



ALZHEIMER  
RESEARCH  
FORUM

# ALZHEIMER RESEARCH FORUM: A KNOWLEDGE BASE AND E-COMMUNITY FOR AD RESEARCH

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## 1. INTRODUCTION

This centenary year of Alois Alzheimer's seminal study also marks the tenth anniversary of the Alzheimer Research Forum website ([www.alzforum.org](http://www.alzforum.org)), known popularly as "Alzforum" by AD researchers around the world. The Alzforum is an independent, not-for-profit resource dedicated to Alzheimer disease and related disorders. Founded in 1996, the website has become a true global online community, with approximately 30-50 percent of all active Alzheimer researchers visiting it regularly.

From its humble beginnings as a small set of HTML pages featuring manually curated lists of articles, the Alzforum has grown tremendously. Today, the website contains more than 40,000 literature citations, 1,300 research news articles, 4,000 comments, 10,000 antibodies, 200 research models, 350 genes from published association studies of late-onset AD, as well as all known mutations causing familial Alzheimer disease and frontotemporal dementia with parkinsonism (FTDP-17). The site receives over one million visits per year. More than 3,200 people have registered as members of Alzforum, representing a significant portion of AD researchers worldwide.

Although it is difficult to gauge the precise impact of Alzforum, many researchers have told us that we have succeeded to a substantial degree in opening our readers' minds to more diverse areas of research, fostering healthy discussion of novel and controversial topics, and serving as a central repository for core data sets such as genetic association studies, research models, clinical trials and antibodies.

While the Alzforum today enjoys a high profile in the Alzheimer field, few people are familiar with the website's background or inner workings. On the occasion of the Alzheimer 100 conference, we would like to share some stories about how the Alzforum began and developed over the years, and to present our vision of some future initiatives.

## 2. ORIGINS OF THE ALZFORUM

The idea for the Alzheimer Research Forum website was spawned over a lunch conversation between one of the authors (Kinoshita), a philanthropist, and a foundation leader who were concerned about barriers to progress in Alzheimer research. The time was late 1995, and the AD field was caricatured as a battle zone between "BAPTists" and "TAUists." At the same time, research was exploding with new findings driven by the landmark discoveries a few years earlier of familial Alzheimer genes and the association between late-onset AD and the epsilon4 allele of apolipoprotein E. It seemed that AD research might benefit from more open dialogue and better management of the diverse streams of data pouring out of laboratories.

The Internet was not yet a household word, but the philanthropist had seen this technology begin to transform business communications and was convinced that the World Wide Web would quickly become a ubiquitous tool for scientific and medical research. The participants in the lunch believed that a Web-based information source, with expert editorial moderation and professional management, would fill a real need in the community. An anonymous foundation stepped forward to fund the concept and assemble the project team, and in July of 1996, the website made its debut at the International Conference on Alzheimer's Disease and Related Disorders in Osaka, Japan.

During the planning phase, the team considered whether the website should be hosted at an academic institution, but initial research indicated that individual and

institutional rivalries could undermine the goal of creating an open community resource. The Alzforum was therefore established as an independent, not-for-profit entity.

Without an institutional imprimatur, the Alzforum faced the challenge of establishing its credibility within the scientific community. The Editor invited prominent leaders with diverse scientific backgrounds to join the scientific advisory board. Happily, most agreed at once. (The founding members were Eva Braak, Joseph Coyle, Peter Davies, Bradley Hyman, Gerald Fischbach, Zaven Khachaturian, Kenneth Kosik, Virginia Lee, Elliott Mufson, Donald Price, John Olney, and Robert Terry.) The composition of the board was intended to signal that the site is dedicated to high scientific standards; that it is neutral with regard to hypothesis or dogma; and that perspectives from multiple disciplines are welcome.

At its launch, the Alzforum featured a “Papers of the Week” list of peer-reviewed publications in the AD field, virtual seminars (slide and audio), and a Milestone Papers list of seminal publications dating back to Alois Alzheimer’s original paper describing the case of Auguste Deter. Although the initial Alzforum offerings seem modest in retrospect, the feedback was positive. By the end of its first year, the site had 1,200 registered members.

### **3. A NEW NICHE FOR SCIENTIFIC DISCOURSE**

Having established a foothold in cyberspace, the challenge for Alzforum was and continues to be to define new types of scientific publishing that take advantage of the speed and wide distribution of the Web, and to curate and add value to information available from other public sources. This is a perennial challenge thanks to the rapid advances in biomedical resources on the Web.

This uphill struggle, however, seems less strenuous when we compare the current situation with the “old days.” Recall that in 1996, PubMed did not exist! (PubMed was launched in June of 1997.) Medical institutions had access to Medline, but in order for Alzforum to produce its Papers of the Week listings, the Editor had to ask the Countway Medical Library at Harvard Medical School to provide weekly text files listing newly indexed AD papers. The Alzforum hired a curator to paraphrase each abstract so that this information could be posted without violating journal copyrights. These documents were manually edited, sent out in a weekly email to the advisors for comments, and compiled into a static HTML page. Looking back, we can see that the entire process seems as antiquated as the hand-copying of manuscripts in the Middle Ages.

Soon after launching Alzforum, we found that scientists were eager to experiment with the informal, rapid communication made possible by the Web. We began to host live chats and post comments on recently published papers. We were also seeking a project to demonstrate how the Alzforum could serve as a community repository.

The first opportunity came in 1997 when geneticists John Hardy and Richard Crook, both then at the Mayo Clinic in Jacksonville, Florida, approached Alzforum about posting a comprehensive list of familial AD mutations in the genes for amyloid precursor protein (APP), presenilin 1 and presenilin 2. Jennifer Kwon at Washington University in St. Louis volunteered to curate a list of FTDP-17 tau mutations and Michael Hutton of the Mayo Clinic Jacksonville helped to edit and update this list. These resources were well received. Scientists contacted Alzforum for permission to reproduce the diagrams in their lectures and papers. “These tables and reviews are incredibly useful for people like

me, who don't closely follow the genetics field," observed one well-known AD biochemist.

Another way that the Alzforum adds value is by integrating information. Editors link primary research articles to related news, papers, databases, discussions and so on. In the early years, we were severely limited in this regard, because we had to program each link by hand. This changed dramatically in the year 2000, when the Alzforum converted to a data-driven, dynamic system. The new system automatically searches and downloads PubMed citations into a database every night, and provides tools to let editors post news and comments and crosslink them to related material.

In addition, we made sure that the new server could be maintained entirely by Alzforum editors and programmers, without an intermediary company to make changes. This flexibility is essential to the Alzforum's ability to develop new ways of providing value-added services, and to keep up with the rapidly evolving landscape of Web resources for scientific research.

Most importantly, perhaps, we overhauled the look and feel of the site, from a staid (some said funereal) look to a bright, colorful style that highlights the richness of content and provides modern navigational tools to help readers wend their way through the ever-expanding menu of offerings.

#### **4. THE ALZFORUM IN 2006**

A guiding principle of the Alzforum homepage is that the site should be "the daily tabloid for AD research," one that AD researchers would want as their personal homepage. To keep our readers coming back, we work hard to keep the homepage dynamic, useful and entertaining. Almost daily, the readers will find something of interest: the latest news, a live discussion, conference reports, commentaries, grant and job postings, new genes and mouse models, and so on.

The Alzforum team strives to make the website an essential resource for scientists by adding value to information that is already available in the public domain. How we pursue this goal is illustrated by specific examples of our major content areas:

**4.1 PAPERS OF THE WEEK.** Many AD researchers keep up with the literature by browsing the Papers of the Week because it provides a high-quality list of articles about AD, related disorders, key genes, relevant developments from broad areas of basic research, and advances in technology — a list that would require multiple searches on PubMed. The "POW" citations are enriched with news stories and commentaries, as well as links to related articles. High-impact articles are designated as "ARF Recommended" papers and "Milestones". For many scientists, the real-time reaction by peers supplies context that is missing from traditional journal publications.

Papers of the Week is essential for the knowledge management role of the Alzforum, and it drives much of the content development on the site. Editors screen the citations for news, and for data to send to curators of the AlzGene database, Telemakus AD biomarkers database, mutations directory, research models database, antibody database, and so forth. The scientific advisory board annotates new citations on a weekly cycle. Thus, the "firehose" of PubMed citations is channeled into multiple streams and helps ensure that the Alzforum's information resources are up-to-date.

**4.2 RESEARCH NEWS.** Our news operation has been directed by Gabrielle Strobel since 2001. It has become one of the most important ways in which Alzforum delivers value, by providing reporting and analysis of news of broad relevance to AD research, by journalists with extensive knowledge of the field. Our writers aim to place new findings in the context of other research. With their detailed conference coverage, they have mastered the art of informing the field of new developments many months ahead of formal publication to accelerate the spread of new ideas, without interfering with formal publication. They also scout for discoveries and methods from other fields that could be useful to Alzheimer disease research, conduct interviews with thought leaders, and prepare the background texts for discussion forums.

**4.3 COMMENTARIES AND DISCUSSION FORUMS.** The Alzforum provides scientists with a forum to respond quickly and publicly to new findings. Readers can post commentaries on any Papers of the Week citation or news story via a “Vote/Submit Comment” text-entry box. Every week, Alzforum editors invite individual scientists to comment on news or journal articles. At 75 percent or better, the response rate is high, and scientists pay close attention to what is being discussed (especially about their own work!).

Over the years, many scientists have remarked on how effective the Alzforum has been in nurturing productive discussion of their ideas and findings. For example, in 2005 Vincent Marchesi, a cell biologist at Yale University, published an alternative interpretation of the amyloid hypothesis that might ordinarily have been quietly ignored by most AD researchers. Instead, when the paper was featured by Alzforum, 17 scientists posted lengthy, detailed and productive commentaries. “The postings on the Alzforum site regarding my PNAS paper have been incredibly rewarding for me, and I suspect, for many of the others that participated,” wrote Marchesi. “I don’t see how so many candid exchanges could have taken place any other way.

**4.4 COMPENDIA AND DATABASES.** Data about key findings and reagents are curated into databases designed by the Alzforum. These data are published in disparate articles and formats, and scientists expend much time and effort to keep up-to-date. Because there is little incentive for individuals to carry out and share this task on behalf of the scientific community, the Alzforum considers the development and upkeep of open databases to be a high priority. Data sets on the Alzforum include the following:

- Familial AD mutations. All published mutations in the amyloid precursor protein (APP), presenilin-1 and presenilin-2, as well as tau mutations that cause frontotemporal dementia with parkinsonism (FTDP-17). Individual mutations are displayed in a table along with clinical, pathology and biochemical data and primary publications.  
(<http://www.alzforum.org/res/com/mut/default.asp>)
- AlzGene. All published genetic association studies for late-onset AD, conceived and curated by Lars Bertram and his colleagues at Massachusetts General Hospital. The database can be browsed by chromosome or searched by gene, polymorphism, protein, keyword or author. Each gene is summarized in a table listing details of all published studies, and a meta-analysis of the

findings can be calculated with a single click.

(<http://www.alzforum.org/res/com/gen/alzgene/default.asp>)

- Antibodies. More than 10,000 antibodies to proteins that are widely studied by AD researchers have been entered into this database. The database includes noncommercial and commercial antibodies, and displays the data in a table summarizing points of interest to researchers.  
(<http://www.alzforum.org/res/com/ant/default.asp>)
- Drugs in Clinical Trials. This database contains all drugs that we have confirmed to have entered Phase 2 clinical trials and beyond, including drugs that were discontinued following clinical trials. We are planning to re-design this database to include preclinical compounds and additional data of value to preclinical researchers.  
(<http://www.alzforum.org/drg/drc/default.asp>)

## 5. WHO ARE OUR MEMBERS, AND WHAT ARE THEY SAYING?

The Alzforum is freely accessible to the public, so we do not have statistics on our entire user population. However, more than 3,200 individuals have registered as members, of whom more than 2,000 have also filled out the “researcher profile” form. Thus, we assume a lower limit of 2,000 on scientists and clinicians who use the site, and estimate that around the same number are using the site without registering. This implies that 30-50 percent of the global community of AD researchers are regular visitors.

Feedback has been strongly positive. Many of our scientific advisory board members (all very busy researchers and clinicians) visit the website around one to three times per week. “[Alzforum] is the local newspaper for Alzheimer research,” writes John Hardy, Director of the Laboratory of Neurogenetics at the National Institutes of Aging. “I visit it one to two times a week just to see what's going on... to check up on recent papers,...to see who's hiring people and so on. I read people's comments on papers, and I go from there to PubMed for anything I've missed. I think pretty much everyone in the field uses it in the same way, and I have often seen my informal reviews on the site cited.”

Scientists mention a variety of reasons why they find the Alzforum valuable. One is that the Alzforum enriches published papers with news analysis and rapid peer commentary. “This is the major e-forum for AD ideas,” observes Jeffrey Cummings, of the University of California in Los Angeles. “The discussion forums have shaped and sharpened my ideas. It's a great way to get a grasp of the literature and to follow emerging events in real time.”

Many researchers value the breadth of the Alzforum's coverage, which is intended to communicate diverse developments with which no specialist could possibly keep up. “Instead of relying only on published papers and meetings, you provide rapid insights into new developments and introduce us to areas that are related to our work but yet we fail to notice were it not for you,” writes Gunnar Gouras of Weill Medical College of Cornell University. The databases also are frequently mentioned as resources that help scientists stay abreast of advances in fields outside their own.

Another important aspect of Alzforum is its community-building function. Through commentaries and live discussion forums, the website provides a neutral ground for scientists to get comfortable with one another. Scientists are directly involved in

creating resources on Alzforum, volunteering significant time to report on meetings, propose and lead discussions, consult on databases and offer unvarnished feedback. To all of them, we are deeply indebted.

## **6. FUTURE DIRECTIONS**

A constant challenge for the Alzforum is to find new ways to apply information technology to significant problems in AD research. The most ambitious effort to date is the SWAN (Semantic Web Applications in Neuromedicine), a collaboration between Alzforum and Massachusetts General Hospital.

One of the key drivers behind SWAN is the realization that the Alzforum, for all its content and community activity, still is little more than collections of documents and data with some links. This information is not embedded in a knowledge model. Rather, the human user carries the knowledge model in his or her head. When a person reads a paper or follows a link, he or she fills in the contextual blanks, such as “this paper challenges hypothesis X,” or “So-and-so draws the opposite conclusion from this data.” With SWAN, we will provide scientists with a tool to embed their documents, data and other digital materials in a knowledge model, and then to share the entire model with other scientists and communities, who can then build upon it.

Another key concept informing the design of SWAN is that scientific ideas, documents, data and other materials evolve within a “scientific ecosystem.” SWAN will incorporate the full biomedical research life cycle in its ontological model, including support for personal data organization, hypothesis generation, experimentation, lab data organization, and digital pre-publication collaboration. Community, laboratory, and personal digital resources may all be organized, interconnected and shared using SWAN’s common semantic framework.

Individuals will use a version called “MySWAN” as a personal tool to find and organize information, to extend their knowledge, motivate discoveries and to form and test hypotheses. At the community level, the same software and the same ontological framework can be used to organize and curate the research of a laboratory or of an entire research community (such as the Alzforum). Therefore, elements of the personal SWAN can be shared with the community at a low incremental effort in curation. What’s more, community SWAN contents may be shared back with individuals and re-used in new contexts.

The SWAN content will develop through the type of partnership that already exists between the Alzforum editors and the AD community, with editors laying the groundwork and inviting community members to contribute. We look forward to rolling out this next generation of Web technology for AD research in the coming years.

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