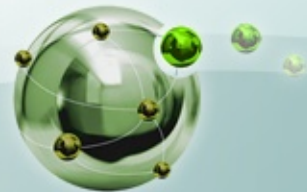


Many foresee more than one

A collaborative approach to *in silico* science

Christine Chichester, Herman van Hagen, Barend Mons
Knewco and Leiden University Medical Center

3rd annual iFQ conference December 11th-12th, 2008



Knowlet Building Blocks

<Source concept>



<Connected Concept>



<Relations>:



<Type F1> Database facts

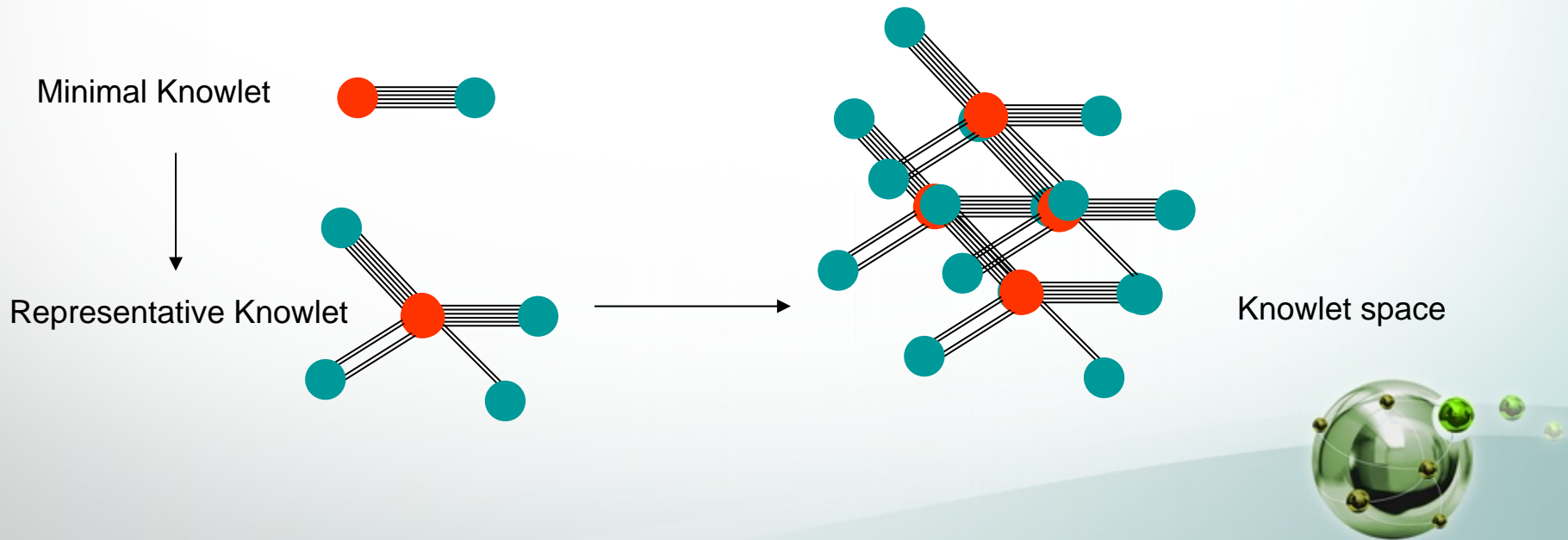
<Type F2> Community Annotations

<Type C1> Co-occurrence of concepts in one sentence

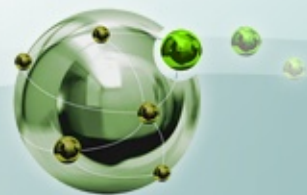
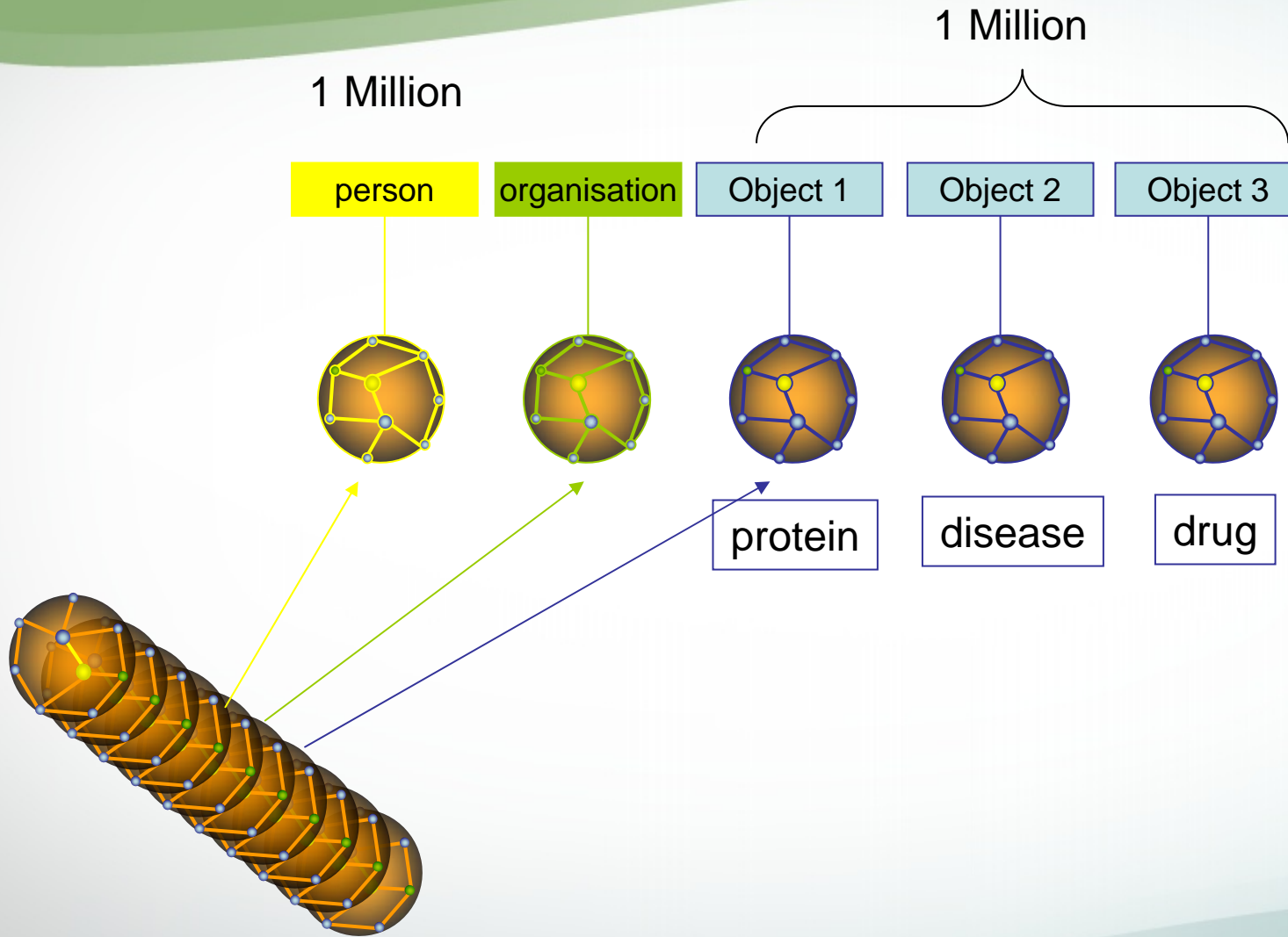
<Type A1> Concept Profile Match

<Type A2> Sequence similarity (BLAST score Genes and Proteins only)

<Type A3> Co-expression (microarray results)

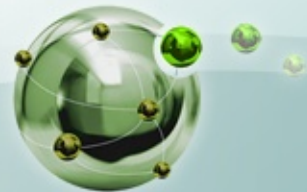


Generate the Knowlet space from large data sources



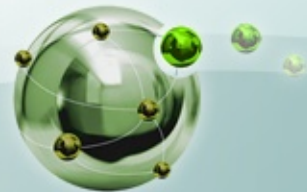
Putting the Knowlet to use

- Semantic Exploration: exploring the Knowledge Space to get an overview of the domain
- Newness Alerting: monitoring all semantic connections regarding a particular topic and providing alerts when significant changes occur
- Science Management: quick overview of other scientists' concepts of interests, maintaining and organizing your personal WikiPeople page, etc.
- Knowledge Discovery: finding new associations between medical and biological entities (protein-protein interactions)

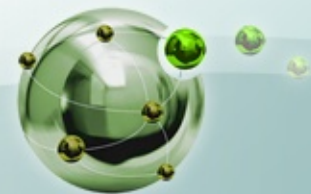
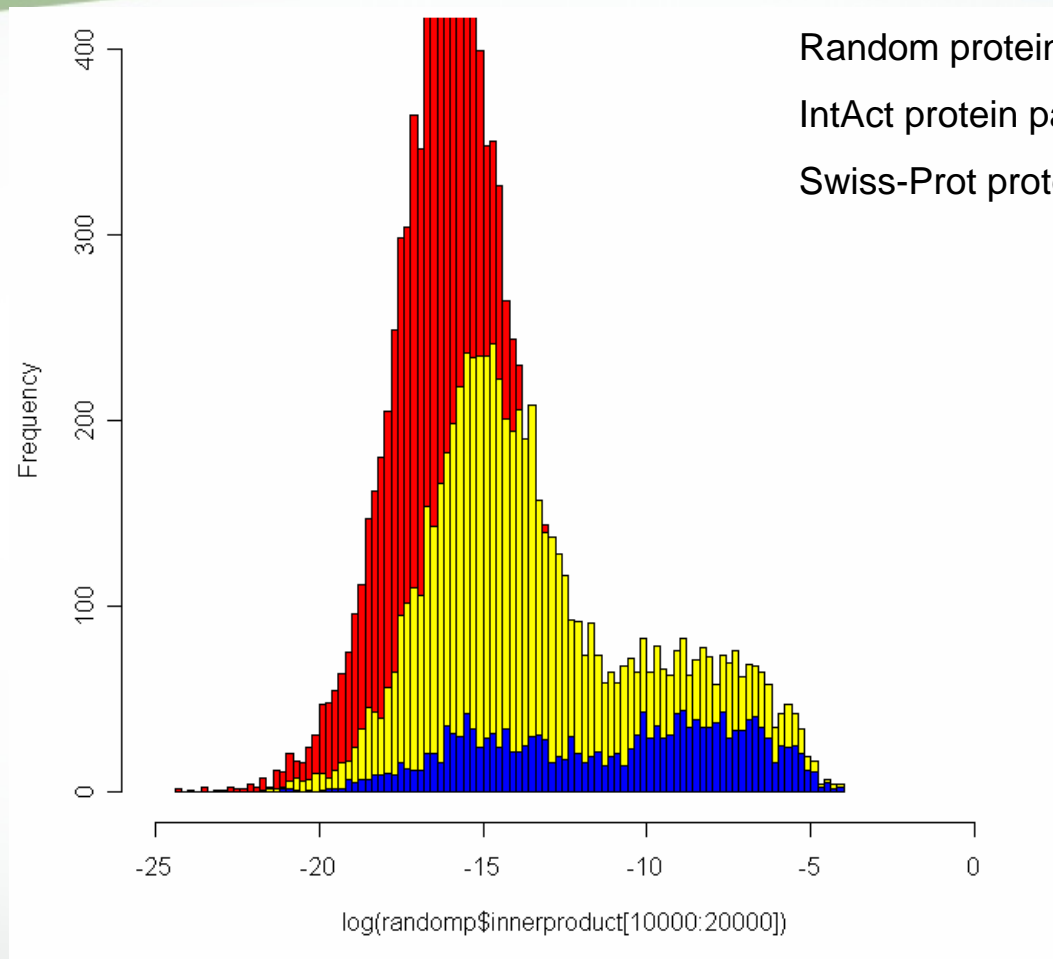


Protein-Protein Interactions (PPI)

- Methods for prediction:
 - phylogenetic distribution
 - homologous proteins
 - co-expression
 - others
- Using biomedical literature
 - Calculate the concept-based similarity between the profiles of two proteins

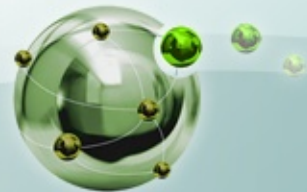


Conceptual overlap (association) of protein pairs



Curated PPIs

- 32% can be found in Medline abstracts using direct query (direct relation in abstract)
- 76% can be found using conceptual overlap
- Retrospective study: using 2005 literature predicted 52% of the PPIs described in Swiss-Prot in 2007 at a specificity of 95%

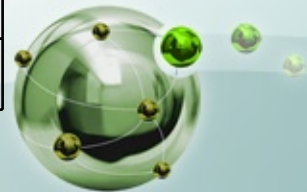


Evaluation of Calpain-3 PPI

Interacting protein	In database	In literature (full text)	Direct relation (abstract)
Dysferlin	Yes	Yes	Yes
Titin	Yes	Yes	Yes
Filamin C	Yes	Yes	Yes
Alpha-actinin	No	Yes	Yes
Calpastatin	No	Yes	Yes
IkappaBalpha	Yes	Yes	Yes
Myosin light chain 1	No	Yes	No
Alpha-spectrin	Yes	Yes	No
Filamin A	No	Yes	No
Ezrin	No	Yes	No
Vinexin	No	Yes	No
Talin	No	Yes	No

Predicted PPIs

Epsilon-sarcoglycan	No	No	No
Beta-parvin	No	No	No

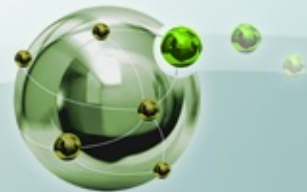


The Million Minds Approach: Wiki technology



Defining characteristics:

- Pages are easily created and updated
- Any registered user can edit
- Results of work are immediately visible and attributed to the user
 - there is no official review of modifications



Acknowledgment of contributions



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[+ Preferences](#)

Cytochrome P450 1A1 (Homo sapiens)

Identifier: 74026242

[+ Also known as](#)

[- Functional information](#)

Connection	Element	Community	Swiss-Prot
performs	EC 1.14.14.1	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
gene product has molecular function	cytochrome P450 activity	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
induced by	By 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD).	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
has catalytic activity	RH + reduced flavoprotein + O(2) = ROH + oxidized flavoprotein + H(2)O.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
has cofactor	heme group	<input checked="" type="checkbox"/> Christine Chichester	
has function	Cytochromes P450 are a group of heme-thiolate monooxygenases. In liver microsomes, this enzyme is involved in an NADPH-dependent electron transport pathway. It oxidizes a variety of structurally unrelated compounds, including steroids, fatty acids, and xenobiotics.	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

[+ Localization and spatial information](#)

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Add predicted interactions to the appropriate concepts for review



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Preferences

Calpain-3 (Homo sapiens)

Identifier: 23245655

+ Also known as

- Functional information

Connection	Element
performs	EC 3.4.22.54
gene product has molecular function	calpain activity
gene product has molecular function	signal transducer activity
interacts with	Beta-parvin (Homo sapiens)
has catalytic activity	Broad endopeptidase activity.
has function	Calcium-regulated non-lysosomal thiol-protease.
enzyme regulation by	Activated by micromolar concentrations of calcium and inhibited by calpastatin.

+ Localization and spatial information

+ Structural and physical information

+ Conceptual and other information

+ Reference information

+ Tags

+ Pointers to Calpain-3 (Homo sapiens)

+ Information in other websites

Colleagues with interest in Calpain-3



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Preferences

Calpain-3 (Homo sapiens)

Identifier: 23245655

Also known as

Functional information

Localization and spatial information

Structural and physical information

Conceptual and other information

Reference information

Tags

Pointers to Calpain-3 (Homo sapiens)

Other concept	Connection	Concept	Reference information	Community	NLM
Calpain	has a broader relationship	Calpain-3 (Homo sapiens)	Reference information	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Muscle Proteins	has a broader relationship	Calpain-3 (Homo sapiens)	Reference information	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
CAPN3 (Homo sapiens)	has relationship other than synonymous, narrower, or broader	Calpain-3 (Homo sapiens)	Reference information	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Corrado Angelini	has interest	Calpain-3 (Homo sapiens)		<input checked="" type="checkbox"/>	
Stefania Aurino	has interest	Calpain-3 (Homo sapiens)		<input checked="" type="checkbox"/>	
Burcu Balci	has interest	Calpain-3 (Homo sapiens)		<input checked="" type="checkbox"/>	
Marc Bartoli	has interest	Calpain-3 (Homo sapiens)		<input checked="" type="checkbox"/>	

Alert people to new predictions



WikiPeople

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Go Search

search person

First name
Middle initial
Last name
Search person

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concept edit history merge

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Barend Mons

Identifier: 101668678

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Have your friends and colleagues *authorized* their pages yet? Please alert them to the [possibility](#)

Also known as

Mons, Barend
B Mons
Mons, B
Barend Mons

Personal information

Concepts of interest

Genes
Gene Symbol
Text
Internet
Natural Language Processing
Mining
Literature
Information Storage and Retrieval
Microarray

Calpain-3 (Homo sapiens)

Publications


Co-authors

Reference information

Tags

Pointers to Barend Mons

View individual publication record



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+ Also known as

+ Personal information

+ Concepts of interest

- Publications

Publication	Author position	Listed a
Localization of circumsporozoite protein in the sporogonic stages of <i>Plasmodium vivax</i>.	3	Mons B
T cell epitopes of the circumsporozoite protein of <i>Plasmodium vivax</i>. Recognition by lymphocytes of a sporozoite-immunized chimpanzee.	3	Mons B
<i>Plasmodium berghei</i>: in vivo generation and selection of karyotype mutants and non-gametocyte producer mutants.	last	Mons B
Chromosome translocation in <i>Plasmodium berghei</i>.	last	Mons B
Bromo-deoxyuridine is not incorporated into DNA of malaria parasites.	last	Mons B
Variation in karyotype and gametocyte production during asexual multiplication of <i>Plasmodium berghei</i>.	last	Mons B
Generation of chromosome size polymorphism during in vivo mitotic multiplication of <i>Plasmodium berghei</i> involves both loss and addition of subtelomeric repeat sequences.	last	Mons B
Long insertions within telomeres contribute to chromosome size polymorphism in <i>Plasmodium berghei</i>.	5	Mons B
<i>Plasmodium falciparum</i>: studies on mature exoerythrocytic forms in the liver of the chimpanzee, <i>Pan troglodytes</i>.	3	Mons B
<i>Plasmodium berghei</i>: gametocyte production, DNA content, and chromosome-size polymorphisms during asexual multiplication in vivo.	8	Mons B
Host cell specificity and schizogony of <i>Plasmodium berghei</i> under different in vitro conditions.	last	Mons B
Presence of contaminating mitochondrial DNA from host reticulocytes in experimental infections of <i>Plasmodium berghei</i>.	last	Mons B

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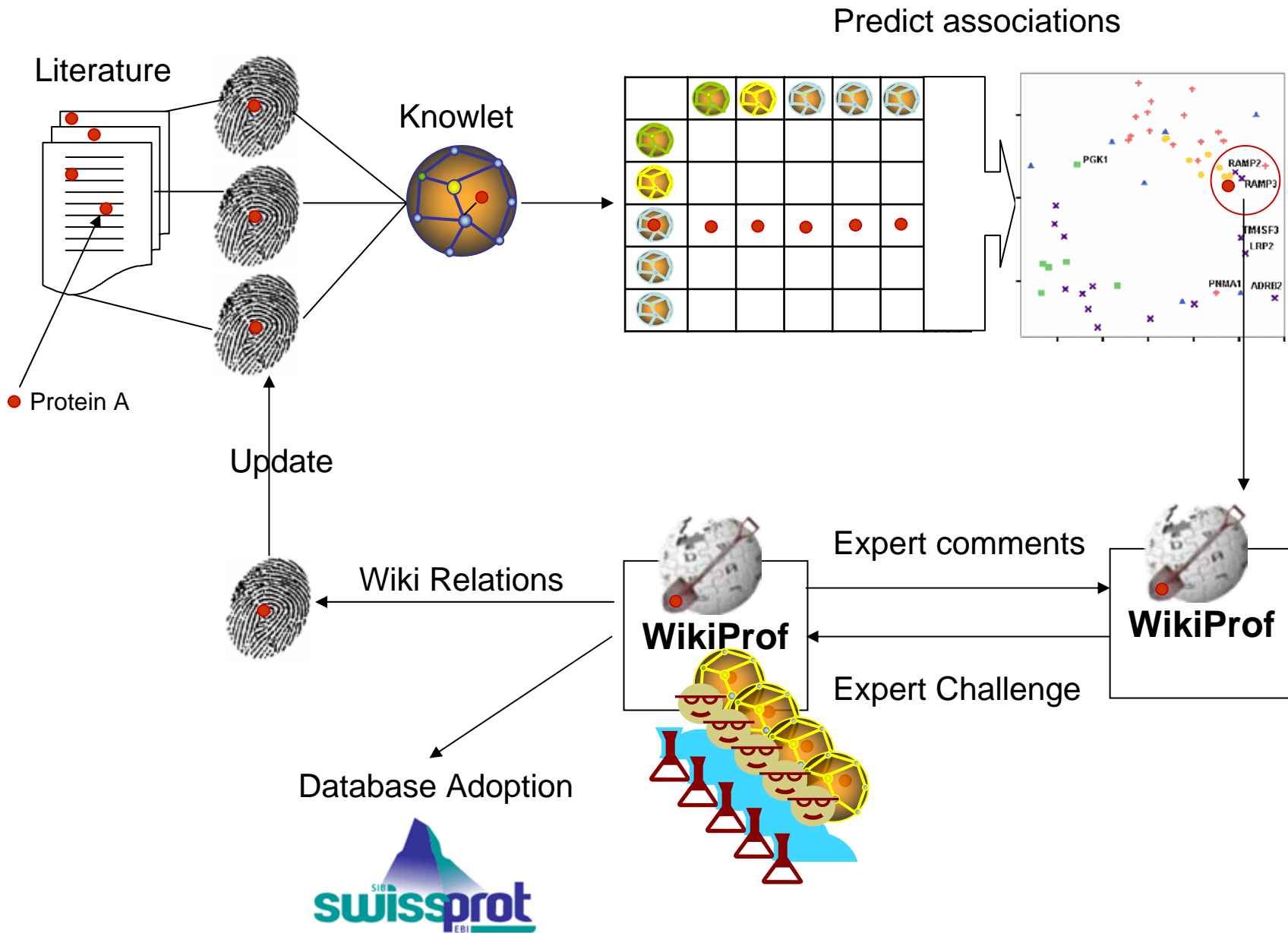
search

search person

First name
Middle initial
Last name

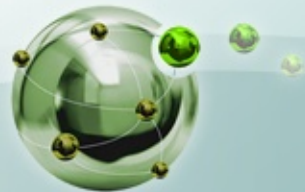
toolbox

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New technologies generate new ideas

- Facilitate social networking
- Easily present scientific identity
- Opportunity to participate
- For a WikiProf to work
 - Dedicated community
 - Incentives
 - Easy to use system



Access Knowlet Space and WikiPeople

- Knowlet Space: www.wikiprofessional.org
- WikiPeople (demo only, edits not saved):
<http://proteins.wikiprofessional-staging.org/>
- Publications: www.knewco.com
- Email: chichester@knewco.com



3rd annual iFQ conference December 11th-12th, 2008

