

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.

Welcome to the SWAN Alzheimer Knowledge Base

SWAN is the participatory knowledge base of Alzheimer Disease that YOU can help develop. SWAN is all about how you interpret, debate, ask questions and advance the science.

» Featured Contributions

H Axonal transport is not impaired by changes in tau gene expression levels. Yuan Aidong et Al.

Dewachter and Van Leuven, on Marchesi Dewachter Ilse et Al.

H Rapid appearance and amyloid-beta plaques in Alzheimer's disease. Meyer-Luehmann Melanie

Click on the image to browse the full content and use the arrows to scroll the list

Contributions from leading researchers

» Hot Topics (browse all hypotheses)

- o Amyloid Hypothesis of Alzheimer Disease (AD)
- o Soluble oligomeric aggregates of A β are toxic to neurons and cause AD pathology. Insoluble fibrillar A β leads to AD
- o Defective mechanisms of A β clearance contribute to AD
- o ApoE contributes to AD through multiple mechanisms
- o Changes in calcium homeostasis may provide a common pathway for the neuropathological changes in AD
- o Changes in presenilin function lead to dementia and neurodegeneration in Alzheimer Disease
- o Misfolded proteins accumulated into protein aggregates characterizes the pathologic lesion of AD
- o The molecular mechanisms of neuronal cell death are involved in the dysfunction and death of neurons in AD
- o Synaptic loss appears to be the most powerful and ubiquitous proximate factor leading to the dementia of AD
- o Failure of axonal transport might be the underlying basis for neurodegeneration in AD
- o Cell membrane properties play a key role in AD Pathophysiology

Key research topics

» Mechanisms

- Functional Changes of Proteins
- Structural Changes of Proteins

Mechanisms of disease

» How to Contribute

- **Build a hypothesis**
- **Critique a hypothesis**
- **Nominate a key paper**
- **Help find connections**
- **Propose new features**
- **Add supporting evidence**

Contribute content

» Knowledge Base

Statements

323 Research Statements

119 Hypotheses

» 21 with Extended annotation

» 98 with Simple annotation

100 Challenges

32 Research Questions

26 Comments

Publications

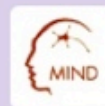
1036 Journal Articles

1 Journal Comments

2 Journal News

30 Web Comments

Inventory of Ideas



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.

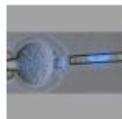
StemBook



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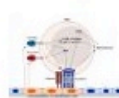
STEMBOOK IS A COMPREHENSIVE, OPEN-ACCESS COLLECTION OF ORIGINAL, PEER-REVIEWED CHAPTERS COVERING TOPICS RELATED TO STEM CELL BIOLOGY. [Read More](#)



Cellular and nuclear reprogramming



Genomics and proteomics



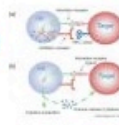
Renewal



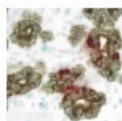
Ectoderm specification and differentiation



Germ cell and somatic stem cell biology in reproduction



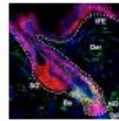
Stem cell immunology



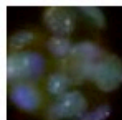
Endoderm specification and differentiation



Mesoderm specification and differentiation



Therapeutic prospects



Epigenetics



Niche biology, homing, and migration



Tissue engineering

News

Behind the Stem Cell Breakthrough

Editorial, *New York Times* 30 November 2007

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](#)



The Scientific Collaborative Framework is a project of the Initiative in Innovative Computing at Harvard University in collaboration with the Harvard Stem Cell Institute, based on the Drupal open source content management system.

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SCF and Drupal are both licensed under the GPL version 2 software license.



[COMMON PATHWAYS OF PATHOGENESIS](#) » [OXIDATIVE STRESS](#) »

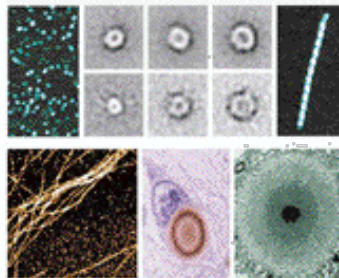


Oxidative Stress Hypothesis

By [Joe Parkinson](#)

Morbus Parkinson [PD (Parkinson's disease)] is a neurodegenerative disorder affecting dopaminergic neurons in substantia nigra. Mitochondrial respiratory complex I deficiency and oxidative stress have been reported 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 > HHAR1 congruent with CHIP > c-Cbl > E6AP). 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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THE ROLE OF α -SYNUCLEIN IN PARKINSON'S DISEASE: INSIGHTS FROM ANIMAL MODELS
Eleonora Maria et al.,
Nature Reviews | Neuroscience SEPTEMBER 2003 |
VOLUME 4 | Page 725

References

- Flowers KJ, Robertson C: **Perceptual abnormalities in Parkinson's disease: top-down or bottom-up processes?**
Perception 1995, 24:1201-1221. [PubMed](#)
- Djambouz MB, Hankins MW, **Hirano J, Archer SN: Neurobiology of retinal dopamine in relation to degenerative states of the tissue.**
Vision Res 1997, 37:3509-3529. [PubMed](#) | [Publisher Full Text](#)

Commentary

[View whole discussion](#)

Role of Prostaglandin E2 in stem cell development

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

Lorem ipsum dolor sit amet, consectetur adipiscing elit. Aliquam vel mauris. Quisque consequat erat sit amet neque. Cras ut risus nec est blandit suscipit. Vivamus libero diam, iaculis ullamcorper, pretium et, sagittis ac, mauris.

John Doe, Director, BioBlah

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

TABLE OF CONTENTS

1. Common Pathways of pathogenesis
 - 1.1 Oxidative Stress
 - 1.2 Role of free radicals
 - 1.3 Mitochondrial Dysfunction
2. Apoptosis
 - 2.1 Excitotoxicity

THERAPEUTIC APPROACHES

1. Antioxidant Therapies
 - 1.1 Coenzyme Q
2. MOA:B inhibitors
 - 2.1 Rasagiline

GENES, PROTEINS & TARGETS

[bac-1](#)
[glutathione](#)
[NADPH](#)

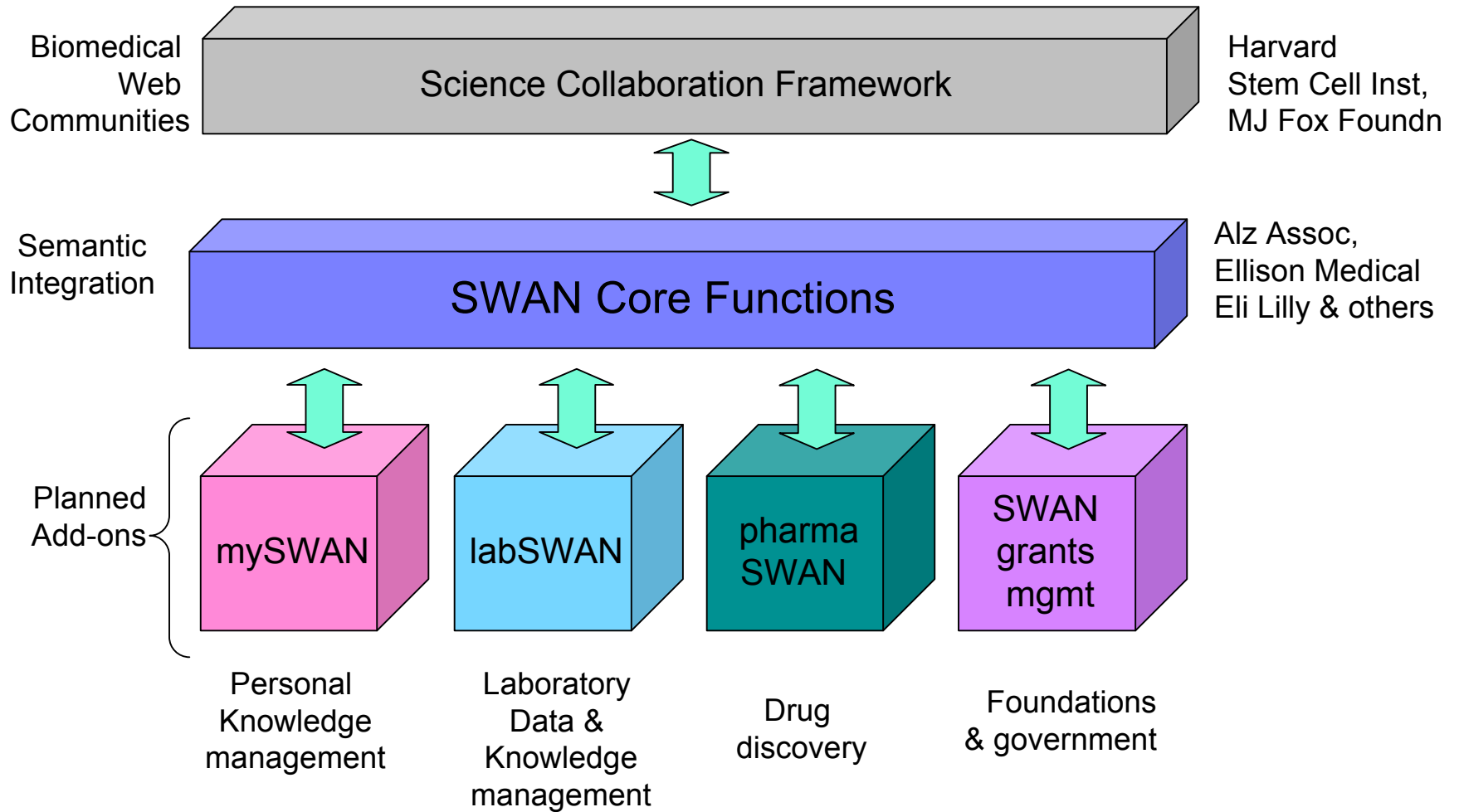
RELATED ARTICLES

The glutathione system and neurodegeneration
by Howard E. Gendelman

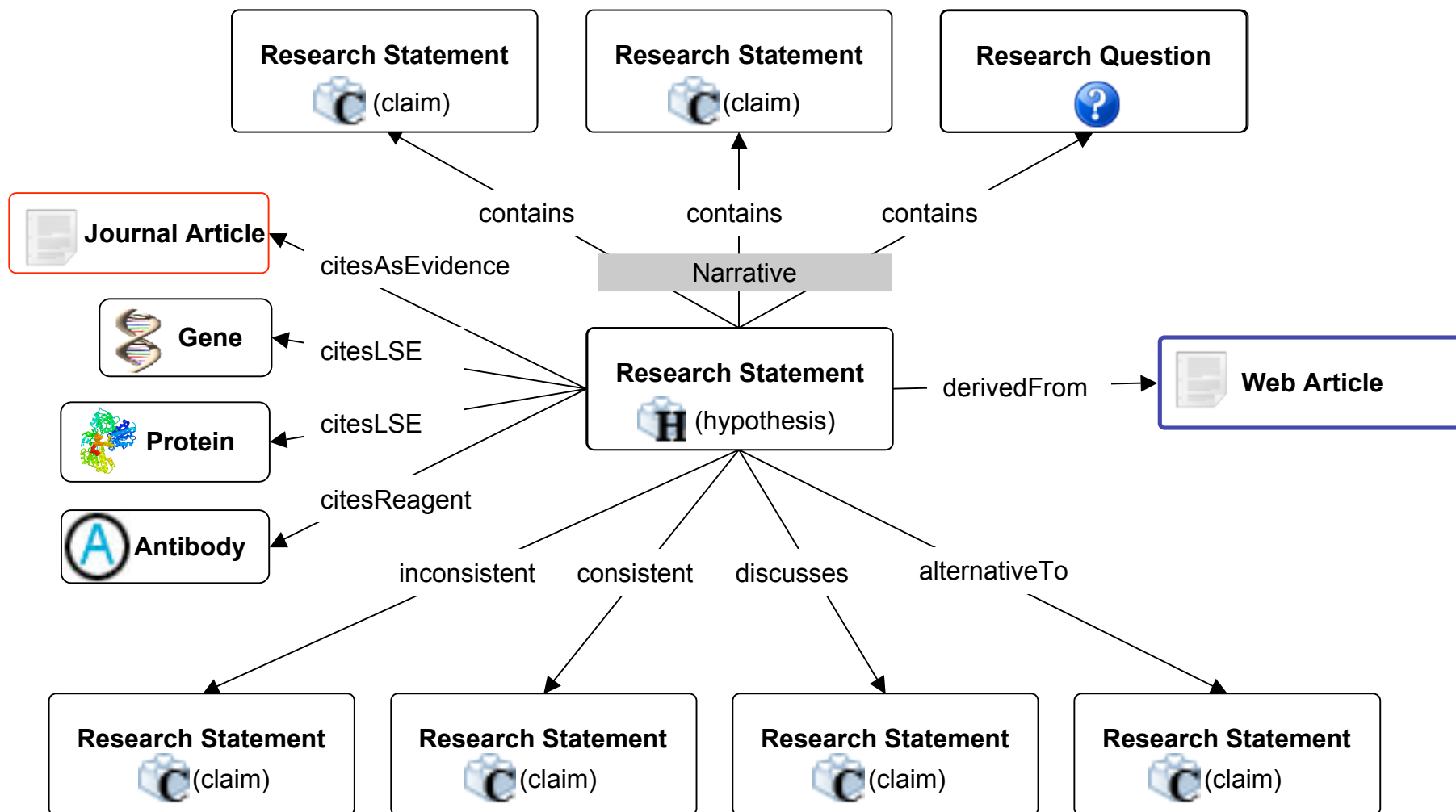
JOE PARKINSON'S CONTRIBUTIONS

- Maecenas posuere urna ut augue lacinia interdum. Curabitur a justo. Vivamus vehicula tellus vitae orci.
- Donec nonummy, neque tristique lacreet nonummy, neque metus iaculis nulla, ut molestie purus dui vitae metus.
- Sed porttitor. Pellentesque hendrerit cursus augue.

SWAN-SCF Components and Applications



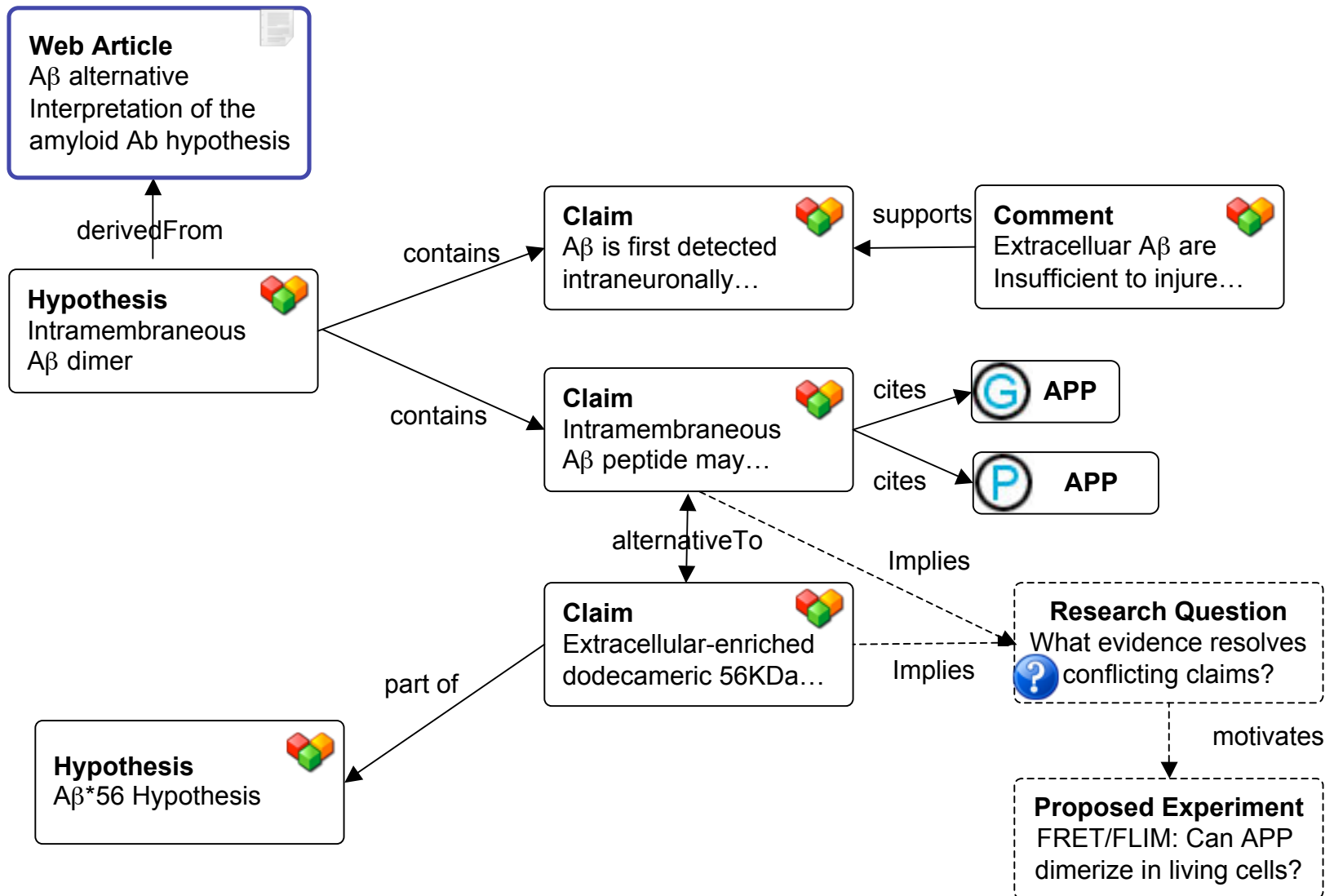
Concept Relationships



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



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

- Ciccarese P, Wu E, Kinoshita J, Wong G, Ocana M, Ruttenberg A, Clark T. **The SWAN Biomedical Discourse Ontology**. Journal of Biomedical Informatics, in press. [PMID: 18583197](#)
- Clark T and Kinoshita J (2007) **Alzforum and SWAN: The Present and Future of Scientific Web Communities**. Briefings in Bioinformatics 8(3):163-171; doi:10.1093/bib/bbm012. [PMID: 17510163](#)
- Das S, Green T, Lewis-Bowen A, Weitzman L and Clark T. (2008) **Linked data in a scientific collaboration framework**. 17th International World Wide Web Conference, Beijing, China (21 - 25 April 2008).

The SWAN Team



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



- Alzforum: Elizabeth Wu, Gwen Wong, June Kinoshita 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)



The Beautiful Swan – by [William Nicholson](#), British (1872–1948), color lithograph after a woodcut, 1900. Campbell 73b.