---------- Ursprüngliche Nachricht ----------
Betreff: Manuscript EMBOJ-2008-*****
Datum: Fr, 16.05.2008, 17:26
An: fandrich@enzyme-halle.mpg.de

Dear Dr. Fändrich,

Thank you for submitting your manuscript for consideration by The EMBO Journal. I have now had the opportunity to read it carefully and to discuss it with the other members of our editorial team as well as with an editorial advisor of suitable expertise who knows the journal very well. I am afraid that the outcome of these discussions is not a positive one.

We appreciate that you were able to put forward for the first time cryo-EM (and 3D reconstruction) data on a panel of different morphologies of amyloid fibrils formed in vitro by Abeta(1-40) under the same solution conditions. Your results suggest that this peptide is able to give rise to a rather diverse set of different fibrils. Clearly, we recognise that the study puts forward an interesting novel structural data set. Still, our expert editorial advisor and the editors all feel that - in order to consider the study for publication in The EMBO Journal - a considerably deeper understanding of the physiological/pathological significance of the different fibers would be required. This is why we are not convinced that the manuscript would fare well under review here, and in order to save you from further unnecessary loss of time, we have decided not to send out the paper for in-depth peer review at this point.

Please note that we publish only a small percentage of the many manuscripts that we receive at The EMBO Journal, and that the editors have been instructed to only subject those manuscripts to external review which are likely to receive enthusiastic responses from our reviewers and readers. As in our carefully considered opinion, this is not the case for the present submission, I am afraid, our conclusion regarding its publication here cannot be a positive one.

Thank you in any case for the opportunity to consider this manuscript. I am sorry that we cannot be more positive on this occasion.

Yours sincerely,

Editor
The EMBO Journal

---------- Ursprüngliche Nachricht ----------
Betreff: PLoS Biology decision [08-PLBI-RA-****]
Datum: Fr, 30.05.2008, 23:23
An: fandrich@enzyme-halle.mpg.de

Dear Dr. Fändrich,

Thank you very much for submitting your manuscript "Abeta(1-40) Fibril Polymorphism Implies Diverse Interaction Patterns in Amyloid Fibrils" for review by PLoS Biology. I have now had a chance to discuss your study with my editorial colleagues. As we understand it, you provide nice 3-D ultrastructural images of the natural diversity of Abeta fibril

morphologies. While we do not doubt the technical quality of your study, I am sorry to say that we are not persuaded the strength of advance reaches the level we must require for PLoS Biology.

I am sorry that we cannot be more positive on this occasion. While we cannot consider your manuscript for publication in PLoS Biology, we very much appreciate your wish to present your work in an Open Access publication. You may want to consider PLoS ONE (www.plosone.org), a swift, high-volume, efficient and economical system for the publication of peer-reviewed research in all areas of science and medicine; a unique publishing forum that will exploit the full potential of the web to make the most of every piece of research.

If you would like to submit your work to PLoS ONE we can transfer your files directly into PLoS ONE's manuscript handling system; please contact the PLoS ONE publication staff (plosone@plos.org) now citing your manuscript tracking number. If you would like more information about submitting to PLoS ONE please either visit its website or email plosone@plos.org.

I hope you appreciate the reasons for this decision, and will consider PLoS Biology for other submissions in the future.

Sincerely,

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Senior Editor, PLoS Biology

www.plosbiology.org

---------- Ursprüngliche Nachricht ----------
Betreff: From the JBC re: Manuscript M8:*****
Datum: Mo, 14.07.2008, 17:59
An: fandrich@enzyme-halle.mpg.de

M8:*****
Dear Dr. Fändrich:

Your manuscript with Jessica Meinhardt, Carsten Sachse, Peter Hortschansky, and Nikolaus Grigorieff, entitled "Abeta(1-40) fibril polymorphism implies diverse interaction patterns in amyloid fibrils", has been reviewed by the Editorial Board. Unfortunately, the manuscript was not recommended for acceptance for publication in the Journal. Although the studies are done well and the data appear solid, concerns were expressed with respect to the novelty of the findings and the appropriateness of the JBC for the dissemination of these findings. The rationales for the focus on only the abeta40 peptide and the selection of buffers are weak. In addition, the relevance of the data produced using PBS is a concern, as the fibrils thus produced were felt to be unrepresentative of those generally obtained by others. Based on these recommendations, we must regretfully decline the manuscript for publication in the Journal.

Thank you for submitting your work for consideration for publication in the Journal. I hope you consider the Journal for your work in the future.

Sincerely,

Associate Editor

Comments #1 for author: M8:*****

Meinhardt et al. use a combination of TEM, cryo-EM, and image reconstruction to study the structures of fibrils formed by the 40-residue amyloid beta-protein (Abeta40). They find that a range of fibril morphologies exist within and between fibril formation processes occurring in PBS or borate buffer. Rigorous analysis of the fibril morphology distribution revealed differences in fibril width (w), cross-over distance (d), and moment of inertia (Iz). This study was beautifully done and confidence exists that the data are accurate. However, the contribution of the work to an improved understanding of mechanisms of fibril formation, and importantly, the biochemistry of amyloidogenesis, is modest at best. It appears that only the model of protofilament organization in Fig. 6 is potentially novel. In light of these issues, it may behoove the authors to consider publication of the work in a specialized structure journal (e.g., J. Structural Biol.).

1. The first section of the results is nicely stated, but the data have existed for many years in the amyloid community. What is new here? Why was only the abeta40 form of Abeta studied, when abundant evidence suggests that parenchymal deposits are primarily formed by abeta42?

2. What is the rationale for studying fibril formation in PBS versus borate? Why are these studies relevant to understanding fundamental aspects of fibril formation?

3. The fibrils formed in PBS look very different from those published by many groups over many years. They are short and look like sheared or truncated fibrils. The value of comparative analyses of these fibrils with those produced in borate thus is questionable.

4. It is curious that the authors argue that ``none of the ten single-fibril reconstructions readily corresponds to any previous structural model'' (p5, c1, l4 ex bot). By what criteria can this statement be made in the light of the actual data, which show generic amyloid fibril characteristics reproduced countless times by laboratories around the world?

5. The discussion point that the discrimination among different fibril types and the ability to manipulate their formation would be relevant for conformational diseases is debatable (p6, c2, l4). Conspicuous by its absence is a discussion of whether fibrils are actually pathologic (as opposed to oligomeric assemblies). Why do we care about fibrils if they are not the key pathologic agents in disease? In contrast, the succeeding sentence regarding prions appears more meaningful.

Minor points:

1. WHO-designated nomenclature specifies that AB, where ``B'' is a lower case Greek beta, is the correct abbreviation for amyloid B-protein, and that ``amyloid B-protein'' is the correct designation for the peptide product of the APP gene. Please correct usage.

2. The meaning of the term ``natural'' is unclear (p2, c1, l3).

3. Please add the parenthetical comment ``see Results'' after ``equation

1'' on p2, c2, l5 ex bot.

4. The meaning of the term ``intermediate fibrils'' is unclear on p3,c2, l24. This reviewer is unaware of any such term.

5. Correct usage required the addition of a comma after ``e.g.'' on p6, c1, l4.

Comments #2 for author: M8:*****

This manuscript does an excellent job demonstrating that the Abeta fibril structure shows high variability (mostly dependent on the conditions in which the fibrils are produced), which partly agrees with previous work from the Tycko lab (ref. 22). The major difference with the present work is that different techniques were used (cryo-EM and TEM), instead of solid state NMR.

There are two issues that need to be addressed: (1) the third paragraph of the Discussion section mentions that the present models were "compared" to previous models and it is not clear how this was done (this is a very important topic), and (2) what is the physiological relevance of the work (this is just mentioned in the final paragraph, and needs to be elaborated further). Is there any rigorous evidence that "native" amyloid fibrils in the human brain are heterogenous? This would go against statements put forth by David Eisenberg and co-workers

---------- Ursprüngliche Nachricht ----------
Betreff: Fändrich ja-2008-****** -- Manuscript Decision 11-Aug-2008
Datum: Mo, 11.08.2008, 17:49
An: fandrich@enzyme-halle.mpg.de

11-Aug-2008

Dr. Marcus Fändrich
Enzymology of Protein Folding
Max-Planck Research Unit
Weinbergweg 22
Halle an der Saale, 06120
Germany

RE: Journal of the American Chemical Society Manuscript Decision
Manuscript ID: ja-2008-******
Manuscript Type: Article
Title: "Abeta(1-40) Fibril Polymorphism Implies Diverse Interaction Patterns in Amyloid Fibrils"
Author(s): Meinhardt, Jessica; Sachse, Carsten; Hortschansky, Peter; Grigorieff , Niko ; Fändrich, Marcus

Dear Dr. Fändrich:

Your manuscript on "Abeta(1-40) Fibril Polymorphism Implies Diverse Interaction Patterns in Amyloid Fibrils" provides interesting microscopic structural detail for this important protein. However, the work lacks the chemical insights needed for JACS. This work is certain to receive favorable reviews in Journals at interface of neurochemistry and/or protein structure. We regret that JACS will be able to review this work.

Thank you for your interest in the Journal of the American Chemical Society.

Sincerely,

Associate Editor
Journal of the American Chemical Society