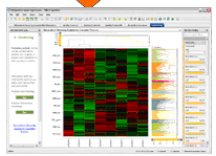
Proteins Information

Protein Grouping

Protein Annotation

Protein Tagging

OmicsHub



Protein Analysis

Export PRIDE Format

Fully Web-based

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OmicsHub Proteomics

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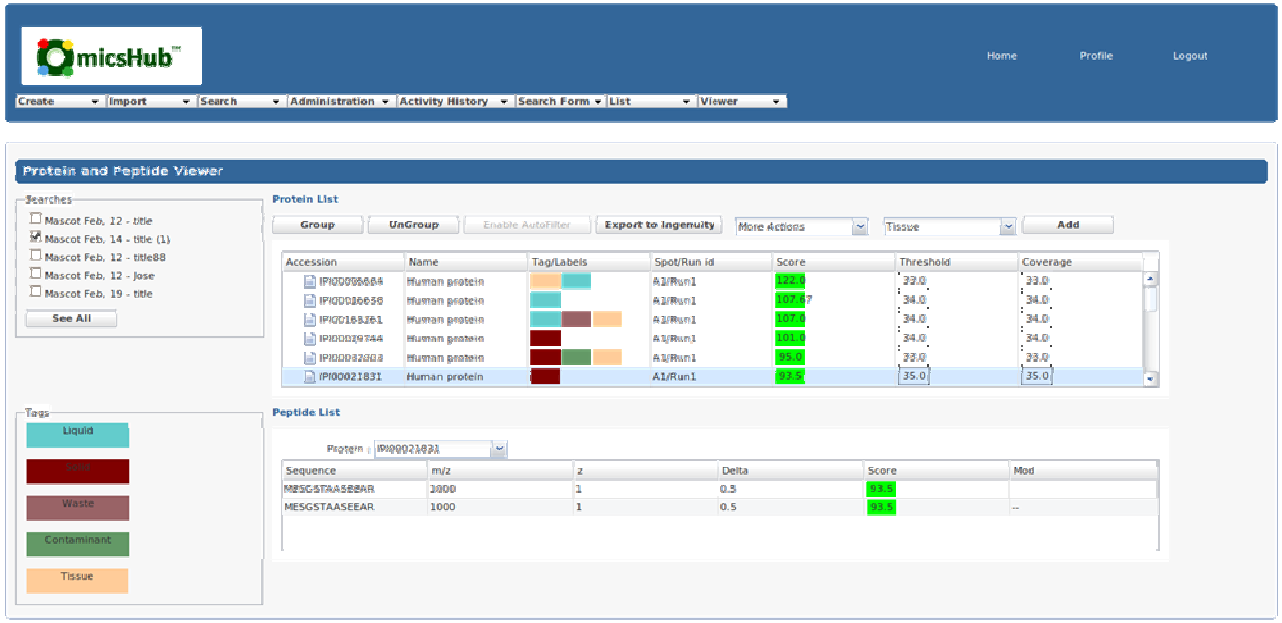
OmicsHub Proteomics

- The solutions
  - Abundant proteins mask low abundance proteins
  - Tissue / cell type “frequent hitters”
    - OmicsHub
      - Uses color labels to “tag” lists of proteins
      - High-lights scoring results



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OmicsHub Proteomics

- The solutions
  - Redundancy (i.e. usage of overlapping DBs)
    - OmicsHub offers a post-processing step to group proteins and reduce the number identified proteins to a manageable number

Identification results redundancy reduction and sequence selection

P1_D

P1_M

P1_H

p1_H

P2_M

P2_D

q1_H

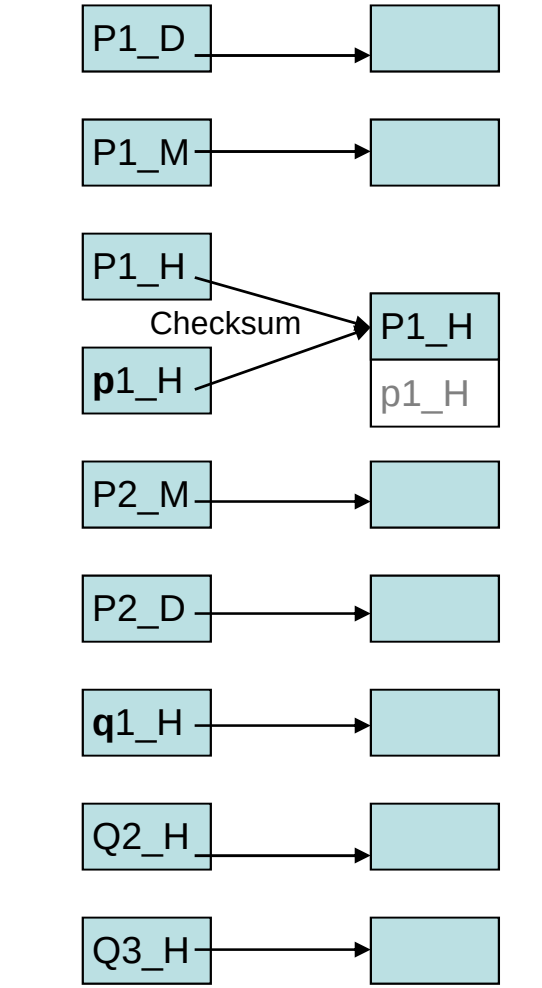
Q2_H

Q3_H

Mascot identification results (1 spot)

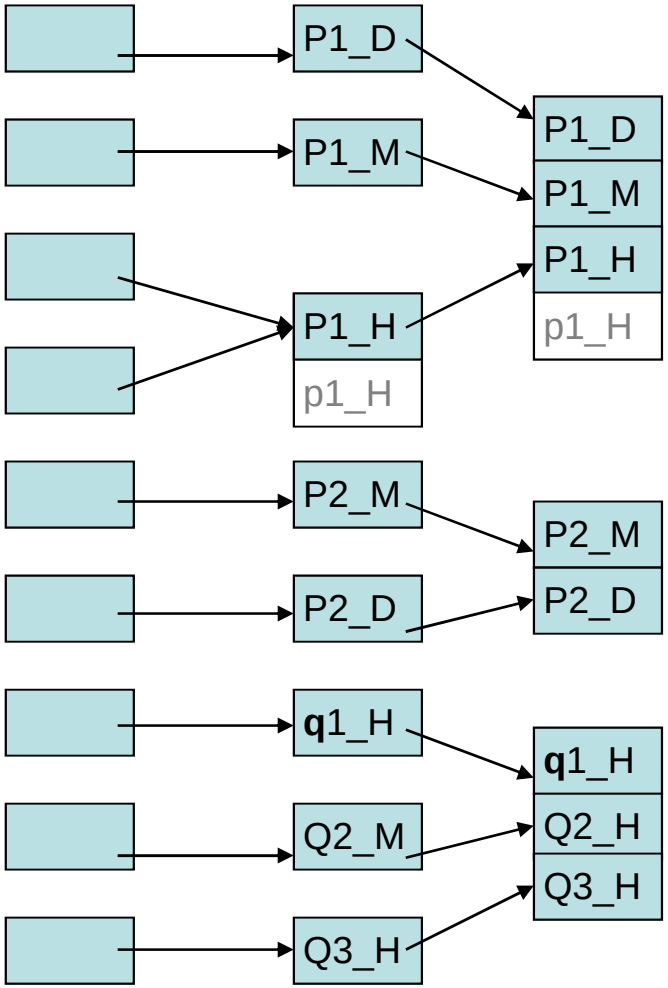
OmicsHub™

Identification results redundancy reduction and sequence selection



OmicsHub™

Identification results redundancy reduction and sequence selection



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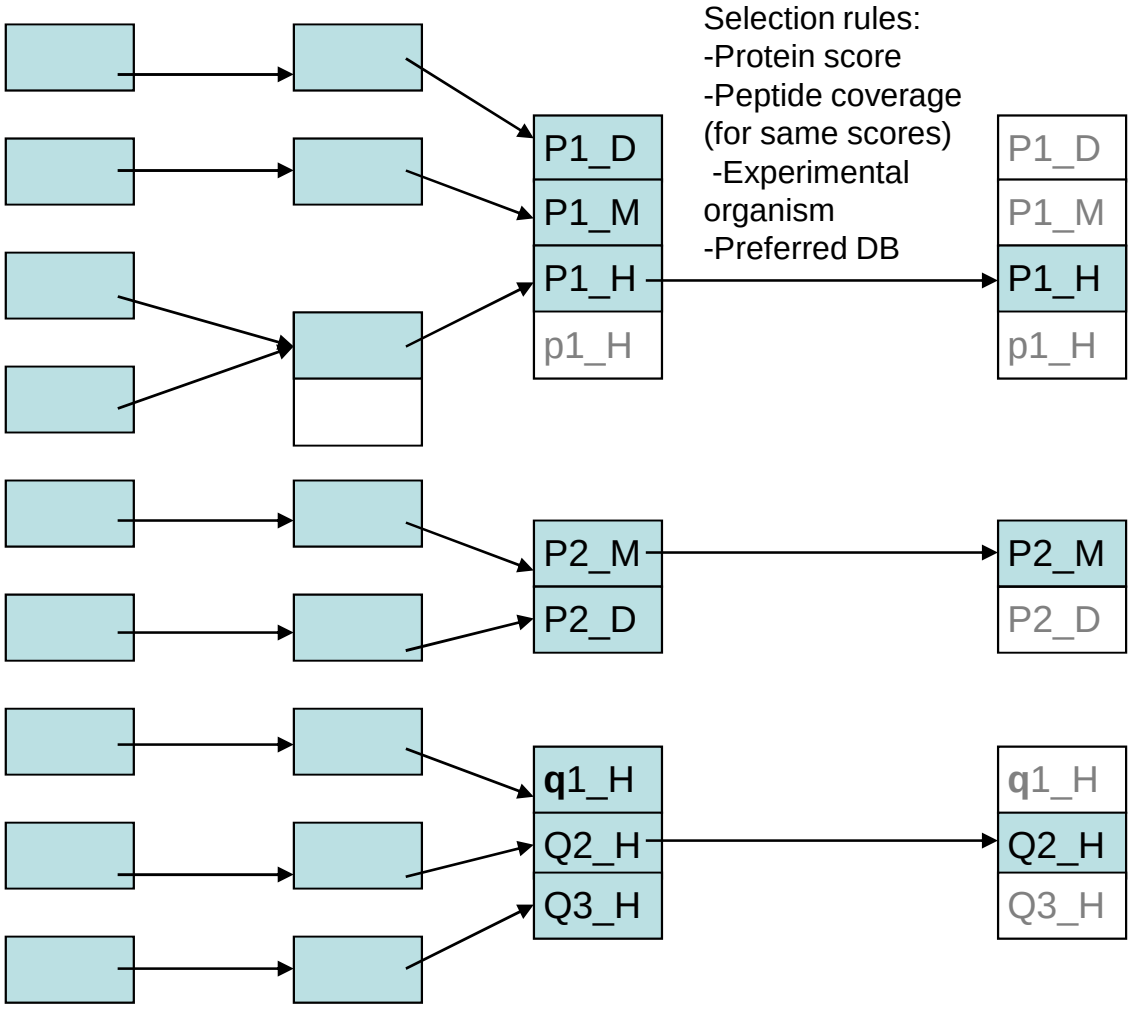
Identification results redundancy reduction and sequence selection



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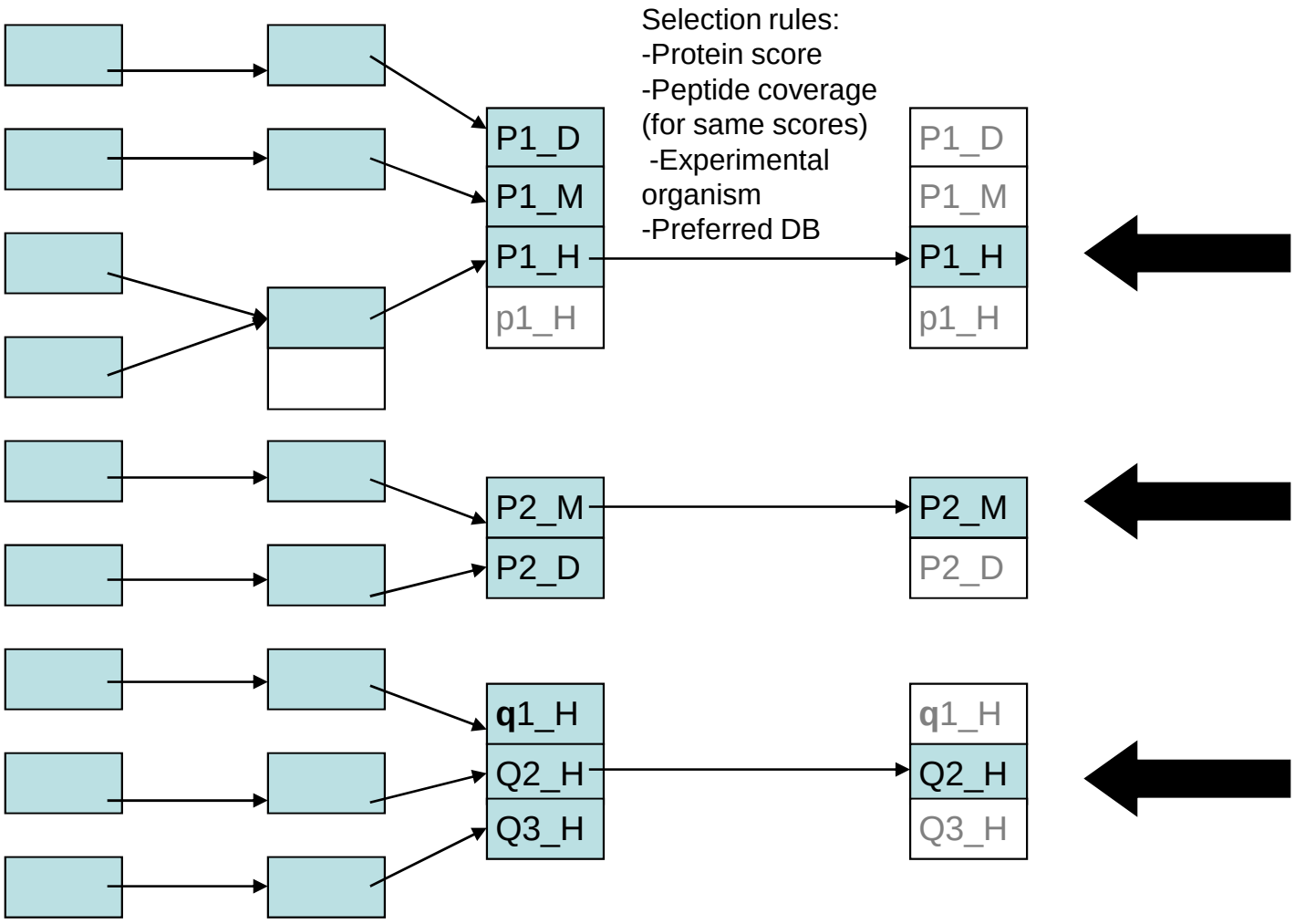

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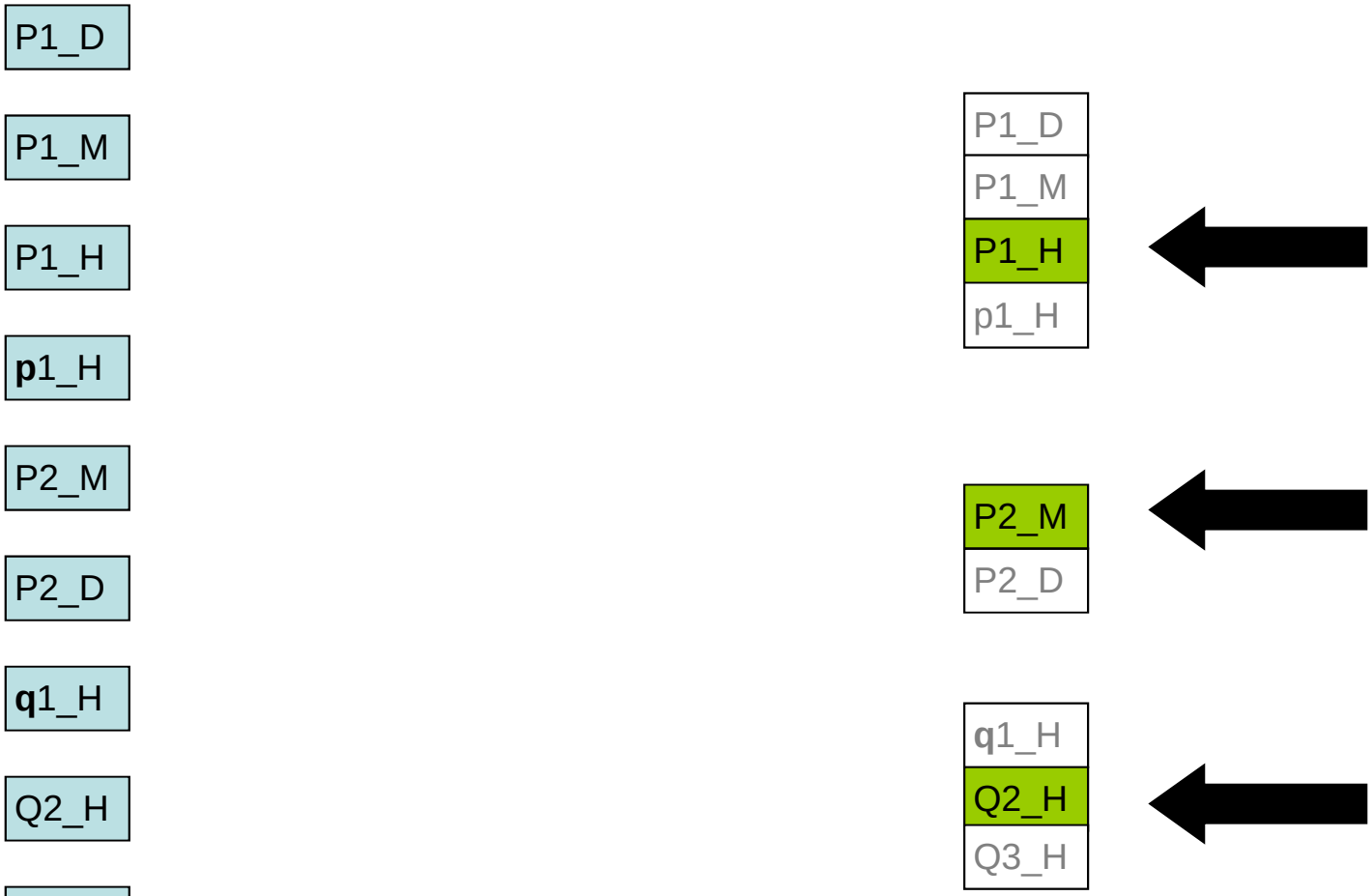
Identification results redundancy reduction and sequence selection



Mascot identification results (1 spot)

Selected sequences

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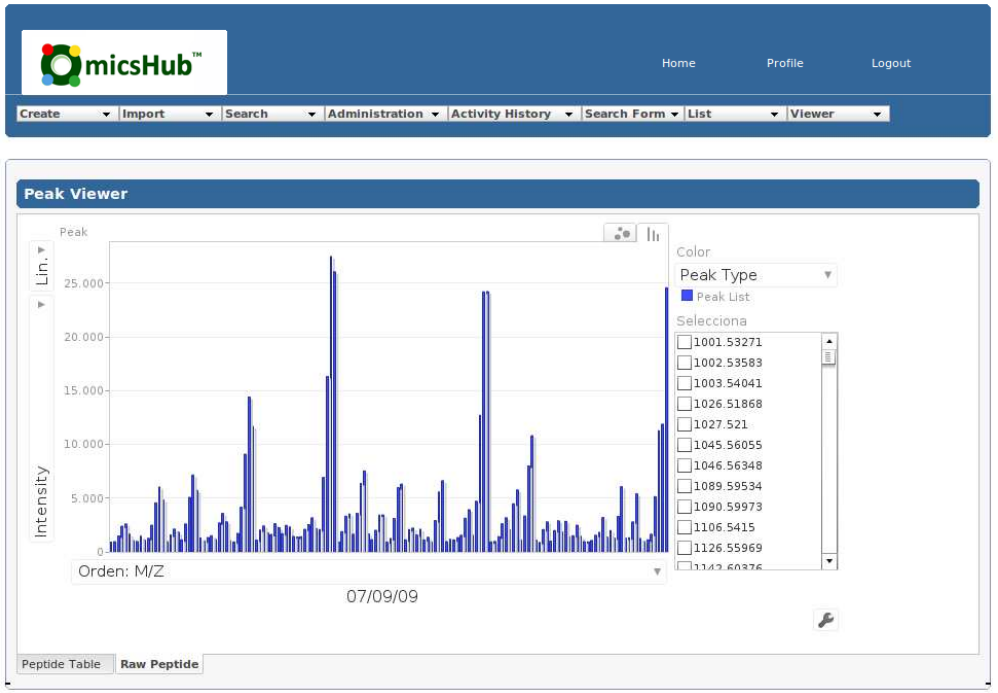
OmicsHub Proteomics

- The solutions
  - Traceability of bioinformatics analysis
    - The bioinformatics workflow of OmicsHub allows tasks automation and full traceability…

      … from peak lists to the final automated customizable report



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OmicsHub Proteomics

- The solutions
  - Few groups act in accordance with proteomics standards
    - OmicsHub is compliant with PRIDE proteomics standard from European Bioinformatics Institute (EBI)

OmicsHub Proteomics Solutions Summary

- Proteomics automated analysis Workflows
  - allow peak list filtering
  - perform storage of software and protocol information using PRIDE standard
  - facilitate searches using Mascot, Phenyx (soon Sequest) with a common user interface
  - group and tag identified proteins
  - annotate identified proteins
  - are integrated with pathways analysis (Ingenuity)
  - **allow customizable HTML report generation summarizing the experiment and the results**

OmicsHub Proteomics Solutions Summary

- Proteomics automated analysis Workflows
  - can also be performed manually
  - can be reused for different mass-spec instruments
  - can be launched for different experiments simultaneously
- OmicsHub Proteomics
  - V1 will be presented at the end of this month a the world HUPO meeting in Toronto
  - V2 will be extended to cover gel-free quantitative proteomics

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Conclusions

- Despite the high mass accuracy of modern mass spectrometers, the general perception of the reliability of MS-based proteomics is that it is **low**.
  NATURE METHODS | VOL.6 NO.6 P. 423 | JUNE 2009
- A major contributing factor to erroneous reporting resides at the level of processing (i.e. databases, search engines) of otherwise valid raw data

- **OmicsHub proteomics directly addresses these issues**

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Conclusions

- OmicsHub NGS is underway for a real “Hub” in “Omics” technologies
- Thanks for your attention !
- Questions ?

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