

To: "Campbell, Philip" <P.Campbell@nature.com>
From: alexekoudinov@neurobiologyoflipids.org
Subject: Selkoe conflict follow up // Re: message from Dr Philip Campbell
Cc: "Boyle, Pauline" <P.Boyle@nature.com>
Bcc: rsmith@bmj.com, rennie@itsa.ucsf.edu, Sharon.Begley@wsj.com, descrowley@eircom.net, weissr@washpost.com, tinkerr@attbi.com, Geoffrey.Cowley@Newsweek.com, kennedyd@stanford.edu, djs@neurobiologyoflipids.org
Attached:

December 2, 2002

Dear Dr.Campbell,

I am writing to remind you regarding my communication with you (below) on Dr.Selkoe non-disclosure of his corporate ties and direct personal financial conflict of interest in his Nature article published in April 2002, and your earlier decision that Selkoe non-disclosure did not break Nature requirement. As a result my communication arising (on Nature article) was accomodated as eResponse to BMJ [1]

I would like to remind you about earlier statement by Nature (see below) that "Dr Selkoe no longer has has any connection with the companies you list because of the 1997 ruling by Harvard University prohibiting such connections among its faculty members". This statement appeared to be false as soon as D. Selkoe conflict of interest is well established [2] and is now acknowledged in Science magazine (September 27 issue correction note).

I share the confidence by others that there there is no expiration date for the ethics break [3, 4]. I therefore would like to ask you whether you had a chance to re-evaluate your decision that in Selkoe article the Nature "conflict of interest guidelines have been adhered to". If not I urge you to do so at your earliest convenience.

My further related questions are:

Why you "help to conceal dishonesty by" (4) Selkoe?

Why Nature and Nature specialist journals help Selkoe and his Elan corporation to publish biased articles on amyloid, a molecule of major direct financial interest to Selkoe and his Elan corporation (see Ref.5 for the list (and associated discussion) of recent articles by Nature family; also see Ref.2).

Sincerely,

Alexei Koudinov, MD, PhD

cc: World Association of Medical Editors, BMJ, Science

References:

1. Koudinov AR. Amyloid hypothesis, synaptic function, and Alzheimer's disease, or: Beware: the dogma is revitalized. BMJ 15 May 2002, Available at: <http://bmj.com/cgi/eletters/324/7338/656#22216>
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5. Koudinov AR. Amyloid was never clearly implicated in Alzheimer's disease, so look at Abeta from a different angle. BMJ 30 Nov 2002, Available at: <http://bmj.com/cgi/eletters/316/7129/446#27397>

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14 October 2002

Dr Philip Campbell
Editor-in-Chief
Nature
Porters South,
4 Crinan St.
London N1 9XW,
UK

14 October 2002

Dear Dr.Campbell,

Thank you very much for your recent response on my inquiry.

Sadly, I have little reason to share your satisfaction that your "conflict of interest guidelines have been adhered to" in case of Dr.Dennis Selkoe nondisclosure of his Elan directorship in his April 2002 Nature research article (see below for our earlier communication details).

I have greater reason to believe Science magazine that published in September 27, 2002 issue a correction note on D. Selkoe conflict of interest.

Based on the above I still do see the basis to believe that either D.Selkoe or one of his close scientific collaborators (like Dr.C.Haass, for example) was a bias reviewer for Schenk et al. article that was published in Nature in summer 1999 to become the basis for the Alzheimer's vaccination development.

I would like to share with you an additional concern that I discovered. How it could happen that two teams of overlapping authors (appeared in two separate Nature articles of 1992, three months apart) list in their Nature articles either just academic (December 17, 1992 Nature article, p.672) or just corporate (September 24, 1992 Nature article, p.325) affiliation (PubMed imprints are attached for your convenience).

Sincerely yours,

Alexei Koudinov, MD, PhD

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At 01:43 PM 11/9/2002 +0100, you wrote:

>Dear Dr Koudinov

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>I have now looked into the files of the papers you have raised in your
>concerns about the involvement of Dr Selkoe. It is a strict policy of Nature
>that we do not discuss the identity of referees involved in our decision
>making. However, I can assure you that there is absolutely no basis for any
>suspicion that Dr Selkoe might have abused his position as a possible
>referee. My colleagues have examined the situation with patents and we are
>also satisfied that our conflict of interest guidelines have been adhered
>to.

>

>Yours sincerely

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>Dr Philip Campbell

>Editor, Nature

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At 12:28 PM 31/7/2002 +0300, Alexei Koudinov wrote:

Dear Dr.Cotter, Dear Dr.Campbell,

I am writing regarding our earlier commentary (communication arising) manuscript. In May 2002 you decided that our commentary should not be published at Nature (the decision letter follows below).

However, just yesterday I discovered several online documents that make the story much more complicated and unfair to Nature.

Three documents are attached as .PDF imprints for your convenience. Two of these documents indicate that Dr.Selkoe is Elan Corporation director, and specify Dr.Selkoe insider trades.

You may be interested to pay special attention to the date of the last transaction. It is dated 12 December 2001, i.e. one month before Elan announced its' Alzheimer's vaccine problems that yielded the drop in its price (Document 3).

In light of the above I anticipate your inviting us to re-submit the revised version of our commentary for publication in Nature as communication arising letter.

I also demand you to check whether Dr.Selkoe served as a referee for the Nature '99 article by Schenk et al. (Nature Vol.400, 173-177 (1999); that was the basis for vaccine development) and other Alzheimer's/amyloid related articles submitted previously to Nature. I then expect you to make an appropriate statement on Nature pages on this issue. In case you will not respond on this matter, I will consider that Dr. Selkoe served as a biased referee for Nature and will make my own efforts in bringing this information for the research community and to the public.

I appreciate your respecting our doing the best to serve non-biased development of Alzheimer's field. We aim to benefit those who suffer from the disease.

With best regards,

Alexei Koudinov, MD, PhD
<http://neurobiologyoflipids.org>

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At 10:52 AM 17/5/2002 +0300, Alexei Koudinov wrote:

Dear Dr.Cotter, Dear Dr.Campbell,

We respect your decision on our letter to Nature editor (commenting on recent Nature article by Walsh et al.).

However, I am sorry to tell you that the authors reply does not address our points. Moreover, the reply is based on false statements, as illustrated by the specification of the false year of the senior author patent filing (that you could discover yourself by following the fulltext patent links provided in our submission).

Based on the above, we believe that you appreciate our decision and the publication of our letter in another journal.

Should you wish to read it the details follow:

Amyloid hypothesis, synaptic function, and Alzheimer's disease, or: Beware: the dogma is revitalized
Alexei R. Koudinov & Natalia V. Koudinova
BMJ online, published 15 May 2002
<http://bmj.com/cgi/eletters/324/7338/656#22216>

Sincerely,

Alexei Koudinov, MD, PhD
caring neuroscientist and Alzheimer's researcher

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At 02:36 PM 13/5/2002 +0100, you wrote:

>Dear Dr Koudinov

>Thank you for your comment on the Nature paper by Walsh et al. As is our
>policy on these occasions, we showed your complaint to the earlier authors,
>and their response is enclosed. After consultation with Dr Campbell and
>other colleagues, we have decided in the light of this response that this
>matter does not need to be drawn to our readers' attention.

>Instead, we advise both parties to settle the issues between themselves.

>Yours sincerely,

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>Rosalind Cotter

>Associate Editor

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>Reply

>To the editor:

>The statements of Koudinov and Koudinova 1 contain factual errors, and most
>of the references cited are unrelated to the subject of our report. First,
>the authors cite two early papers^{2,3} that used rat brain slices in vitro to
>study synthetic A β 1-40 peptide preparations that were not biochemically
>characterized. This is in contrast to our fully characterized samples (see
>our Figs 1 and 2)⁴ of naturally secreted A β species, which include the
>neurotoxic, AD-implicated A β 1-42 peptide and which were examined in vivo in
>intact, anesthetized rats. Importantly, Wu et al.² monitored HFS for 30 min
>or less, whereas we monitored for 180 minutes and saw a change in LTP only
>after ~60 minutes⁴. Also, Wu et al studied the commissural association
>pathway of dentate gyrus, while we studied CA1, so the results are not
>directly comparable. In the other paper,² the former pathway was again
>studied, and the authors concluded (and latter confirmed⁵) that the increase
>in NMDA EPSCs may, in fact, promote excitotoxicity; this is hardly evidence
>for a beneficial role of A β in synaptic plasticity. Second, Koudinov and
>Koudinova describe the A β 1-40 peptide levels used in these two papers as
>"just above physiological concentrations (100-200 nM)", whereas it has been
>extensively documented during the last decade that physiological
>concentrations of human A β in vivo are 100-fold less, i.e., ~1-2 nM [see
>e.g.⁶⁻⁹]. In this regard, we explicitly provided the A β concentrations of
>the cell medium we microinjected in vivo (3.2 \pm 1.2 ng/ml; i.e., ~0.8 nM) and
>pointed out that this concentration was "very similar to those we previously
>measured in normal human CSF (4.0 \pm 1.9 ng/ml"; i.e., ~1 nM) (see p.537, col.
>2, par. 1)⁴. A strength of our study is that we utilized truly
>physiological concentrations of the heterogeneous human A β species that are
>naturally produced by cells, whereas the papers cited by Koudinov and
>Koudinova used supra-physiological concentrations of a single, defined
>synthetic peptide (specifically, A β 1-40, which is not clearly implicated in
>AD causation). Koudinov and Koudinova cite as their final principal
>reference¹⁰ an abstract from 1996 that did not result in a peer-reviewed
>scientific paper. This abstract used micromolar levels of synthetic A β , and
>no details are available that allow a rigorous comparison to our study.

>

>Then, in their 3rd paragraph, Koudinov and Koudinova cite several unrelated
>studies¹¹⁻¹⁷, most of which are of no direct relevance to either their
>argument or our paper. For example, a report¹¹ that full-length APP
>increases "with learning capacity in rats" does not signify that one of the
>several metabolic products of APP (A β) has a normal synaptic function.
>Similarly, the up-regulation of "a synaptic vesicle protein 2B mRNA

>transcript" in a neuroblastoma cell line exposed to synthetic A β (at ~2
>uM)¹³ certainly does not show that there is a "beneficial role for A β in
>synaptic plasticity". This up-regulation could just as well represent a
>synaptotoxic response, and indeed the authors noted a 50% loss of viable
>cells after the A β treatment¹³. Furthermore, the cited report that
>stimulating the mGluR1a receptor increases secretion of the APP ectodomain
>fragment (i.e., a-APPs)¹⁵ argues directly against the authors' thesis, as
>this would result in decreased A β release at the synapse. Finally, and
>paradoxically, the authors cite 3 papers^{16,18}, all of which suggest that
>(synthetic) A β peptides negatively influence normal synaptic function in rat
>neurons in vitro.

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>It is not inconceivable that low physiological doses of A β will yet be shown
>to have some normal role in synaptic function in vivo. But the authors cite
>no compelling published evidence documenting this, to wit, because there is
>almost none. In any event, our work clearly demonstrates a negative effect
>of A β oligomers, in particular, on synaptic plasticity in vivo, and we used
>extensive controls to show that the natural A β monomers in our cell media do
>not produce any alteration of baseline or induced synaptic activity (Figs. 3
>& 4). If A β monomers or other species had a "beneficial role in synaptic
>plasticity" (whether at physiological or supra-physiological levels) as the
>authors propose, then why have several studies in major peer-reviewed
>journals reported that transgenic mice which express human APP and steadily
>accumulate cerebral A β over time actually show impaired synaptic morphology
>and learning behavior as well as either decreased or normal (not increased)
>LTP [see 19-24]? Thus, our report of impaired hippocampal LTP induced by
>soluble A β oligomers is consistent with numerous earlier in vivo studies.

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>The patents the authors cite were originally filed (and their findings
>published) in 1992, they were out-licensed in 1992, and they provide no
>on-going royalties or opportunity for future financial gain to the authors
>or their institutions. More importantly, these patents are not germane to
>the purpose of our study, which is a basic analysis of the effects and
>neurophysiological mechanism of A β oligomers in rat hippocampus. Finally,
>all of the work in our paper was free of commercial support and commercial
>obligation, and Dr. Selkoe's laboratory does not receive any sponsored
>research funding from industry.

>

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- >24. Fitzjohn, S.M. et al. Age-related impairment of synaptic
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At 02:12 AM 24/4/2002 +0300, Alexei Koudinov wrote:

Dear Dr.Cotter, Dear Dr. Campbell,

Thank you so much for your e.mail and comments.

We do not agree with the arguments explained in your reply (below). We provide the response on these items in the new version of our letter (now entitled 'Alzheimer's amyloid beta and synaptic plasticity') that is attached in the format of word2000 Koudinov230402allnew.doc file, 307 word count) and at length of this e.mail.

We focused our updated letter on just two major items explained below.

The major points (referenced and further explained in the updated letter) are:

1. Our concern is not related to the "scientific inconsistency with previous publications by the Dublin group" and the reports by others. Our concern is that the lack of the discussion/citation of the reports on the beneficial role of amyloid beta for synaptic function/plasticity (that is completely missed in the article) makes the article by Walsh et al. unipolar and misleading with regard to the subject state of the art.

The updated version of our letter is mostly devoted to the above discussion and provides ten references to support possible synaptic function of amyloid beta. Two articles co-authored by Anwyl and Rowan are no longer concerned but just cited in our letter. This discussion also compatibilise the physiological relevance of the concentrations used in the previous reports (Refs.2-3) and specify that one report used the analysis of naturally secreted amyloid-beta peptide (Ref.6) produced under physiological conditions.

As you may figure out the above is different from the misrepresentation of our concern by the authors (see your letter below).

2. Our second point is the compromise of the trust and the 'Nature Competing Financial Interest policy' by Walsh et al. The Competing Interest policy of Nature (P. Campbell, Nature 23 August 2001) describes the following: "Personal financial interests: Stocks or shares in companies that may gain or lose financially through publication; consultation fees or other forms of remuneration from organizations that may gain or lose financially; patents or patent applications whose value may be affected by publication."

The authors arguments [that they likely provided you with on our earlier version of the letter (that we submitted before your requested to feedback "evidence to support your complaint")] seem irrelevant now when we discovered and provide concise official full citations of three patents of Dr.Selkoe dated 1998 and 2001 (with the links to freely available full patent records at US Patent and Trademark Office databases).

These citations and records officially disclose Dr.Selkoe co-inventors and patents' assignees (please see Refs.13-15 of our new letter for names of people and companies).

Furthermore, all three patents of Dr.Selkoe are matching the key words provided by ISI Web of Science for the article by Walsh et al. [ISI keywords plus: insulin-degrading enzyme, Alzheimers-disease, transgenic mice, precursor protein, plaque-formation, neurotoxicity, cells, neurodegeneration, fibrillogenesis, A-beta(1-42)], thus fitting the Nature definition of personal financial interest on "patents or patent applications whose value may be affected by publication."

There is a clear contradiction between the facts and the authors reply to you (see below) as soon as the latest US patent (6,284,221) of Dr.Selkoe is dated September 4, 2001, is co-invented by Schenk, D.B., Schlossmacher, M.G., Selkoe, D.J., Seubert, P.A., and Vigo-Pelfrey, C., and has Elan Pharmaceuticals, Inc., Eli Lilly and Company, and Brigham and Women's Hospital, Inc. as assignees (Ref.13).

We fully agree with Nature that "the best way to maintain readers' trust in the integrity of the research we publish is through a policy of transparency".

We further believe that the trust was compromised in this particular case and resulted in the unipolar discussion that may mislead further development of Alzheimer's field. However, in the updated version of our letter we omit our thoughts (that we share with you previously and in this e.mail) and provide just facts.

In accord with the above we ask you to reconsider the new version of our Letter for publication at Nature. We believe that our communication arising belongs to Nature pages and Nature readership, not to a private correspondence of Nature with us and with the authors, and not to some other third party biomedical publication/ethics resources that we otherwise will have to approach.

We look forward hearing from.

Sincerely,

Alexei Koudinov, MD, PhD
P.O.Box 1665
Rehovot 76100
Israel

Alzheimer's amyloid beta and synaptic plasticity

To the editor:

We read with interest recent Nature article by Walsh et al. entitled "Naturally secreted oligomers of amyloid beta (Ab) protein potently inhibit hippocampal long-term potentiation in vivo"[1]. The study provide important knowledge, but unfortunately does not discuss possible beneficial role for Ab in synaptic plasticity.

Thus it was shown that whereas acute treatment of young rat (70-120 days) hippocampal slices with near physiological concentrations (100-200 nM) of bath applied Ab1-40 did not change basal synaptic transmission, there was an increase in tetanus induced long-term potentiation (LTP) [2]. Moreover, intracellular (100 nM, via the recording pipette) or bath (200 nM) application of Ab1-40 triggered the slow onset potentiation of the NMDA receptor-mediated synaptic currents [3] in the hippocampal slices from young rats (70-120 g weight), and did not affect the basal AMPA receptor-mediated transmission, resting membrane potential or input resistance of the granule cells. Similar results were presented by Schulz, who showed no effect of Ab1-42 on AMPA currents, and demonstrated the increase of NMDA currents by the peptide [4]. This report proposed that Ab peptides (Ab1-42, Ab1-28 and Ab1-40) increase the probability of LTP under the paradigm that induced little LTP in control slices [4].

The above reports favor synaptic function for Ab (rather than synaptotoxicity of Ab claimed by Walsh et al.[1]), and are additionally supported by several recent studies by others, particularly, by an increase of synaptic amyloid b precursor protein with learning capacity in rats [5], by neuronal activity dependent secretion of natural Ab [6], by Ab-mediated upregulation of a synaptic vesicle protein transcript [7], and by a bidirectional modulation between Ab, its precursor protein and both metabotropic and ionotropic receptor molecules [8-12].

Also, we wonder to read in the last sentence of the paper [1] that "the authors declare that they have no competing financial interests." This is because several patents by Dennis Selkoe [13-15], the senior author, disclose his competing interest as it is defined by Nature [16].

Competing interests: none

References

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- Sincerely,
13. Schenk, D.B., Schlossmacher, M.G., Selkoe, D.J., Seubert, P.A., Vigo-Pelfrey, C., inventors; Elan Pharmaceuticals, Inc., Eli Lilly and Company, Brigham and Women's Hospital, Inc., assignees. Method for identifying .beta.-amyloid peptide production inhibitors. US Patent 6,284,221. Sept. 4, 2001 [Full text].
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Alexei Koudinov, MD, PhD

Natalia Koudinova, MD, PhD

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At 04:44 PM 23/4/2002 +0100, you wrote:

>Dear Dr Koudinov

>Thank you for resubmitting your complaint about the recent Nature paper by

>Walsh et al. After careful consideration by my editorial colleagues, we have

>decided that publication of a correction by these authors in response to

>your complaint is not justified for the following reasons.

>First, you are concerned about scientific inconsistency with previous

>publications by the Dublin group: in fact, these earlier studies relate to

>in vitro experiments that used very high, non-physiological concentrations

>of synthetic amyloid-beta peptides, whereas Walsh et al. use naturally

>secreted amyloid-beta peptides produced under physiological conditions and
>show the effects in vivo. It is not unusual for discrepancies to arise
>between in vivo and in vitro studies for these reasons.
>Second, Walsh et al. adequately acknowledge previous work by the Dublin
>group; the omission of your references 4-6 from their reference list is
>because we impose a strict limit of 30 citations on Letters to Nature
>because of the extreme demands on our space and we can therefore only allow
>listing of those most relevant to the study (knowing that other recent
>related publications will show up in web searches).
>Third, regarding the competing financial interests statement, Dr Selkoe no
>longer has any connection with the companies you list because of the
>1997 ruling by Harvard University prohibiting such connections among its
>faculty members. Selkoe's amyloid-beta vaccine patent was independent of
>Elan/Schenk's.
>Thank you again for writing to us.
>Yours sincerely
>Rosalind Cotter
>Associate Editor
>
>

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Editors
Nature
Porters South,
4 Crinan St.
London N1 9XW,
UK

11 April 2002

Dear Colleagues,

Please find below (as plain text) my letter to the editor on April 4, 2002 contribution by Walsh et al. I hope that you will find my viewpoint interesting to share it with your readers on Nature pages. The letter counts 294 words and has eleven important references.

With best holiday regards from the Holy Land,

Sincerely,

Alexei Koudinov, MD, PhD
<http://anzwers.org/free/neurology/>
<http://neurobiologyoflipids.org>

Neurology
P.O.Box 1665
Rehovot 76100
Israel

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At 12:42 PM 18/4/2002 +0300, Alexei Koudinov wrote:

Subject: additional items to accompany my yesterday correspondence with Nature

Dr.Cotter
Nature Editorial Office
Porters South,
4 Crinan St.

London N1 9XW,
UK

cc: Philip Campbell PhD
Editor, Nature
Editor-in-Chief, Nature publications

18 April 2002

Dear Dr.Cotter, Dear Dr.Campbell,

I appreciate Ms.Clarke confirmation of my yesterday communication.

I would like to add several other items in support of my correspondence with Nature.

These are reports on D.Selkoe three patents provided by the US Patent and Trademark Office search system for the period 1996-2002 (that was not covered in the ISI report I that e.mailed to you yesterday). These documents prove the competing interest of Dr.Selkoe and his close relation with Elan Pharmaceuticals, Eli Lilly and Company, Athena Neurosciences, and Elan's Dale Schenk.

The search for patents at US Patent and Trademark Office is available for any user at the following URL:
<http://www.uspto.gov/patft/index.html>

For your convenience I attach these patent documents as Acrobat .PDF imprints and ask you to bind them to my earlier correspondence with you.

Sincerely,

Alexei Koudinov, MD, PhD
P.O.Box 1665
Rehovot 76100
Israel

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At 03:35 AM 18/4/2002 +0300, Alexei Koudinov wrote:

Dr.Cotter
Nature Editorial Office
Porters South,
4 Crinan St.
London N1 9XW,
UK

cc: Philip Campbell PhD
Editor, Nature
Editor-in-Chief, Nature publications

(Ms. Clarke, please confirm that the copy of this correspondence and all attached materials reached Dr.P.Campbell. Also, please confirm the receipt of this communication by you. Thanks)

16 April 2002

Dear Dr.Cotter, Dear Dr.Campbell,

In light of your request to provide you with the "evidence to support the complaint", I performed additional search and found several documents that indicate that the paper by Walsh et al. does not fit Nature policy on competing financial interests (Nature, 23 August 2001). The non-reported competing interest of Dr.Selkoe explains the misleading discussion of the paper by Walsh et al. outlined in our correspondence (ref #0478).

The documents that I succeeded to find include:

1. The list of D.Selkoe patents (posted at ISI Web of Science site), indicating his joint competing interest with Dr.Schenk of Elan Pharm in the subject of the article published in Nature on April 4, 2002,
2. Dr.Selkoe CV (also posted at ISI Web of Science),
3. Dr.Selkoe brief bibliography at his institution, indicating that he is a principal founding scientist of Athena Neurosciences,
4. Elan Pharm company web site notice on the acquisition of Athena Neurosciences,
5. Dr.Schenk brief biography at WebMD, indicating his early affiliation with Athena Neurosciences.

For your convenience, the above documents are attached as an Acrobat .PDF imprints of the corresponding web pages.

The URL links to two of the above pages are now included as references in the updated version of our submission (attached file KoudinovCorrespondenceFinal180402).

As you may figure out from our communication, we aim open, unbiased and unrestricted discussion of our research subject of Alzheimer's disease. For the above reason I am happy to contribute to eradication of the misconduct that was brought on April 4, 2002 to Nature pages by Walsh et al.

In addition for your consideration for publication in Nature our correspondence submission (#0478) I request you to investigate and inform all agencies with which Dr.Selkoe is affiliated (the list of these agencies you can find in the attached CV of Dr.Selkoe posted at the ISI web site), and where his misconduct (as a reviewing agent) may similarly contribute to the unidirected unfair development of Alzheimer's research priorities and thus retard the development of Alzheimer's cure.

Sincerely,

Alexei Koudinov, MD, PhD
P.O.Box 1665
Rehovot 76100
Israel

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At 03:40 PM 11/4/2002 +0300, Alexei Koudinov wrote:

UNIDIRECTED. AGAIN.

Alexei Koudinov, MD, PhD and Natalia Koudinova, MD, PhD

We read with interest recent Nature article by Walsh et al. entitled "Naturally secreted oligomers of amyloid beta protein potently inhibit hippocampal long-term potentiation in vivo" [1]. Two study authors previously co-authored two articles (published in 1995) that reported the opposite results on acute facilitation of tetanus induced long-term potentiation (LTP) and the development of slow onset potentiation in the absence of tetanic stimulation by low dose of amyloid peptide (Ab1-40) [2, 3]. Unfortunately, these papers were neither cited nor discussed in the recent Nature article by Walsh [1]. Several other papers that favor synaptic function for Ab (rather than synaptotoxic Ab function claimed by Selkoe's team [1]) are also ignored [4, 5, 6].

It's a pity that such subject misrepresentation and the unfair discussion is possible. It is disappointing that it happens on Nature pages.

Such a way of limited science delivery is, however, very similar to the other Nature story on Alzheimer's and amyloid that was fueled during summer 1999 and then come to death at the beginning of this year 2002 [7, 8, 9]. It thus took two and a half years of public confidence waving. Too high toll for Alzheimer's victims.

It would be irresponsible to postpone the public awareness of the other undisclosed [2-6] knowledge related to the April 4, 2002 Nature article. Fortunately, the connected world makes the possibility to fix this unjust easier than to be caught by the Nature heavy and surely very important publication schedule.

Also, it seems strange to read in the article [1] last sentence that "the authors declare that they have no competing financial interests." This is because senior author Dr. Selkoe is an Elan consultant [10] and because he was affiliated with the Athena Neurosciences (that was acquired by Elan [11]).

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