Building an Ecosystem of Biomedical Web Communities

SWAN-SIOC Integration Project
Background Presentation
Tim Clark       Harvard/MGH

July 24, 2008
SWAN and SIOC are highly complementary approaches to integrating communities of discourse.
The emerging SWAN-SCF ecosystem provides a focused laboratory for SIOC integration.
Active participation of biomedical bench researchers in the ecosystem grounds the project in realistic use cases.
SWAN

• Project of Massachusetts General Hospital and Alzheimer Research Forum.
• Represents core knowledge on AD, highlights open questions and conflicts, provides a roadmap for researchers.
• Researcher-friendly UI, data in RDF.
• Focus: hypotheses, claims and evidence.
Contributions from leading researchers

Key research topics

Mechanisms of disease

Inventory of Ideas

Contribute content
SCF - Science Collaboration Framework

- SCF is a special distribution of Drupal
  - Designed to support biomedical web communities.
  - Collaboration of Harvard, Alzforum, MGH.
  - Initial focus communities: Stem Cells, Parkinson’s Disease

- SCF is specifically designed to work with SWAN.
  - Drupal “Node proxy” architecture reads RDF triples.
  - Specific models for many biomedical entities.

- Vision
  - Many SCF-based communities
  - Resource, information and discourse sharing via triple stores.
  - Semantic annotation and integration across communities.
Behind the Stem Cell Breakthrough


The stunning announcement by Japanese and American research teams that they have obtained highly promising stem cells without having to destroy an embryo could help free scientists from shackles that have long hobbled their efforts. It is especially important for a critical field of research that is far behind where it could have been if the Bush administration and Congressional conservatives had not thrown up so many roadblocks.

Commentaries

May 30, 2008
Genomic approaches provide insights into the molecular basis of pluripotency

more
Oxidative Stress Hypothesis

By Joe Parkinson

Morus Parkinson (PD, Parkinson's disease) is a neurodegenerative disorder affecting dopaminergic neurons in substantia nigra. Mitochondrial respiratory complex I deficiency and oxidative stress are known to occur in these neurons, and cytoplasmic aggregates ('Lewy bodies') of α-synuclein and other proteins have been observed in the affected neurons.

Autosomal recessive mutations within the Parkin gene are associated with degeneration of the substantia nigra and locus coeruleus and an inherited form of Parkinson's disease (PD). As loss-of-function mutations in parkin are responsible for a familial variant of PD, conditions that affect wild-type parkin are likely to be associated with increased risk of idiopathic disease. Previous studies uncovered a unique vulnerability of the parkin protein to dopamine (DA)-induced aggregation and inactivation. In this study, we compared several proteins that share structural elements or ubiquitinating activity with parkin. We report that oxidative stress in several cell lines and primary neurons induces the aggregation of parkin into high molecular weight species, at least a portion of which are self-associated homo-multimers.

While parkin was preferentially affected by excess DA, each of the E3 proteins tested were made more insoluble by oxidative stress, and they varied in degree of susceptibility (e.g., parkin > HHAR > CHIP > NQO1 > BAP). These conditions of oxidative stress were also associated with decreased parkin E3 ligase activity. Similar to recently conducted studies on α-synuclein processing, both macroautophagy and the proteasome participate in parkin degradation, with the proteasome playing the predominant role for normal parkin turnover and macroautophagy being more important in the degradation of aggregated parkin. These data further highlight the selective vulnerability of parkin to DA-induced modifications, demonstrating for the first time the ability of both endogenous and ectopically expressed parkin to transition into an insoluble state in part through self-association and next page.

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References


Commentary

Role of Prostaglandin E2 in stem cell development

Added: Wednesday, 22 August, 2007, 15:51 GMT 16:51 UK

John Doe, Director, BioBlah

Added: Wednesday, 22 August, 2007, 15:51 GMT 16:51 UK
SWAN-SCF Components and Applications

Science Collaboration Framework

Biomedical Web Communities

Semantic Integration

SWAN Core Functions

planned Add-ons

mySWAN
Personal Knowledge management

labSWAN
Laboratory Data & Knowledge management

Pharma SWAN
Drug discovery

SWAN grants mgmt
Foundations & government

Harvard Stem Cell Inst, MJ Fox Foundn

Alz Assoc, Ellison Medical Eli Lilly & others
Not Just Facts

• Among the 20 top candidate hypotheses about how AD works, there are at least
  — 49 key scientific disagreements and
  — 32 key open questions to be resolved.

• Surfacing the gaps and conflicts along with the agreement is very important.
Relationships Between Hypotheses in SWAN

Web Article
Aβ alternative
Interpretation of the amyloid Ab hypothesis

Hypothesis
Intramembraneous Aβ dimer

Claim
Aβ is first detected intraneuronally…

Claim
Intramembraneous Aβ peptide may…

Claim
Extracellular-enriched dodecameric 56KDa…

Comment
Extracellular Aβ are Insufficient to injure…

Research Question
What evidence resolves conflicting claims?

Proposed Experiment
FRET/FLIM: Can APP dimerize in living cells?

motivates

Hypothesis
Aβ*56 Hypothesis

derivedFrom

contains

contains

alternativeTo

part of

Implies

Implies

Implies

supports

cites

cites
Researcher Support

- Software features reviewed before release by over thirty senior AD researchers.
- Content reviewed before release by over twenty senior AD researchers.
- Extensive feedback incorporated into SWAN - this is a community tool.
Recent SWAN-SCF Publications


The SWAN Team

- **Harvard/MGH**: Paolo Ciccarese, Marco Ocana, Tim Clark

- **Alzforum**: Elizabeth Wu, Gwen Wong, June Kinoshita [www.alzforum.org](http://www.alzforum.org)

with many thanks to: Brad Hyman (Harvard/MGH), Carole Goble (University of Manchester, UK), Andy Seaborne (HP Labs), Sean Martin and Lee Feigenbaum (Cambridge Semantics)

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