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June 27, 2011

Marie-Therese Heemels, PhD
Senior Editor
Nature

Re: Resubmission of manuscript "Molecular changes in the aging systemic milieu negatively regulate neurogenesis and cognitive function" (manuscript Nature 2009-07-08848LFAH)

Dear Therese,

Thank you very much for offering publication of the above referenced manuscript. We have completed the editorial changes necessary for our manuscript to comply with the guidelines outlined for publication of a Biology Letter in *Nature*. Specifically, we have now included only 4 figures in the main text, and moved information to the supplemental information.

In response to the observation by reviewer 1 "that the influence on neurogenesis only makes minor contributions to the influence of old environment on learning and memory" we have toned down our conclusions regarding the correlations between the aging systemic milieu and neurogenesis versus behavior.

As you suggested, we present now the data most central to the conclusions in the main part of the paper and streamlined the supplement to leave out unnecessary data, which do not directly contribute to the main message. Consequently, in the second part of the paper, we removed data concerning CCL2 and focused instead on CCL11 for which we have strong *in vivo* data. Based on the Excel worksheet to calculate the size of the final paper the total number of pages is now within 5 pages.

Lastly, we would like to suggest as a possible cover illustration the painting "Dos Fridas" from Frida Kahlo. We think this would just be perfect to convey the message of aging and rejuvenation central to our study. We have thus contacted Ms. Fernanda Meza from the Artists Rights Society, who is in charge of supervising the distribution rights for the Kahlo estate and are able to obtain a license for publication use specifically as a cover for *Nature* should the image be chosen.

With best wishes,

A handwritten signature in black ink, appearing to read 'A. Wyss-Coray'.

Tony Wyss-Coray, Ph.D.
Associate Professor, Stanford University School of Medicine
Research Career Scientist, VA Palo Alto



Suggested Cover Illustration. “Dos Friday” by Frida Kahlo. This is a self-portrait of Frida Kahlo painted in 1939. On the right is an image of a young Frida Kahlo in Mexican Tehuana costume clasping in her left hand to a memory of her lover’s youth. The younger more vibrant Frida is connected by vasculature – in essence parabiosis – to the older more cosmopolitan Frida. While the older Frida bleeds from heartbreak onto her white dress, her life is sustained from the blood source the youthful Frida provides.

We have corresponded with Ms. Fernanda Meza (mfmeza@arsny.com), from the Artists Rights Society, who is in charge of supervising distribution rights for the Kahlo estate and are able to obtain a license for the use of the “Dos Fridas” image for publication use.