

MARC TESSIER-LAVIGNE

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Theo Baker
Staff Writer, The Stanford Daily
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Dear Theo:

I am saddened that you seem intent on publishing an article that misrepresents so completely our 2009 Nature paper and our subsequent work. I would like to ask that you please pause and consider the points I make in this letter.

Let me start with the science, which I lay out in detail in the attached backgrounder titled "Scientific context to the 2009 Nature paper." I hope you and the scientists you are consulting will read it in full. In brief:

- The 2009 paper implicated several players in degeneration (DR6, APP and Caspase-6, but not Caspase-3). It also proposed a model for the interaction of DR6 and APP.
- Importantly, as the backgrounder explains, the data that led to those proposals were reproducible and many were independently reproduced by other groups (the Raff and Milbrandt groups). Let me underscore this: the data were reproducible.
- It is our own extensive experiments that made us realize over time that interpretation of the experiments (ours and those of other groups) was affected by off-target effects of inhibitors and other reagents, and by other factors, and that led us to show that Caspase-3 is in fact involved and to revisit the model for APP-DR6 interaction. The backgrounder explains this in detail. Again, please read it.

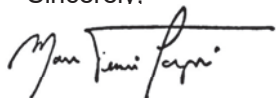
It is perplexing that you seem to think that revisiting models based on new data somehow impugns the integrity of the earlier models; instead, that process is exactly what science is about.

Let me now turn to the purported investigation. There was never to my knowledge an investigation of the paper; **Third-Party Material Redacted**

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The RRC typically meets six hours a week to review essentially all programs at Genentech, and to portray this as anything but a regular check-in would be a misrepresentation.

In short, we published important findings, many of which have withstood the test of time, and when our experiments told us that we needed to revisit aspects of our models we did so and published those findings too. Our revised models for Caspase-3 involvement and for the DR6-APP interaction have been validated and, for DR6 and APP, extended to adult brain and to neurodegenerative disease. It is deeply troubling to me that you would consider presenting this in any other way.

Sincerely,



Marc Tessier-Lavigne