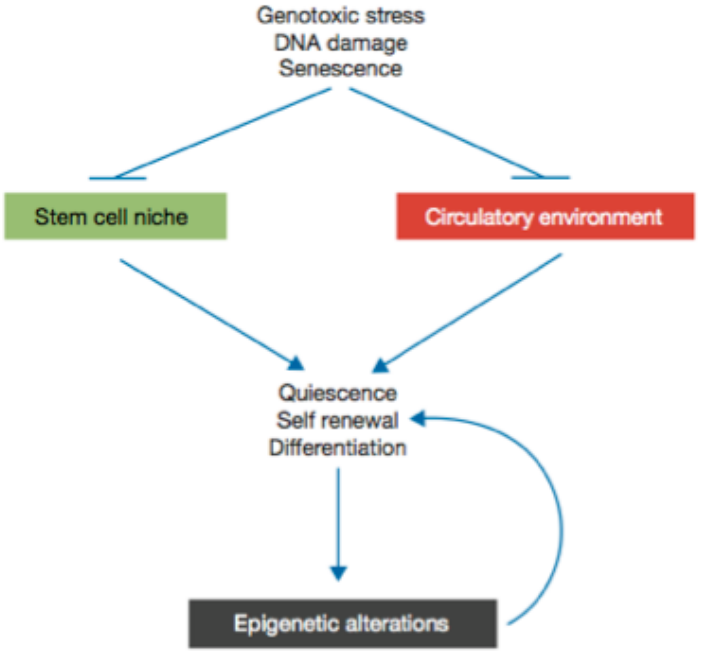
Cours du 3-11-2014

Impact of genomic damage and ageing on stem cell function

Behrens A, van Deursen JM, Rudolph KL, Schumacher B

Nat Cell Biol
2014 vol. 16 (3) pp. 201–7



Young blood rejuvenates old brains

Paul SM, Reddy K

Nat Med
2014 vol. 20 (6) pp. 582–3

Endothelial Cells Stimulate Self-Renewal and Expand Neurogenesis of Neural Stem Cells

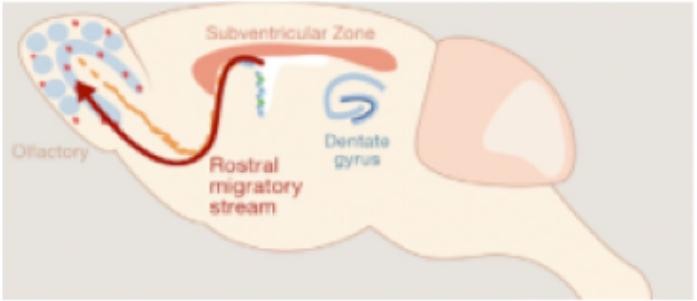
Qin Shen,[1] Susan K. Goderie,[1] Li Jin,[1] Nithin Karanth,[1] Yu Sun,[1] Natalia Abramova,[1] Peter Vincent,[2] Kevin Pumiglia,[3] Sally Temple[1]*

28 MAY 2004 VOL 304 SCIENCE

Off the beaten track: new neurons in the adult human striatum

Kempermann G

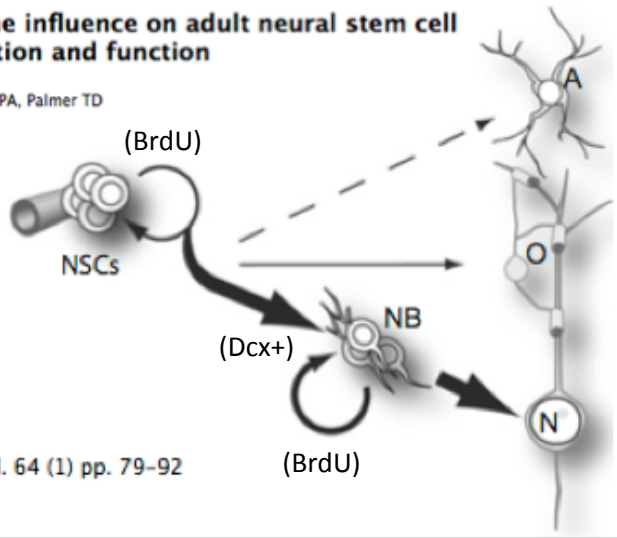
Cell
2014 vol. 156 (5) pp. 870–1



Immune influence on adult neural stem cell regulation and function

Carpentier PA, Palmer TD

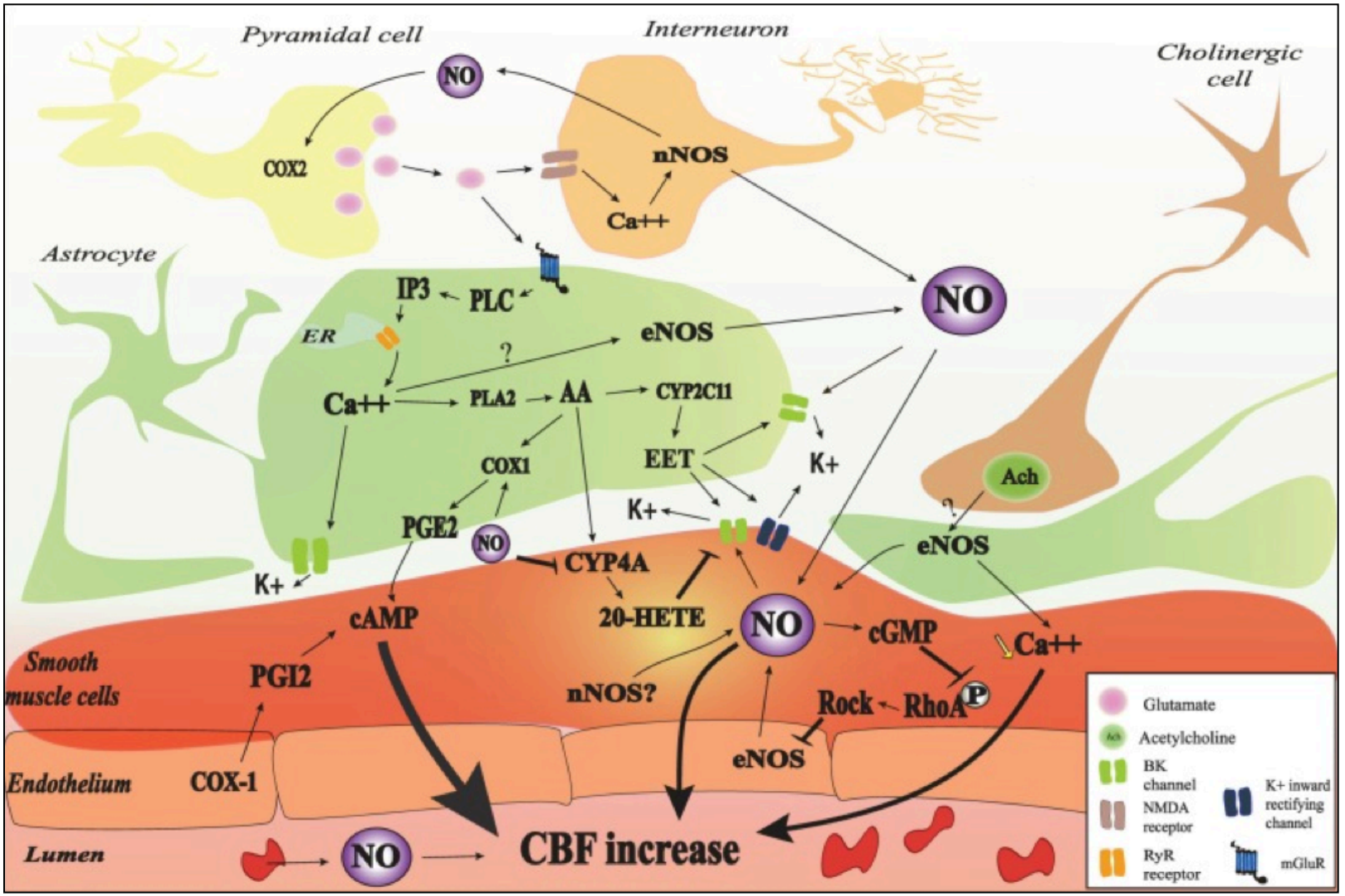
Neuron
2009 vol. 64 (1) pp. 79–92



Front Neural Circuits. 2012;6:51. Epub 2012 Aug 9.

The complex contribution of NOS interneurons in the physiology of cerebrovascular regulation.

Duchemin S, Boily M, Sadekova N, Girouard H.



The ageing systemic milieu negatively regulates neurogenesis and cognitive function

Villeda SA, Luo J, Mosher KI, Zou B, Britschgi M, Bieri G, Stan TM, Fainberg N, Ding Z, Eggel A, Lucin KM, Czirr E, Park J, Couillard-Després S, Aigner L, Li G, Peskind ER, Kaye JA, Quinn JF, Galasko DR, Xie XS, Rando TA, Wyss-Coray T

Nature

2011 vol. 477 (7362) pp. 90–4

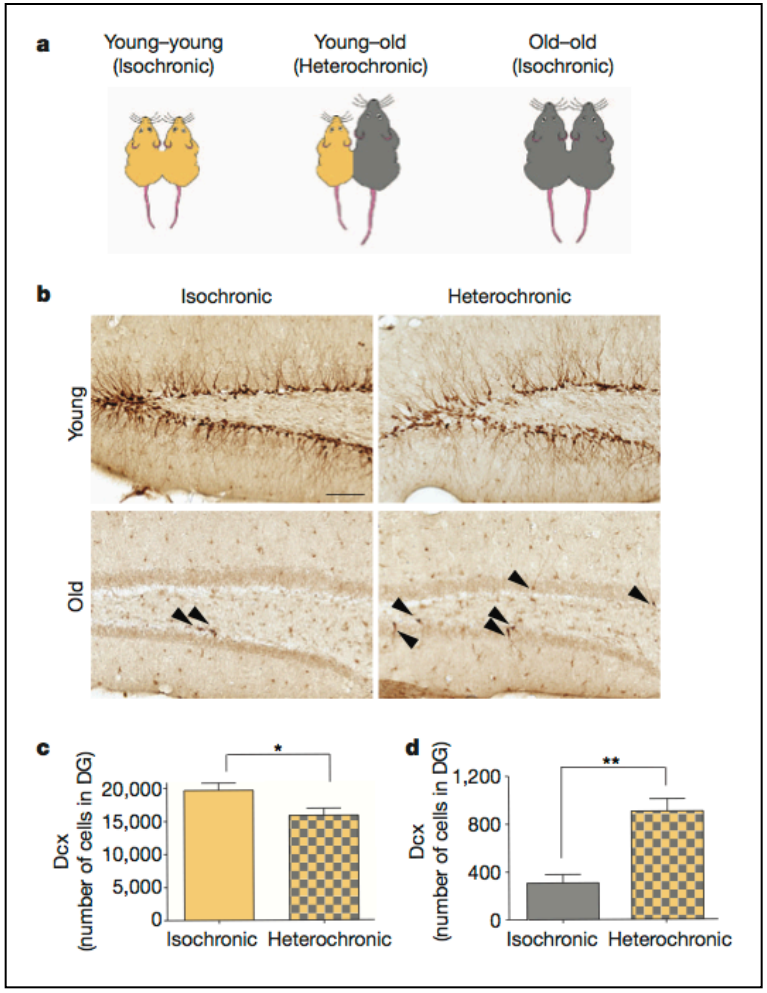
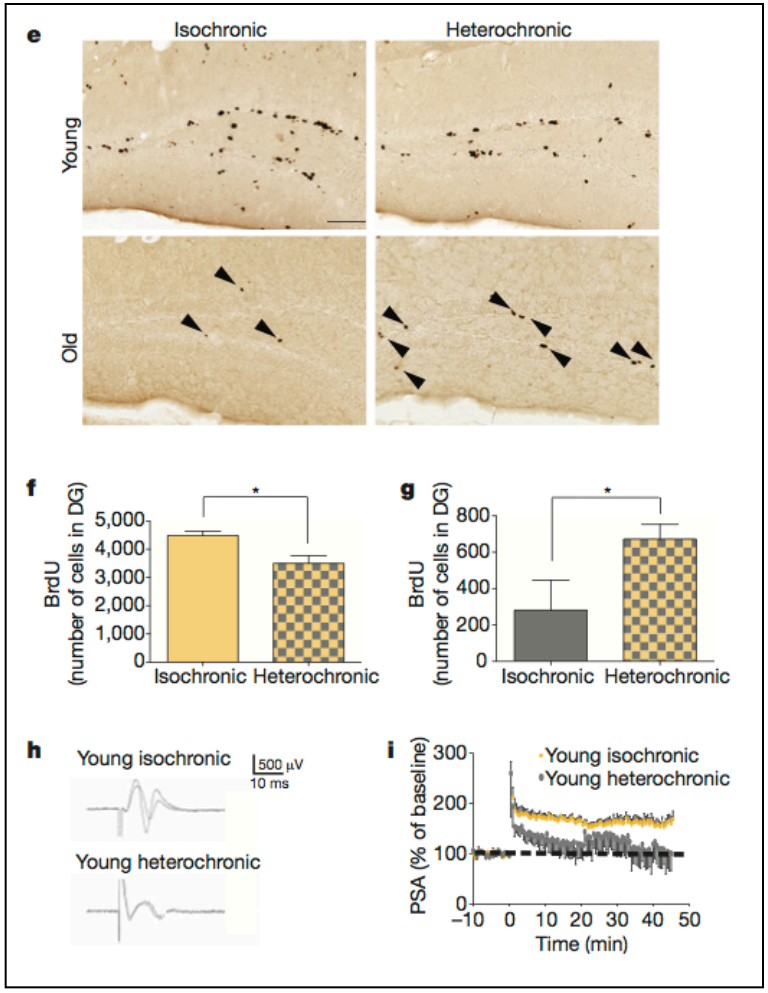


Figure 1 | Heterochronic parabiosis alters neurogenesis in an age-dependent fashion. **a**, Schematic showing parabiotic pairings. **b**, **e**, Representative fields of Dcx (**b**) and BrdU (**e**) immunostaining of young (3–4 months; yellow) and old (18–20 months; grey) isochronic and heterochronic parabionts 5 weeks after parabiosis (arrowheads point to individual cells; scale bars, 100 μm). **c**–**f**, Quantification of neurogenesis (**c**, **d**) and proliferating cells (**e**, **f**) in the young (**c**, **e**; top) and old (**d**, **f**; bottom) dentate gyrus (DG) after parabiosis. Data from 12 young isochronic, 10 young heterochronic, 6 old isochronic and 12 old heterochronic parabionts. **g**, **h**, Population spike amplitude (PSA) was recorded from the dentate gyrus of young parabionts. Representative electrophysiological profiles (**g**) and LTP levels (**h**) are shown for young heterochronic and isochronic parabionts. Data from 4–5 mice per group. All are data represented as mean + s.e.m.; $*P < 0.05$; $**P < 0.01$, *t*-test.



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Nature
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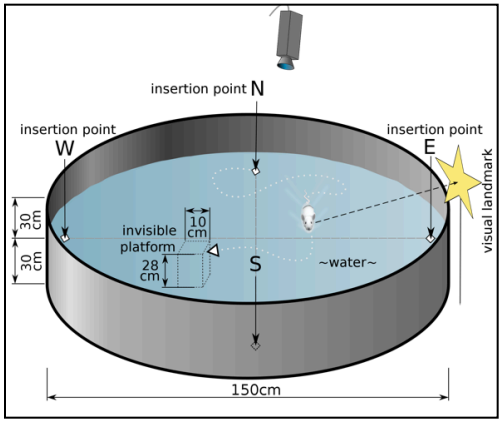
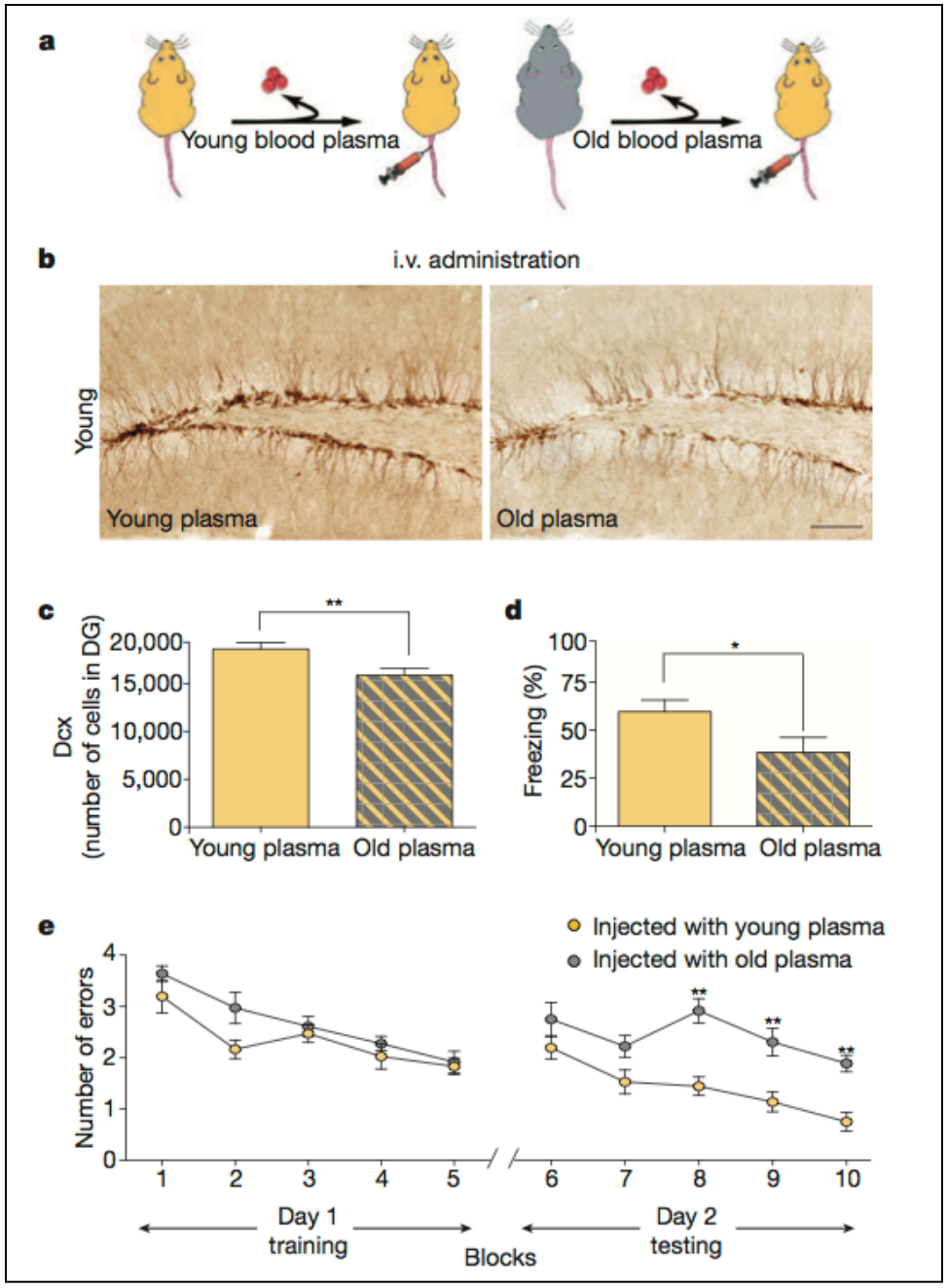
Figure 2 | Factors from an old systemic environment decrease neurogenesis and impair learning and memory. **a**, Schematic of young (3–4 months) or old (18–22 months) plasma extraction and intravenous (i.v.) injection into young (3 months) adult mice. **b**, Representative field of Dcx immunostaining of young adult mice after plasma injection treatment four times over 10 days (scale bar, 100 μm). **c**, Quantification of neurogenesis in the young dentate gyrus after plasma injection. Data from 8 mice injected with young plasma and 7 mice injected with old plasma. **d**, **e**, Hippocampal learning and memory assessed by contextual fear conditioning (**d**) and RAWM (**e**) paradigms in young adult mice after young or old plasma injections nine times over 24 days. **d**, Percent freezing time 24 h after training. Data from 8 mice per group. **e**, Number of entry arm errors before finding platform. Data from 12 mice per group. All data represented as mean ± s.e.m.; $*P < 0.05$; $**P < 0.01$, *t*-test (**c**, **d**), repeated measures ANOVA, Bonferroni post-hoc test (**e**).





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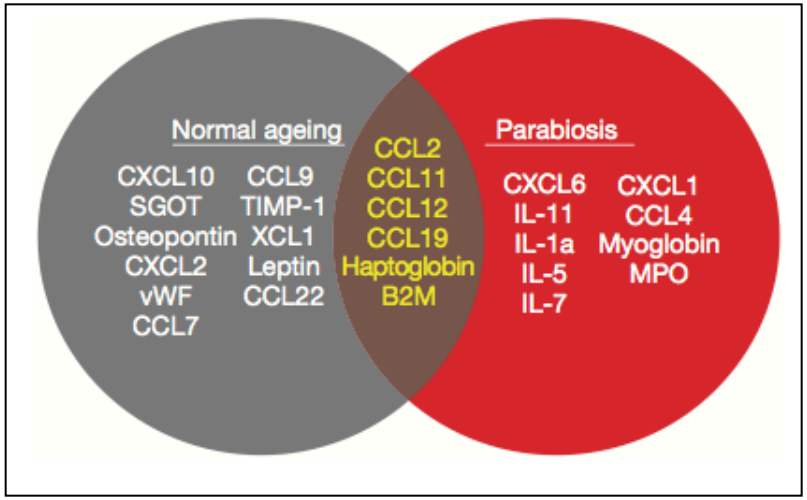
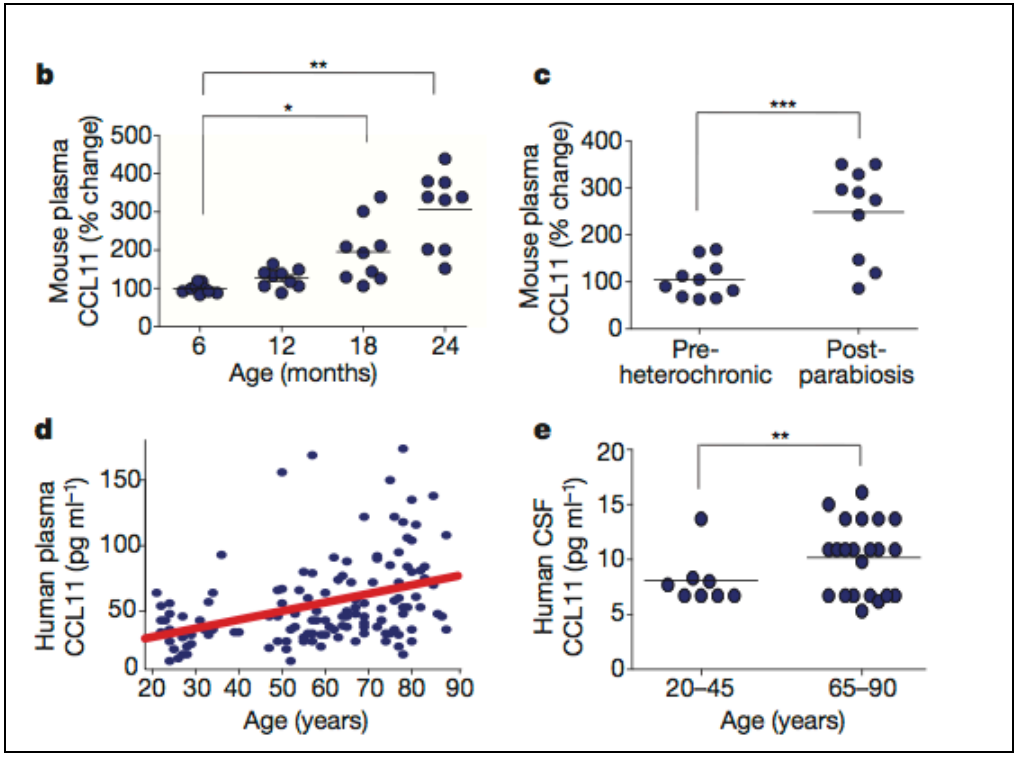


Figure 3 | Systemic chemokine levels increase during ageing and heterochronic parabiosis, and correlate with decreased neurogenesis. **a**, Venn diagram of results from ageing and parabiosis proteomic screens. In grey are shown the seventeen age-related plasma factors that correlated most strongly with decreased neurogenesis, in red are shown the fifteen plasma factors that increased between young isochronic and young heterochronic parabionts, and in the brown intersection are the six factors elevated in both screens. Data from 5–6 mice per age group. **b**, **c**, Changes in plasma concentrations of CCL11 with age (**b**) and young heterochronic parabionts pre- and post- parabiotic pairing (**c**). **d**, **e**, Changes in plasma (**d**; $r = 0.40$; $P = 5.6 \times 10^{-7}$; 95% confidence interval = 0.26–0.53) and CSF (**e**) concentrations of CCL11 with age in healthy human subjects. All data represented as dot plots with mean; $*P < 0.05$; $**P < 0.01$; $***P < 0.001$, *t*-test (**c**, **e**), ANOVA, Tukey's post-hoc test (**a**, **b**), and Mann–Whitney U Test (**d**).



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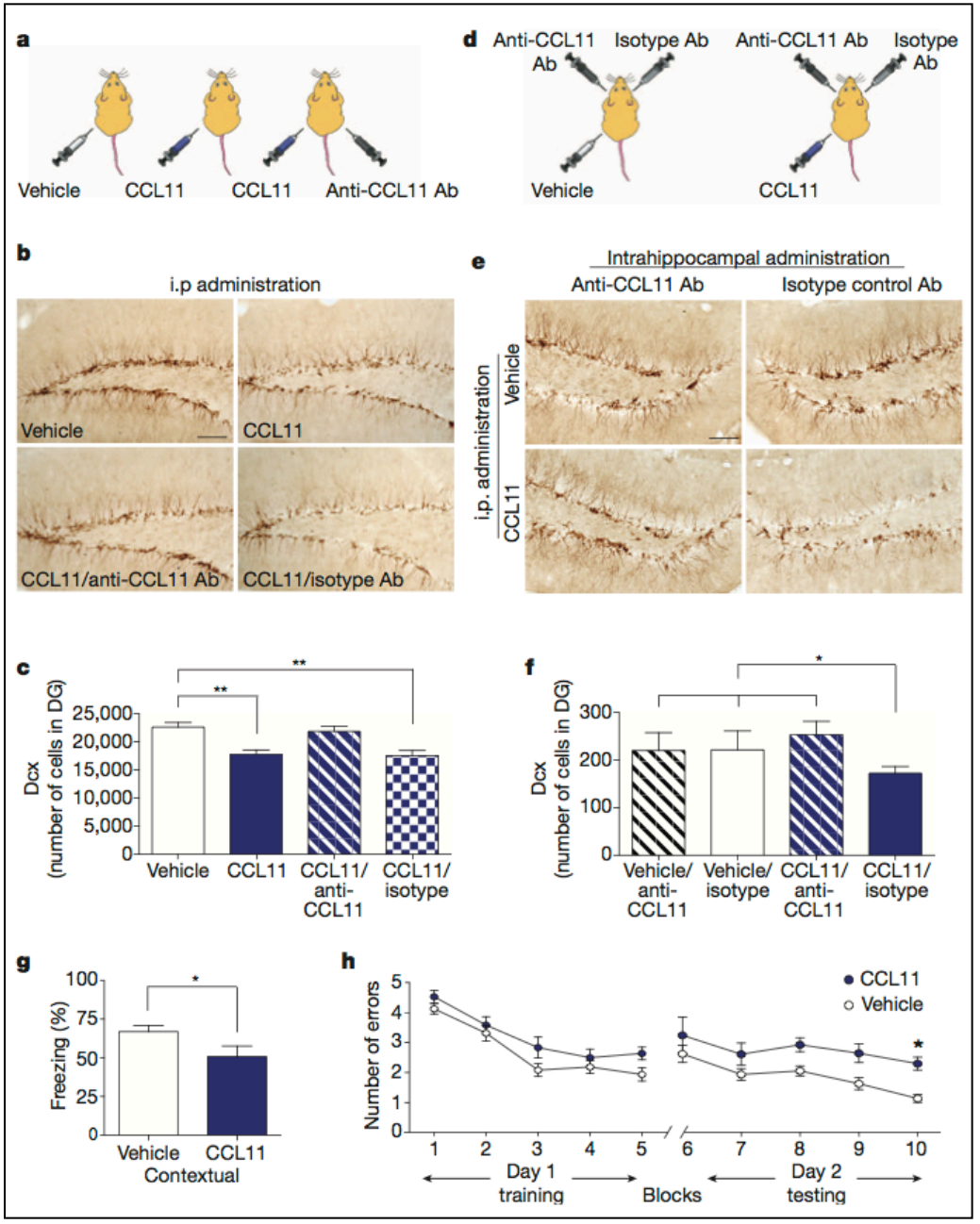
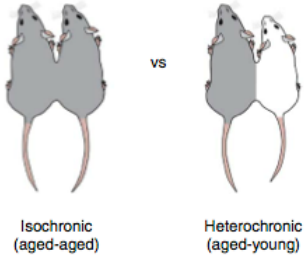


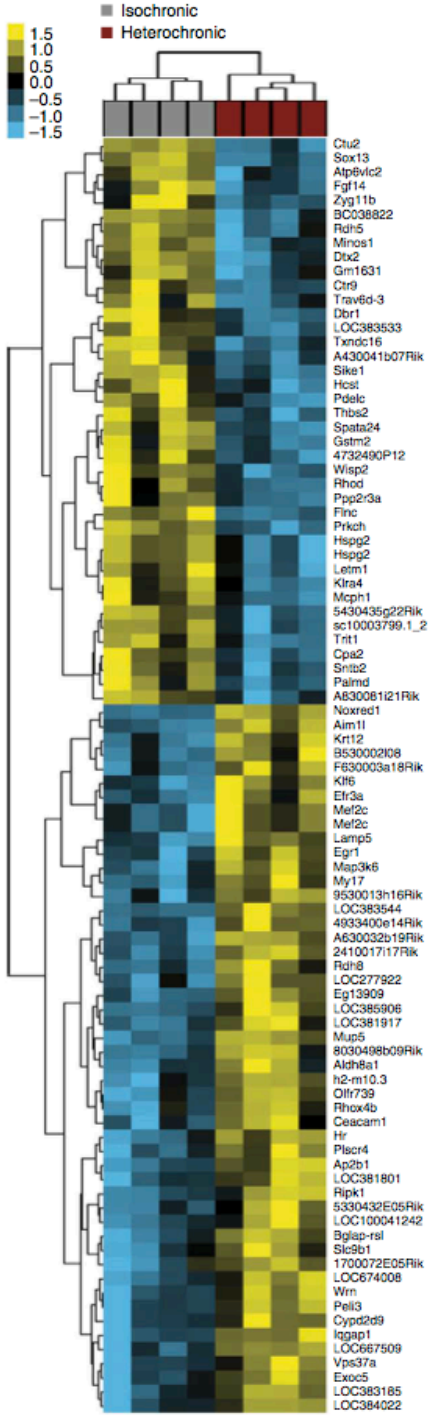
Figure 4 | Systemic exposure to CCL11 inhibits neurogenesis and impairs learning and memory. **a**, Schematic of young (3–4 months) mice injected intraperitoneally with CCL11 or vehicle, and in combination with anti-CCL11 neutralizing or isotype control antibody (Ab). **b**, Representative field of Dcx-positive cells for each treatment group ($n = 6$–10 mice) treated four times over 10 days. i.p., intraperitoneal. Scale bar, 100 μm. **c**, Quantification of neurogenesis in the dentate gyrus after treatment. **d**, Schematic of young adult mice given unilateral stereotaxic injections of anti-CCL11 neutralizing or isotype control antibody followed by systemic injections with either recombinant CCL11 or PBS (vehicle). **e**, Representative field of Dcx-positive cells in adjacent sides of the dentate gyrus for each treatment group ($n = 3$–11 mice). Scale bar, 100 μm. **f**, Quantification of neurogenesis in the dentate gyrus after systemic and stereotaxic treatment. Bars represent mean number of cells in each section. **g**, **h**, Learning and memory assessed by contextual fear conditioning (**g**) and RAWM (**h**) paradigms in young adult mice injected with CCL11 or vehicle every 3 days for 5 weeks ($n = 12$–16 mice per group). All data are represented as mean ± s.e.m.; $*P < 0.05$; $**P < 0.01$; ANOVA, Dunnet's or Tukey's post-hoc test (**c**, **f**); repeated measures ANOVA, Bonferroni post-hoc test (**k**).

Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice

Villeda SA, Plambeck KE, Middeldorp J, Castellano JM, Mosher KI, Luo J, Smith LK, Bieri G, Lin K, Berdnik D, Wabl R, Udeochu J, Wheatley EG, Zou B, Simmons DA, Xie XS, Longo FM, Wyss-Coray T

Nature Medicine
2014 vol. 20 (6) pp. 659-63





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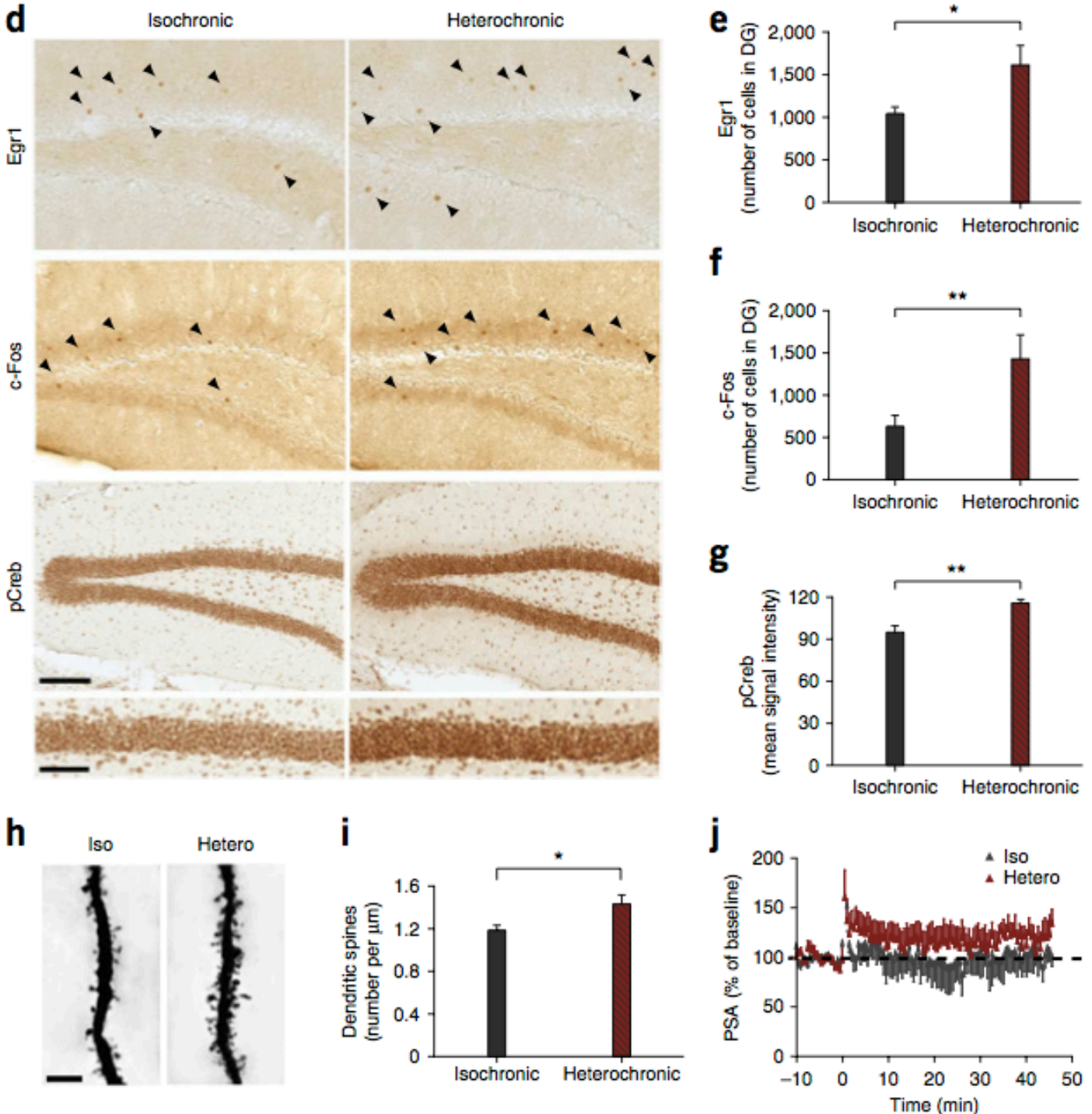

Cellules des grains
du dentate gyrus.
Pas d'augmentaion pour les
pyramidales

Young blood reverses age-related impairments in cognitive function and synaptic plasticity in mice

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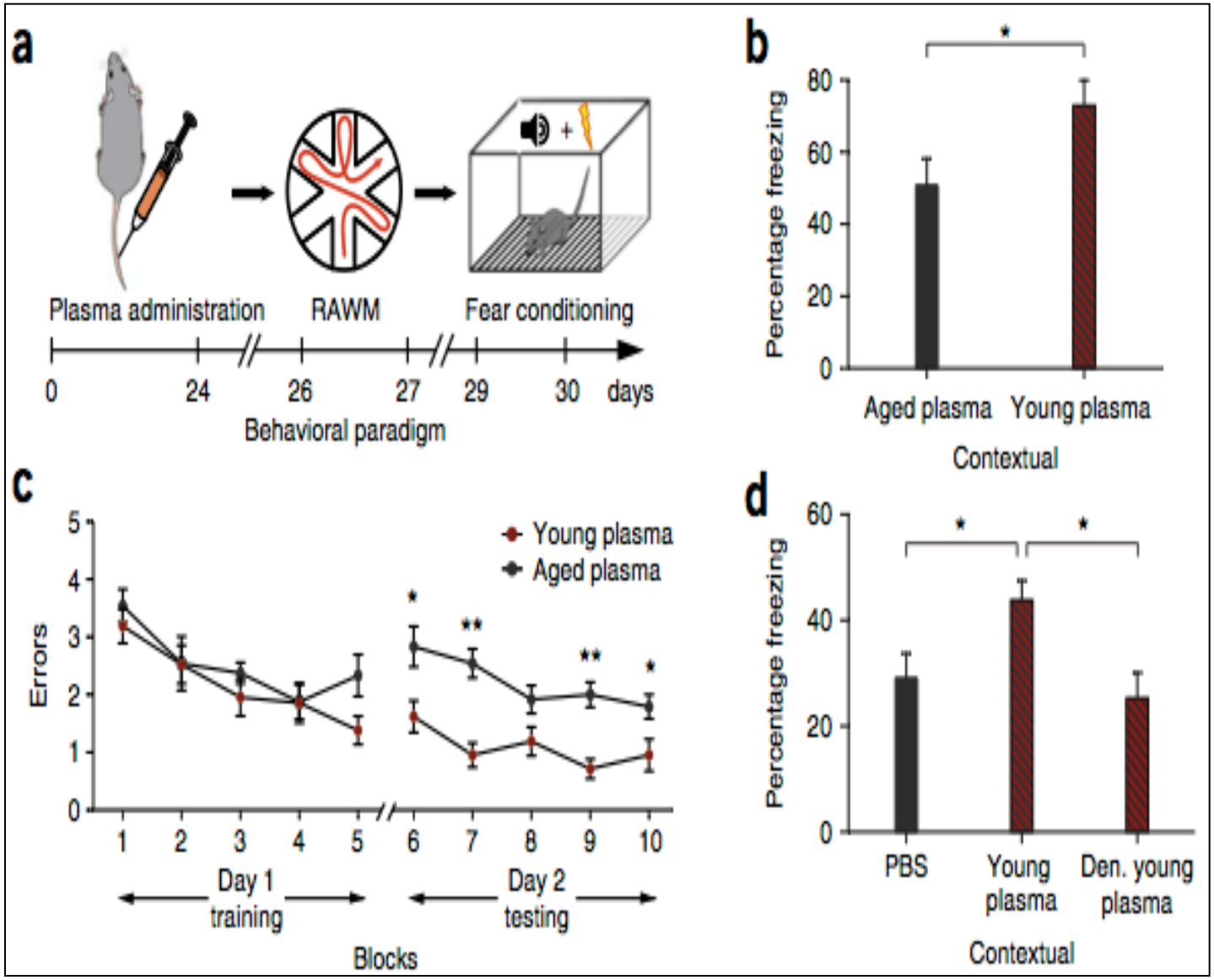

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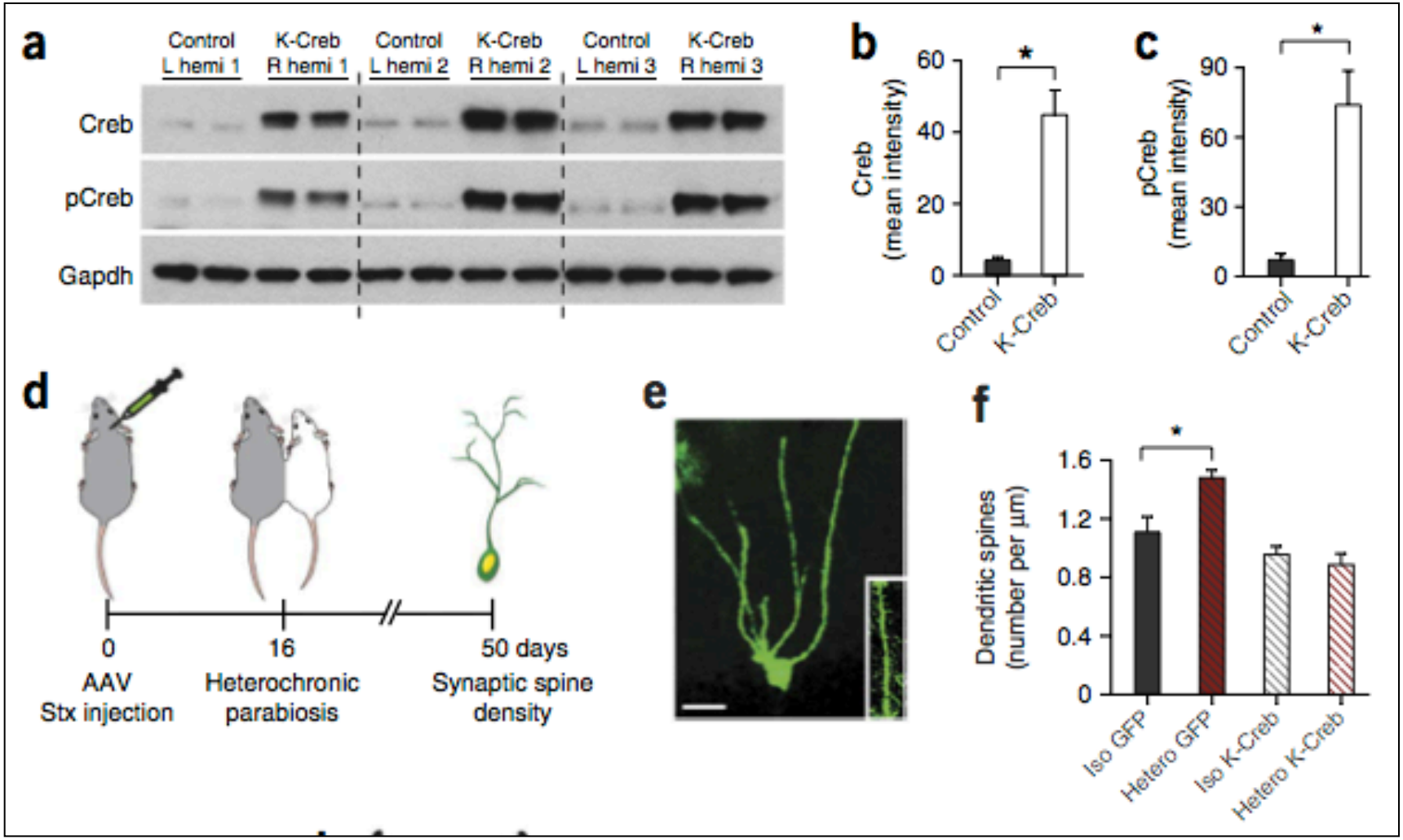

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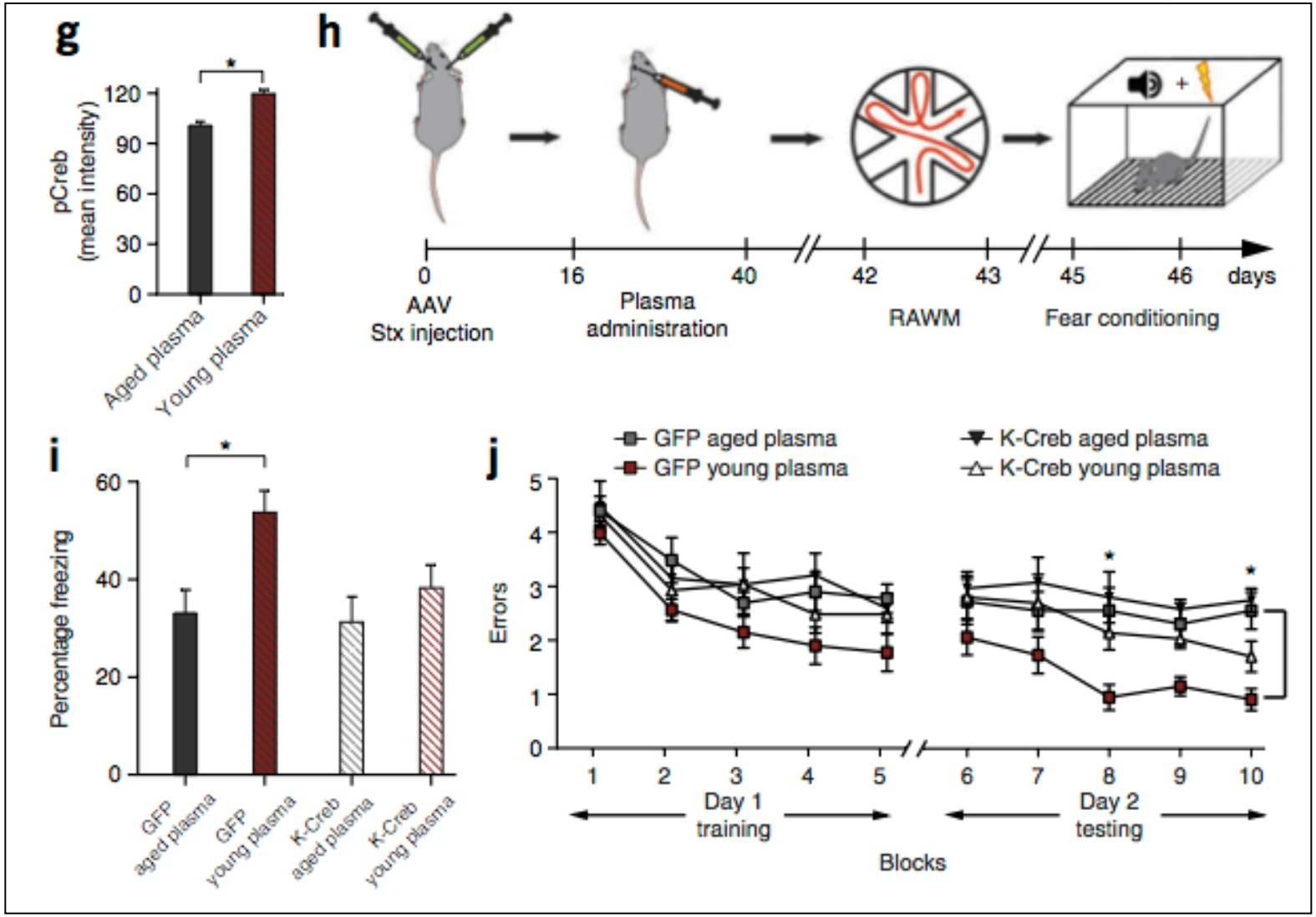


Vascular and neurogenic rejuvenation of the aging mouse brain by young systemic factors

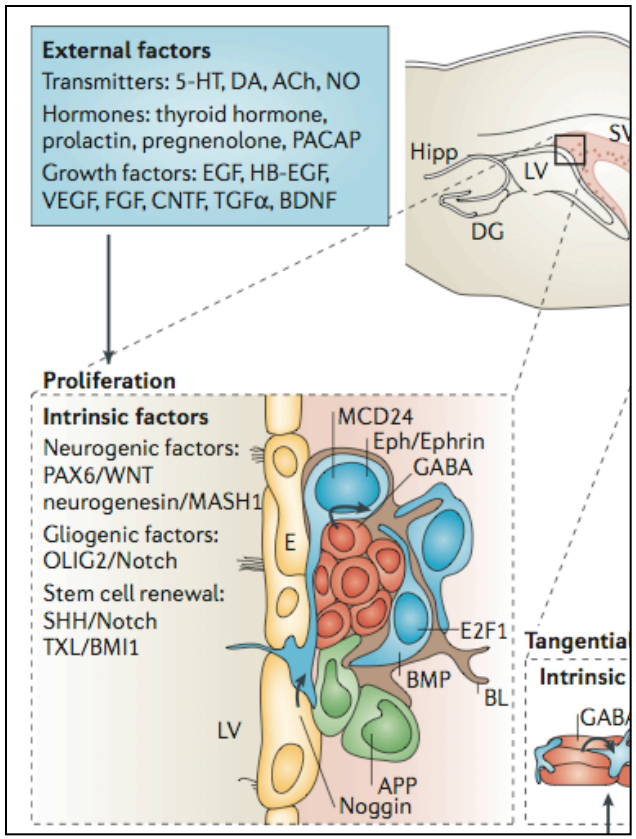
Katsimpardi L, Litterman NK, Schein PA, Miller CM, Loffredo FS, Wojtkiewicz GR, Chen JW, Lee RT, Wagers AJ, Rubin LL

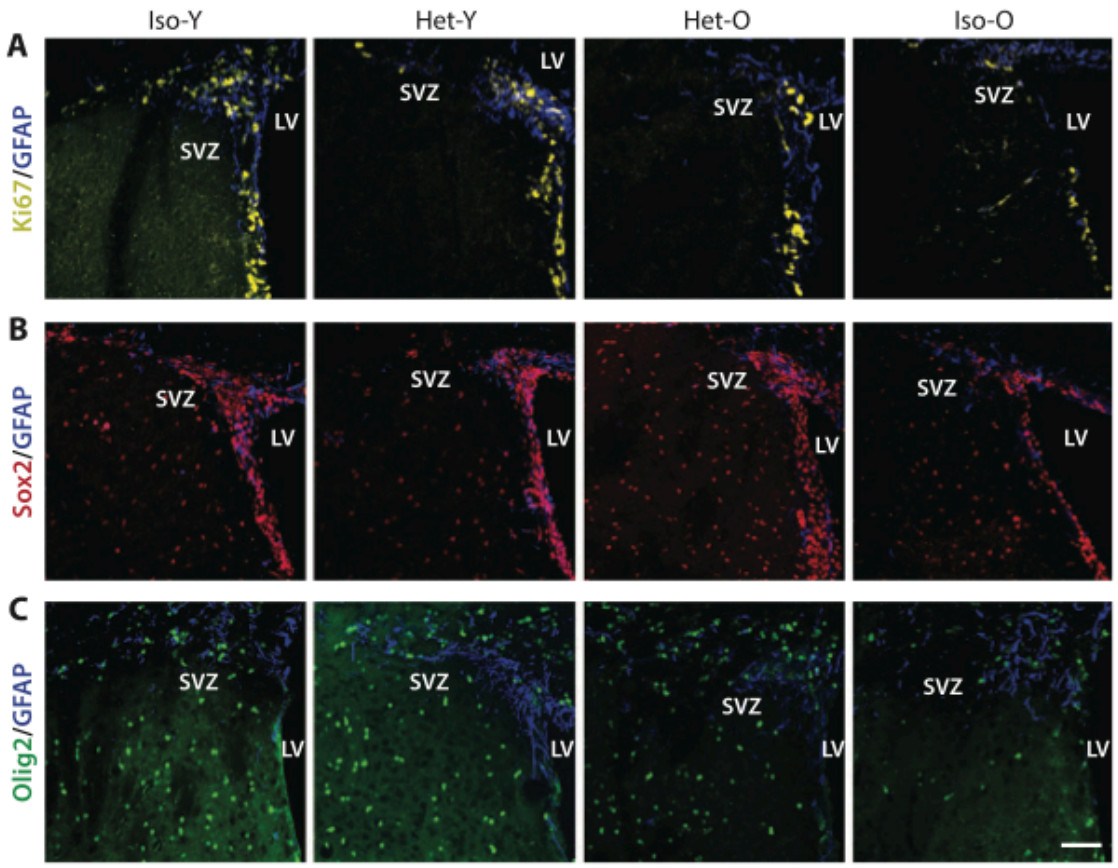
Science
2014 vol. 344 (6184) pp. 630–4

Adult neurogenesis and functional plasticity in neuronal circuits

Pierre-Marie Lledo, Mariana Alonso and Matthew S. Grubb

VOLUME 7 | MARCH 2006 | 179
NATURE REVIEWS | NEUROSCIENCE





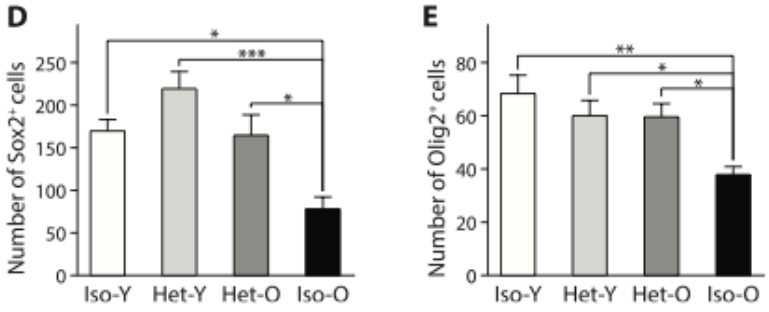


Fig. 1. Rejuvenation of progenitor cells by heterochronic parabiosis. (**A** to **C**) Confocal images showing the effects of parabiosis on (A) proliferative, (B) neural stem, and (C) progenitor cells in the SVZ of isochronic and heterochronic mice. Scale bar, 50 μm. (**D** and **E**) Quantification of (D) neural stem and (E) progenitor cell populations of the above images ($n = 9$ animals for each experimental group, $^{*}P < 0.05$, $^{**}P < 0.01$, $^{***}P < 0.001$). Data shown as mean ± SEM; statistical analysis was performed with analysis of variance (ANOVA).

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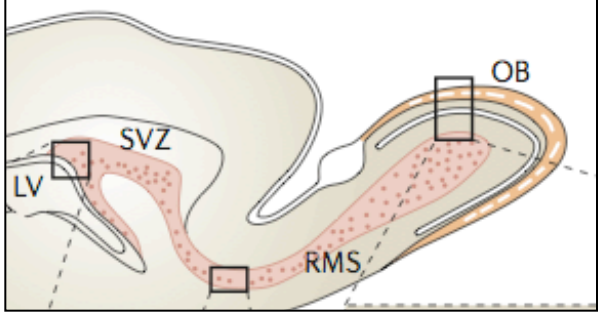

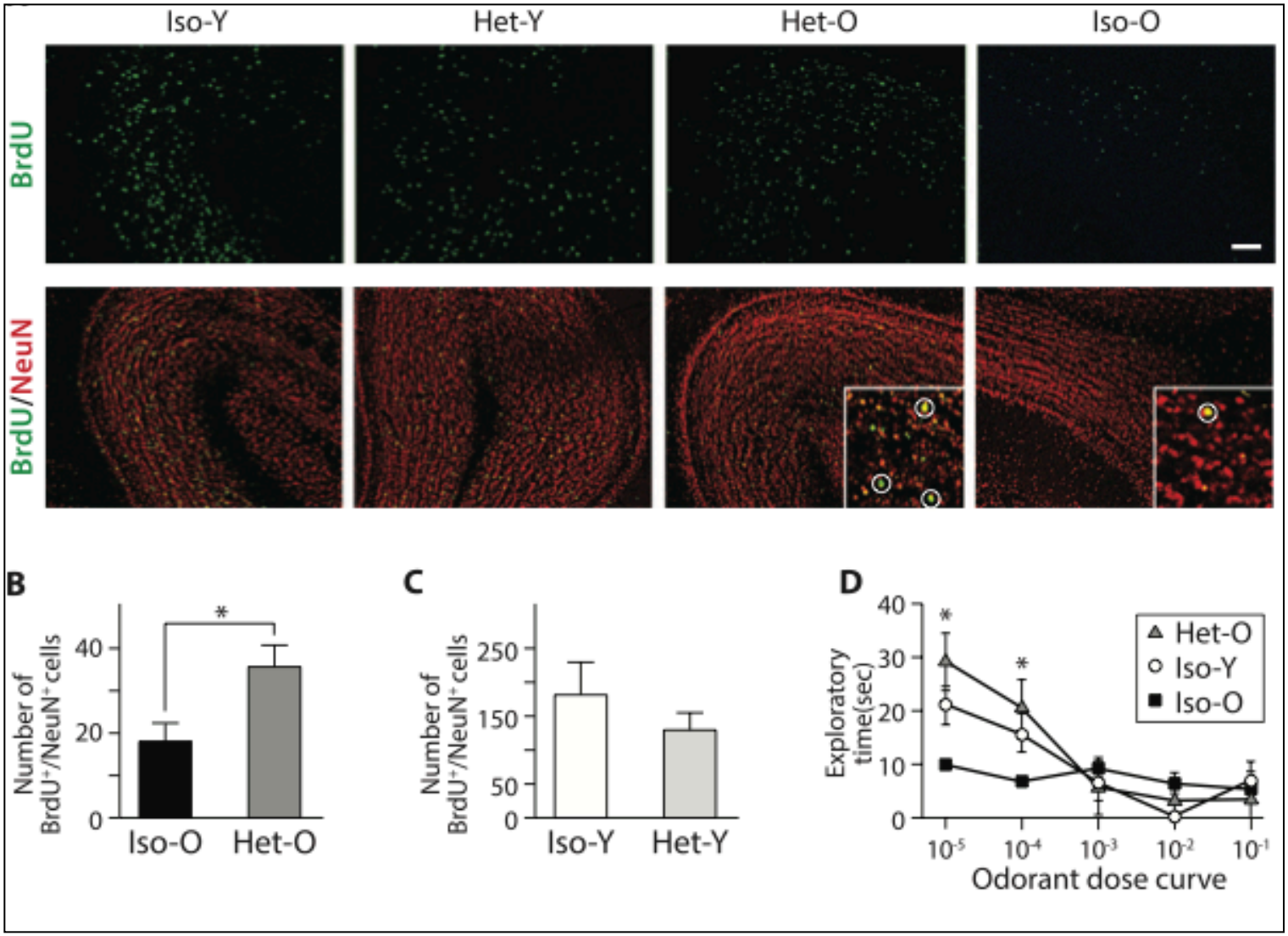

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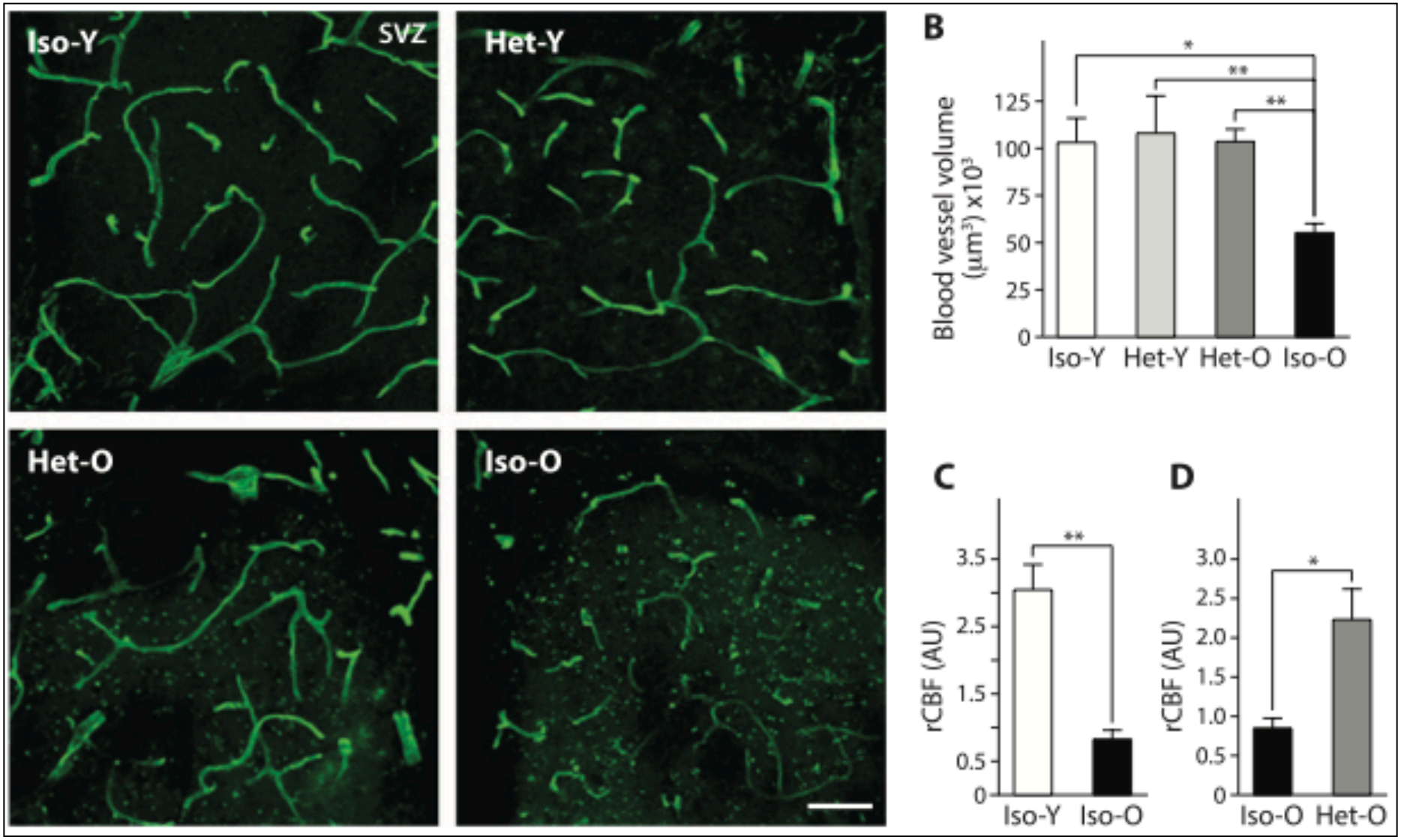

Growth differentiation factor 11 is a circulating factor that reverses age-related cardiac hypertrophy

Loffredo FS, Steinhauser ML, Jay SM, Gannon J, Pancoast JR, Yalamanchi P, Sinha M, Dall'Osso C, Khong D, Shadrach JL, Miller CM, Singer BS, Stewart A, Psychogios N, Gerszten RE, Hartigan AJ, Kim MJ, Serwold T, Wagers AJ, Lee RT

Cell
2013 vol. 153 (4) pp. 828-39

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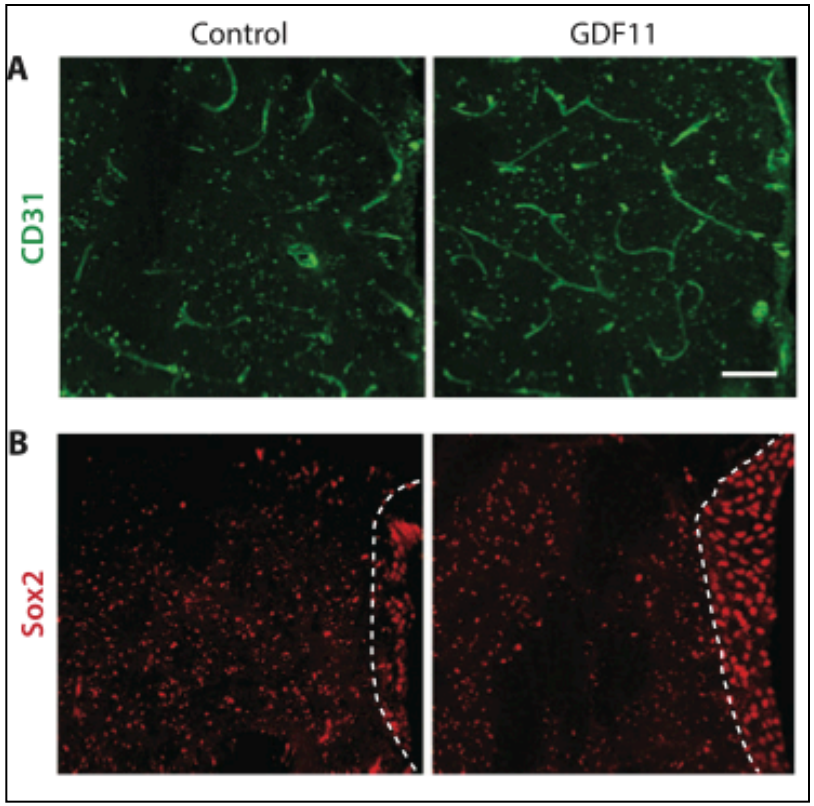
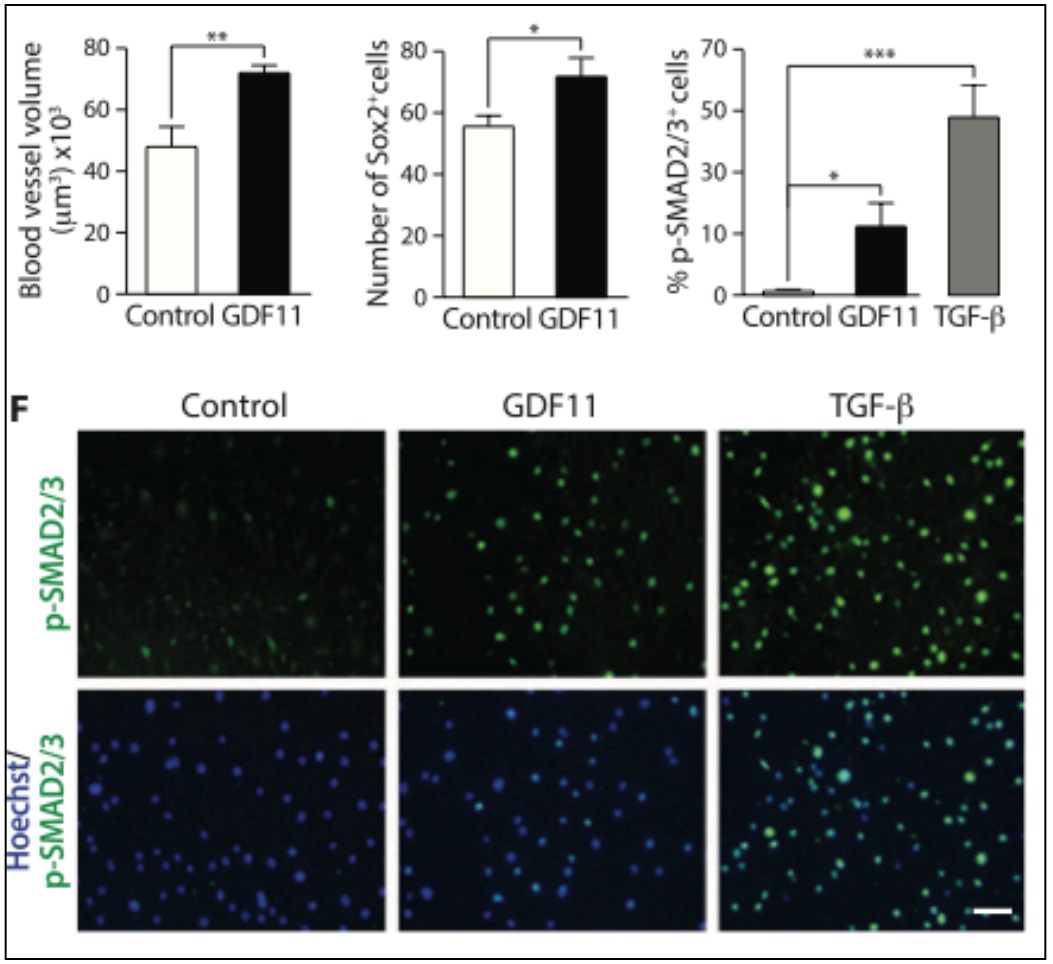




Rejuvenation: It's in Our Blood

Cell Metabolism *20*, July 1, 2014

Alessandro Bitto[1] **and Matt Kaeberlein**[1,*]
[1]Department of Pathology, University of Washington, Seattle, WA 98195-7470, USA
*Correspondence: kaeber@uw.edu
http://dx.doi.org/10.1016/j.cmet.2014.06.007

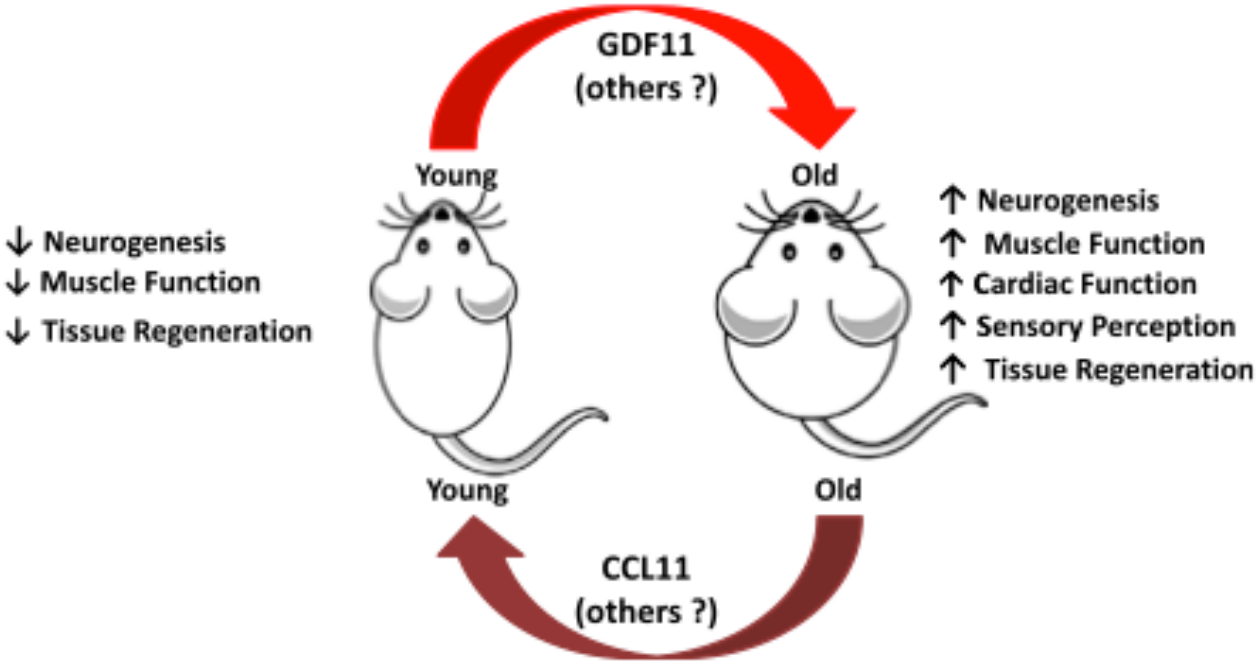
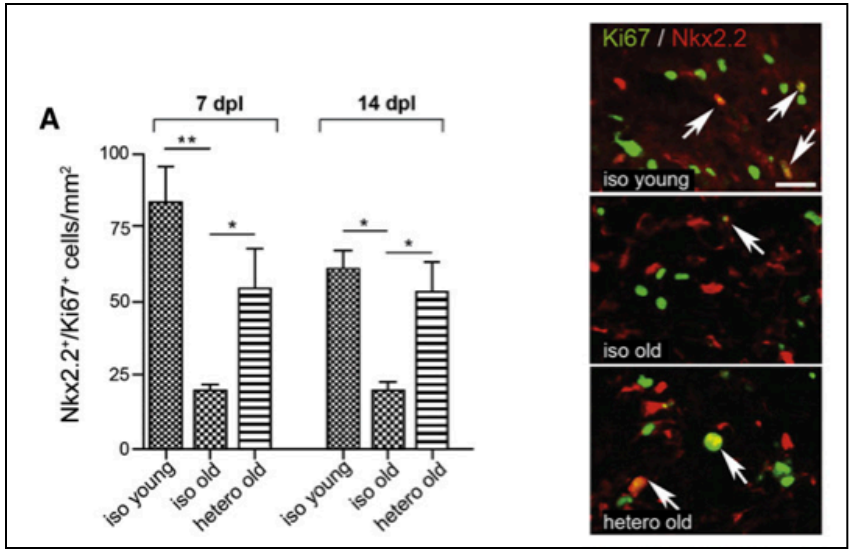


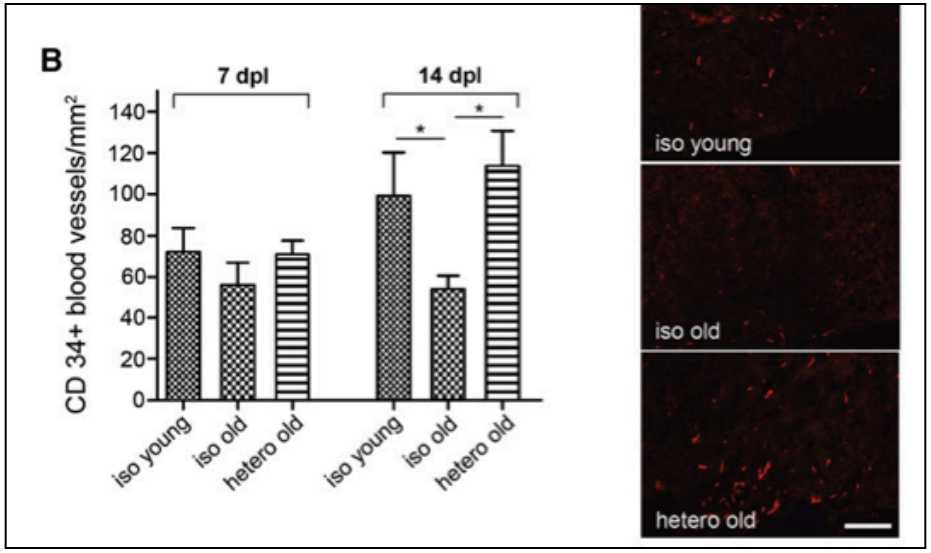
Figure 1. Opposing Effects of Heterochronic Parabiosis in Mice
Heterochronic parabiosis, in which a young mouse and an aged mouse share circulatory systems, improves the health of the aged mouse while having negative health consequences for the young mouse. GDF11 and CCL11 have recently been identified as two of the factors mediating these effects.

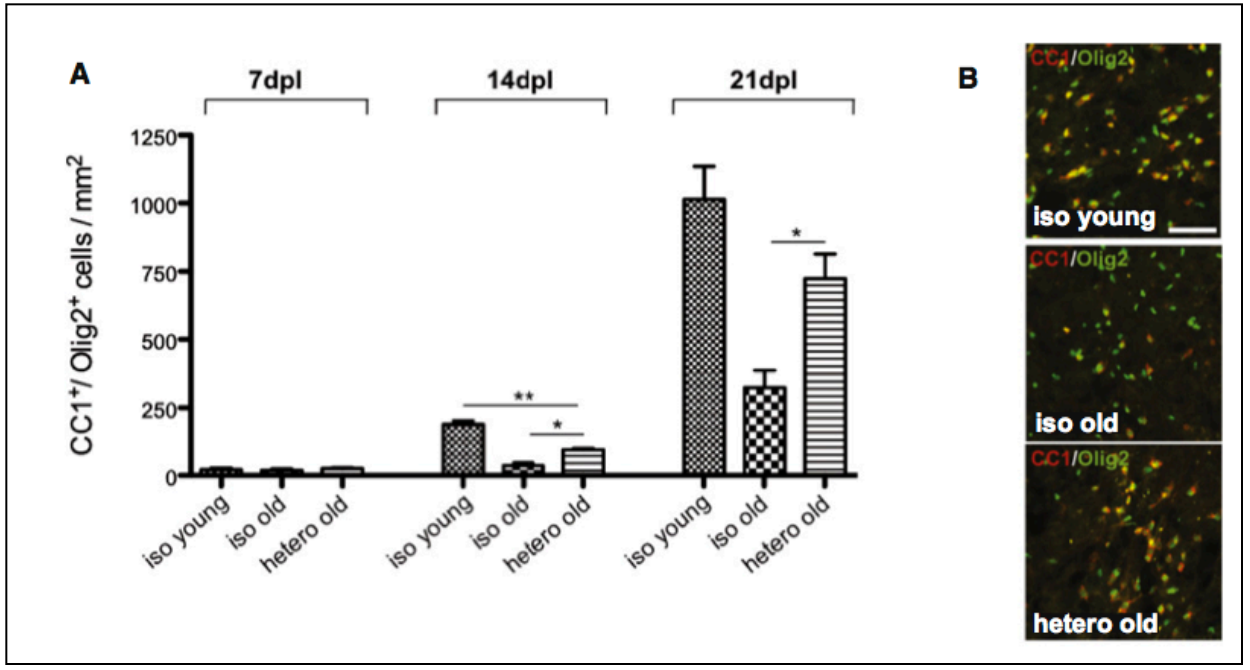
Rejuvenation of regeneration in the aging central nervous system

Cell Stem Cell
2012 vol. 10 (1) pp. 96-103

Ruckh JM, Zhao J, Shadrach JL, van Wijngaarden P, Rao TN, Wagers AJ, Franklin RJ







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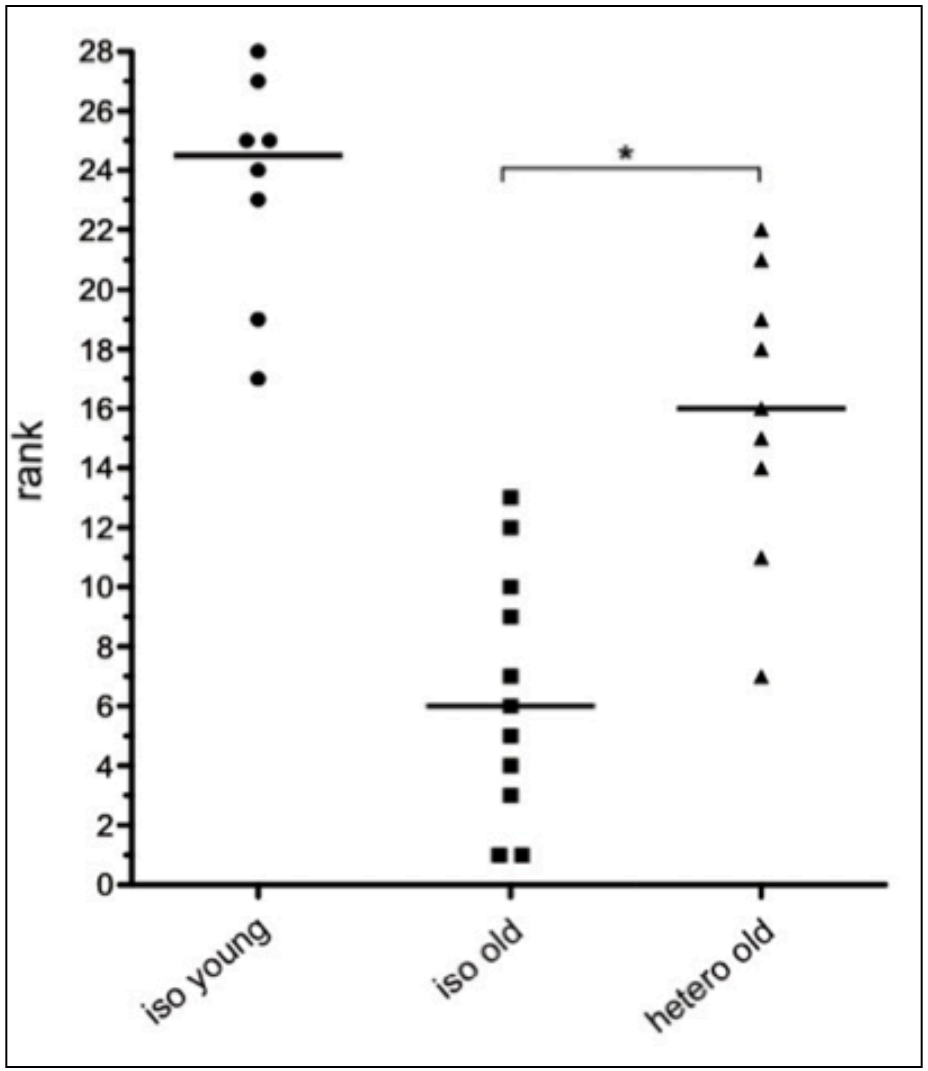

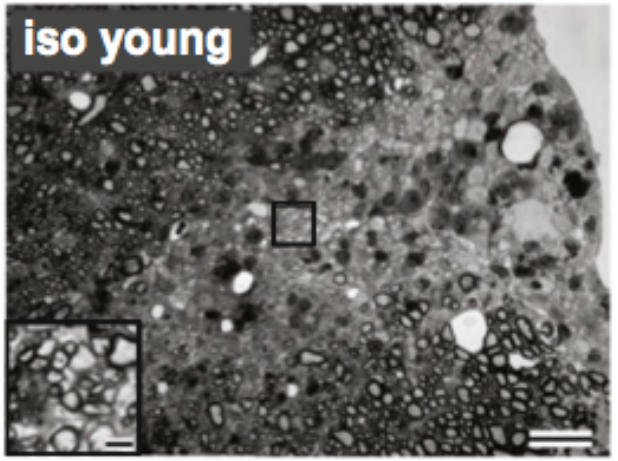

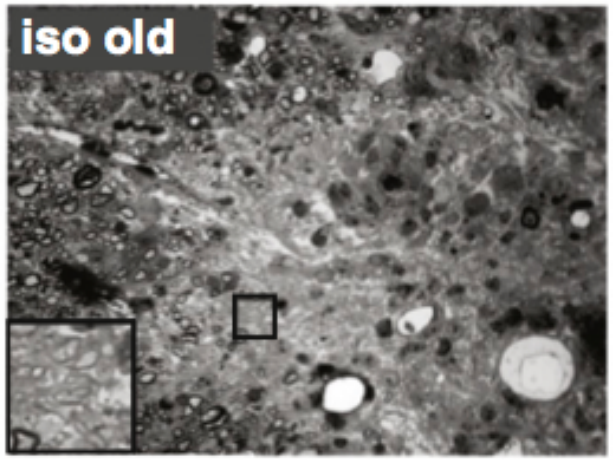

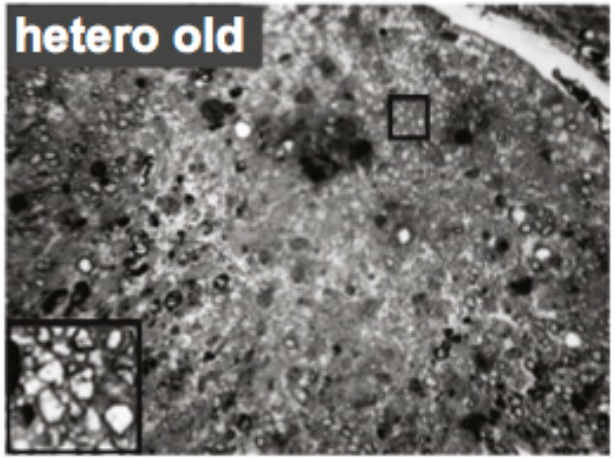

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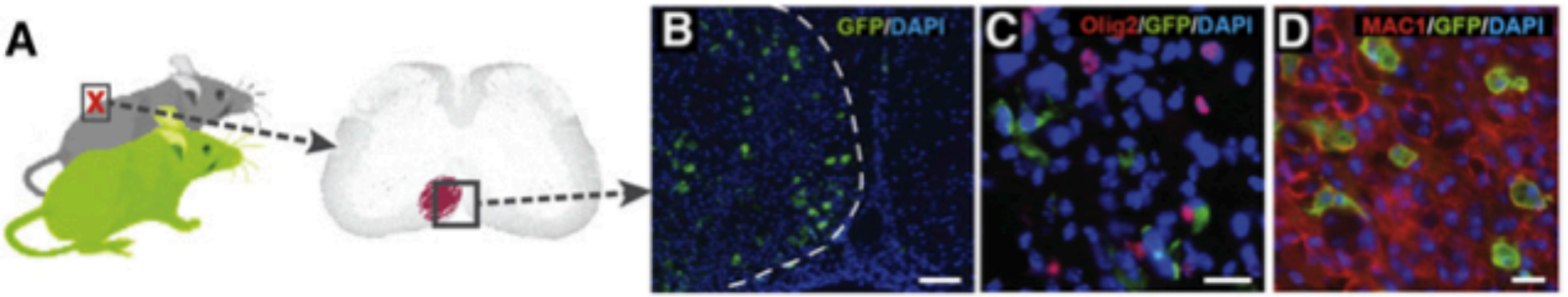

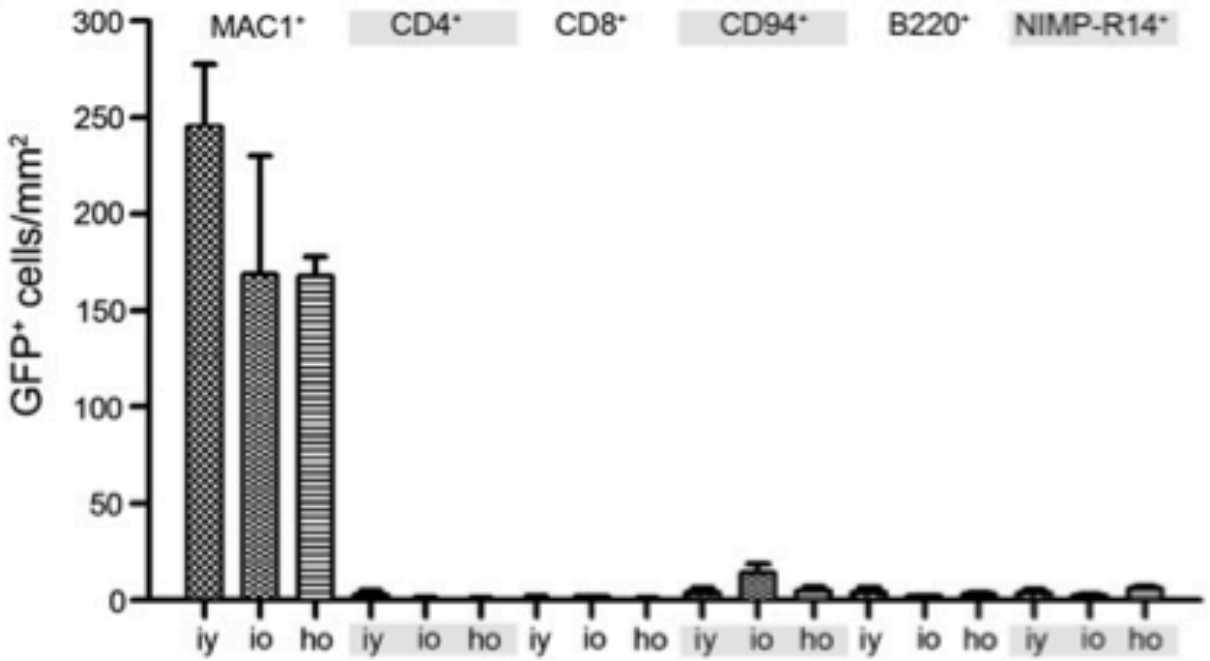

(A) Parabiotic pairings in which cells of the young partner were transgenically labeled by GFP expression were established. In the old partner lesion from each GFP^{young}/WT^{old} pairing, GFP^+ cells were confined to the lesion (B). (C) No GFP^+ cells in old partner lesions were found to colocalize with $Olig2^+$ nuclei. (D) Almost all GFP^+ cells colocalized with the macrophage marker MAC1. (E) Characterization of the GFP^+ inflammatory infiltrate at 5 dpl in isochronic-young (iy) (n = 3), isochronic-old (io) (n = 2), and heterochronic-old (ho) animals (n = 4). No statistically significant differences were found among the parabiotic groups. The overwhelming majority of GFP^+ cells were $MAC1^+$ macrophages. Very few $CD4^+$ T cells, $CD8^+$ T cells, $CD94^+$ natural killer cells, $B220^+$ B cells, and $NIMP\text{-}R14^+$ neutrophils were present in the lesions. Data are means ± SEM. Scale bars: (B), 100 μm; (C) and (D), 20 μm.

Rejuvenation of regeneration in the aging central nervous system

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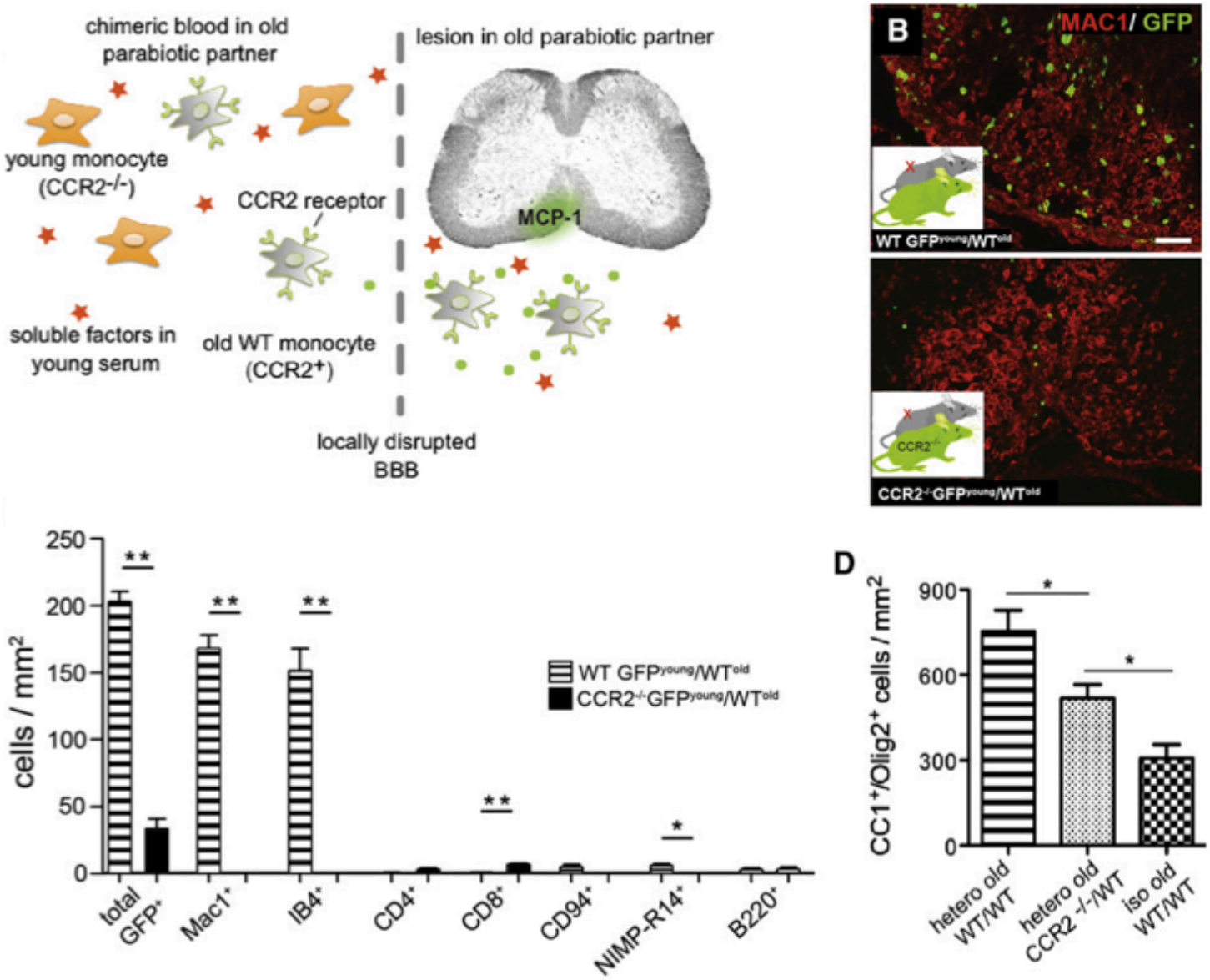

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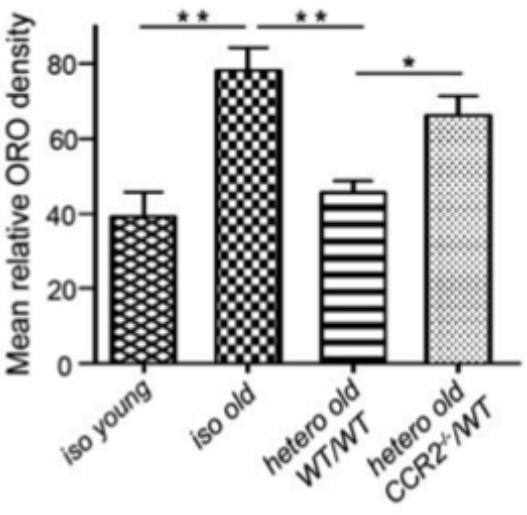
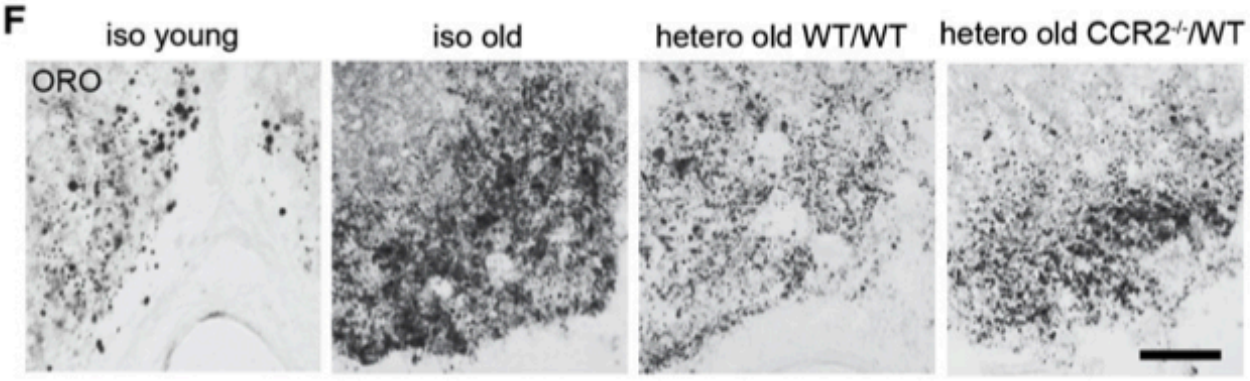
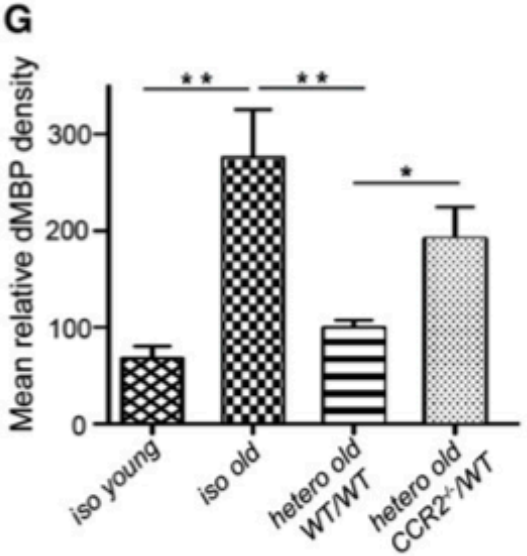
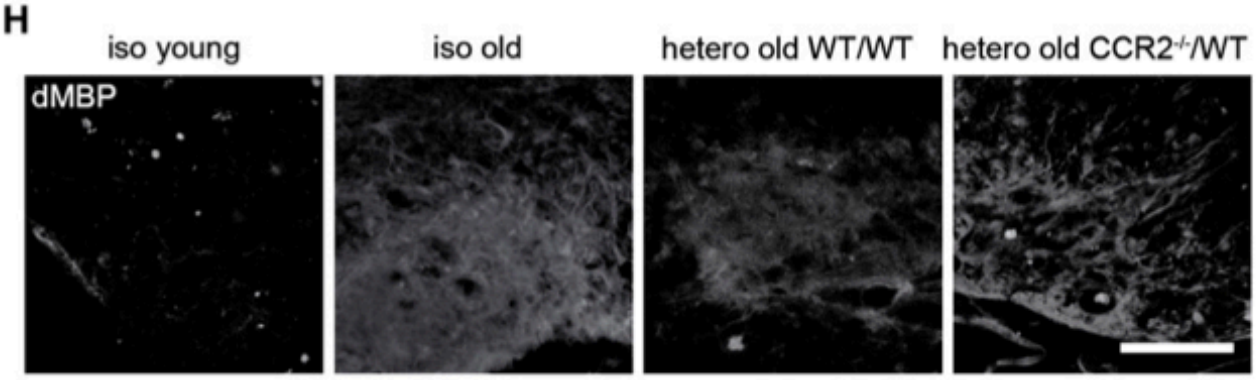




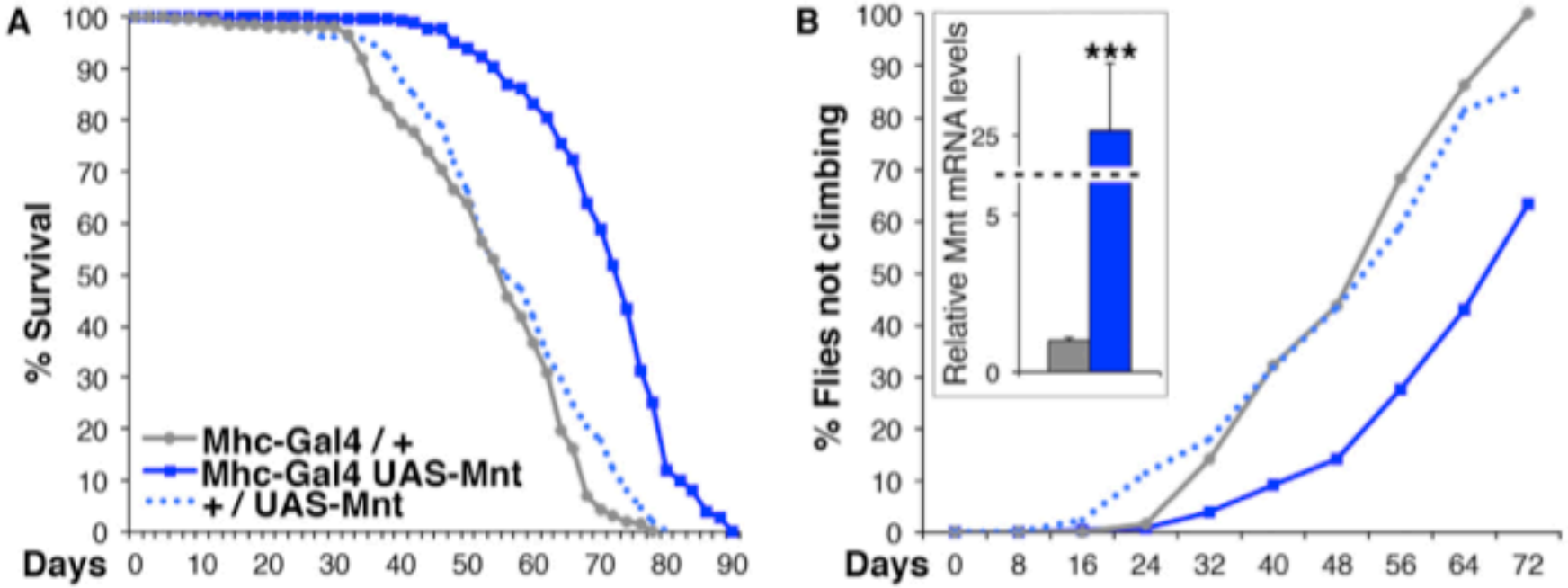




Intertissue control of the nucleolus via a myokine-dependent longevity pathway

Cell Rep
2014 vol. 7 (5) pp. 1481-94

Demontis F, Patel VK, Swindell WR, Perrimon N



C *Microarray analysis (muscle)*

GO categories with decreased expression in response to Mnt transcriptional activity

GOCCID	P value	Odds Ratio	Exp Count	Count	Size	Term
GO:0005730	1.8522E-05	7.09157562	1.54652595	9	56	nucleolus
GO:0000313	0.00014265	5.27509653	1.9883905	9	72	organellar ribosome
GO:0005762	0.00134684	5.59246052	1.24274406	6	45	mitochondrial large ribosomal subunit
GO:0015934	0.00449461	3.35786469	2.6235708	8	95	large ribosomal subunit
GO:0005763	0.0446765	4.12237762	0.80087951	3	29	mitochondrial small ribosomal subunit

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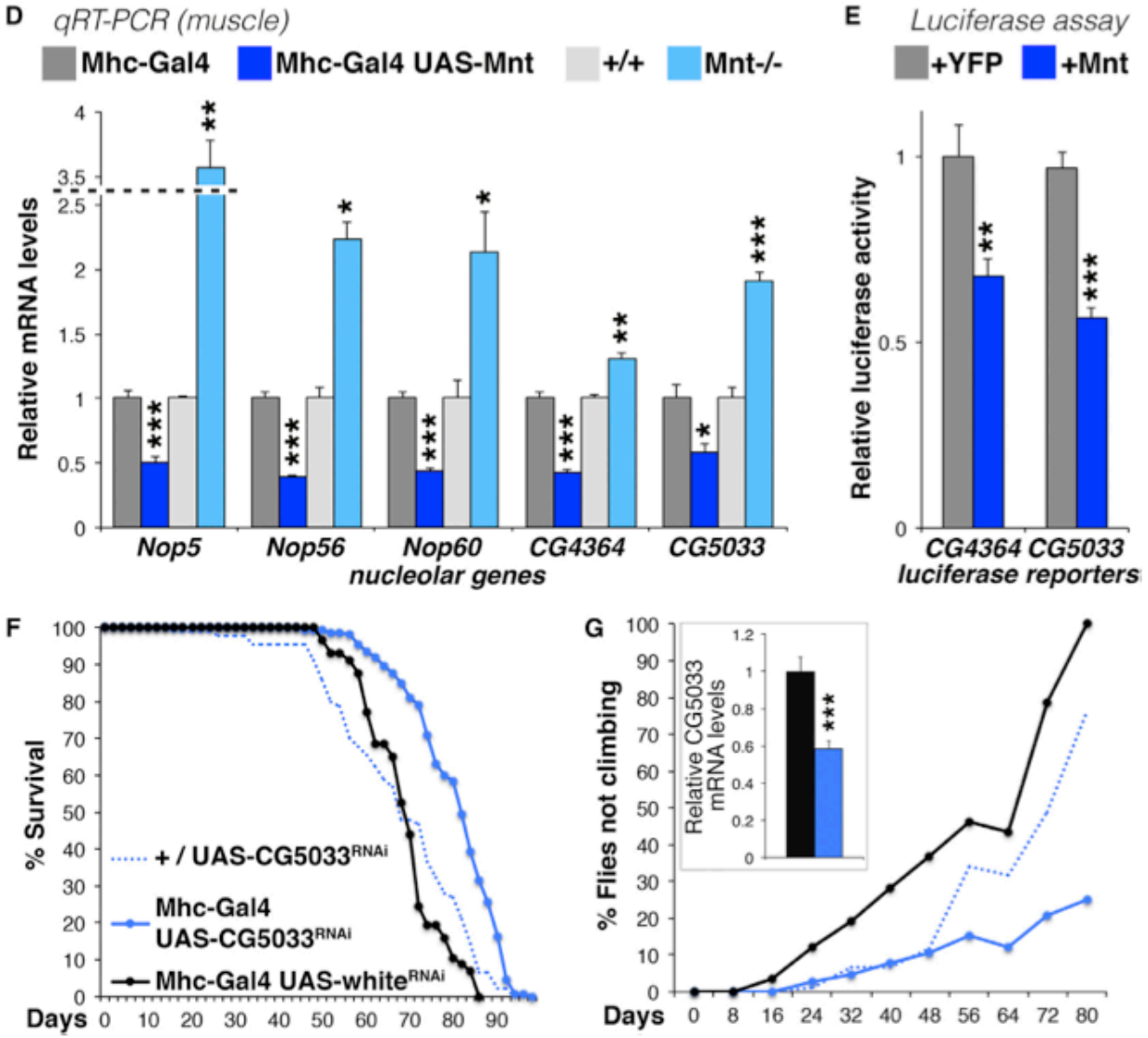

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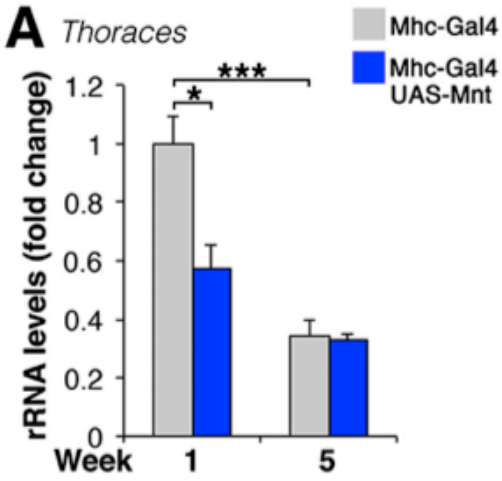

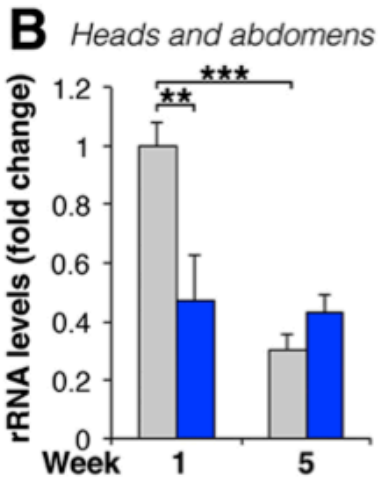

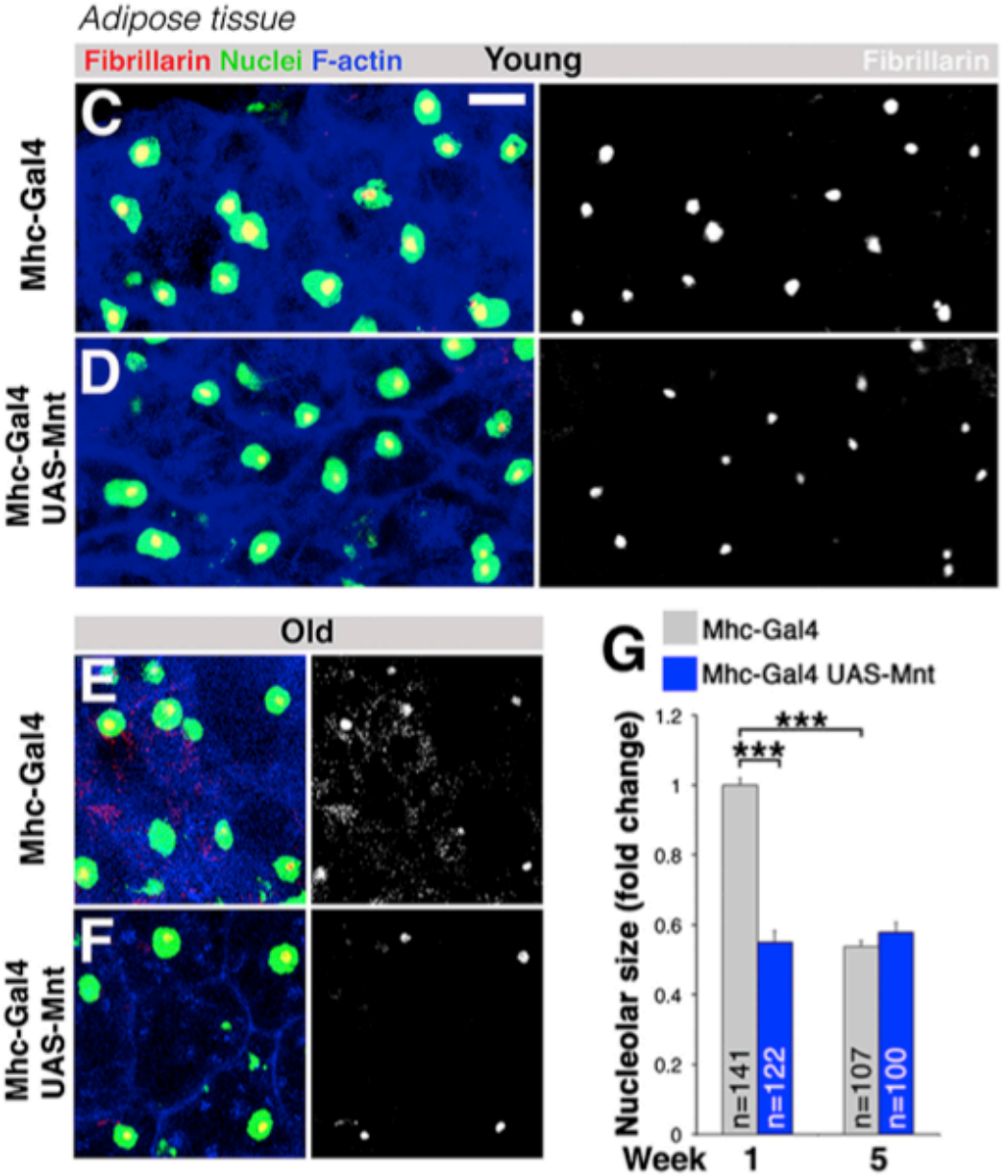

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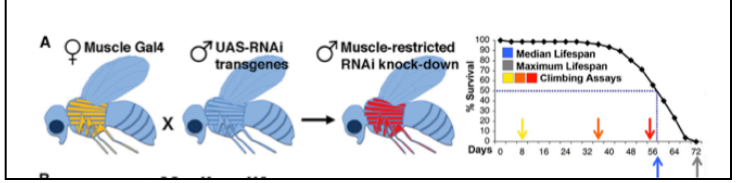

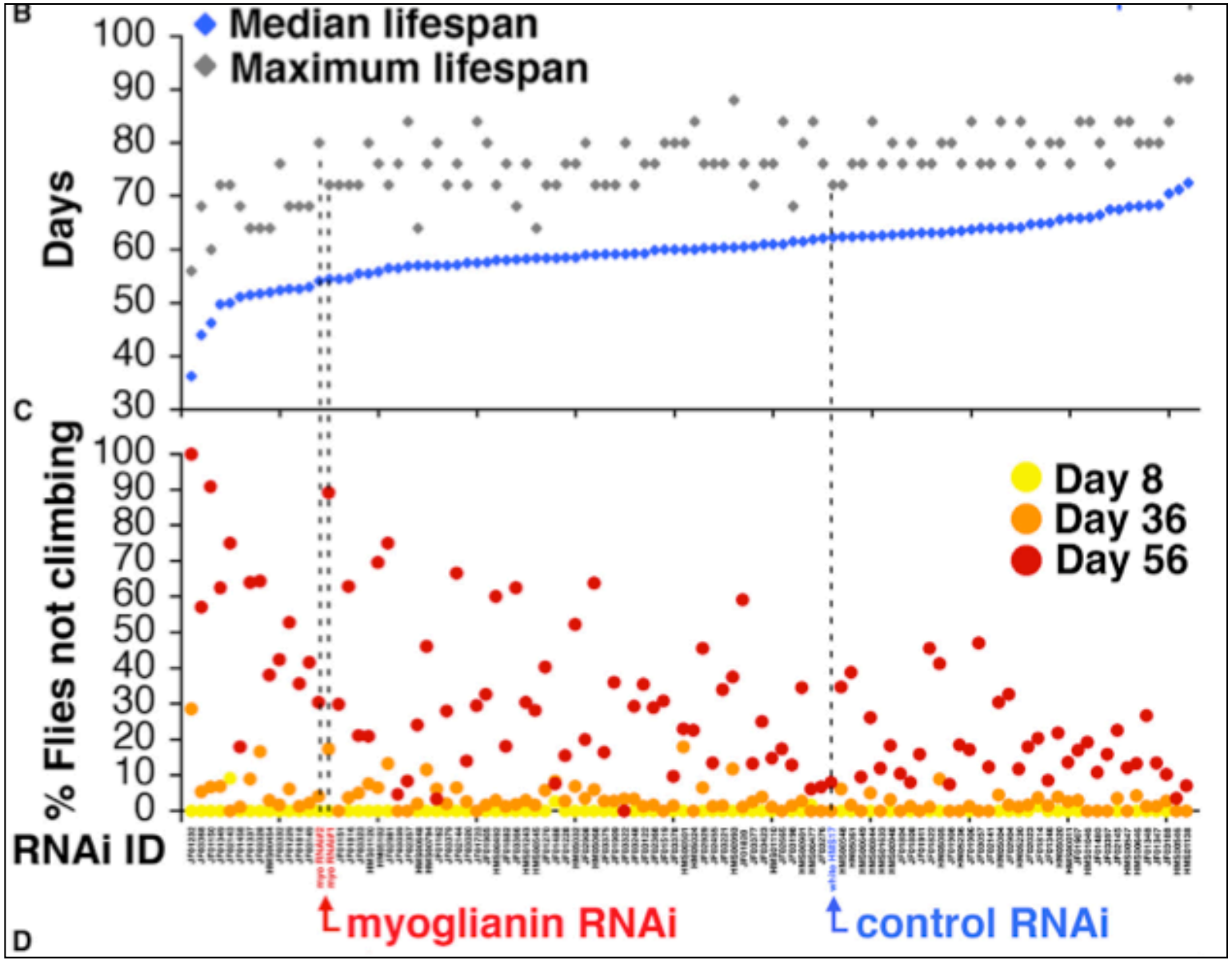

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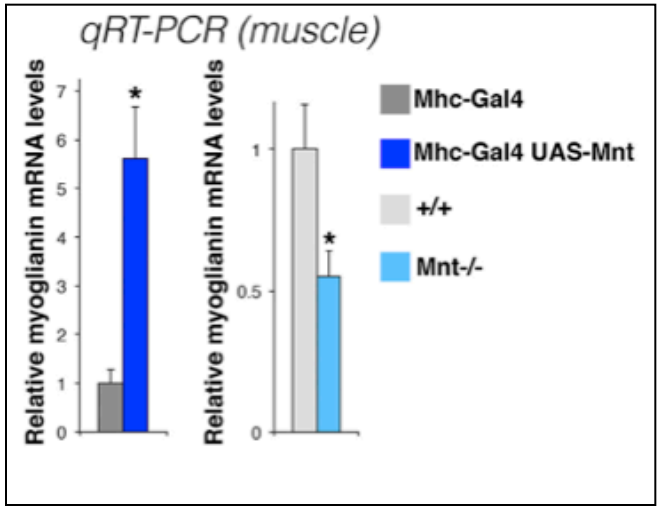

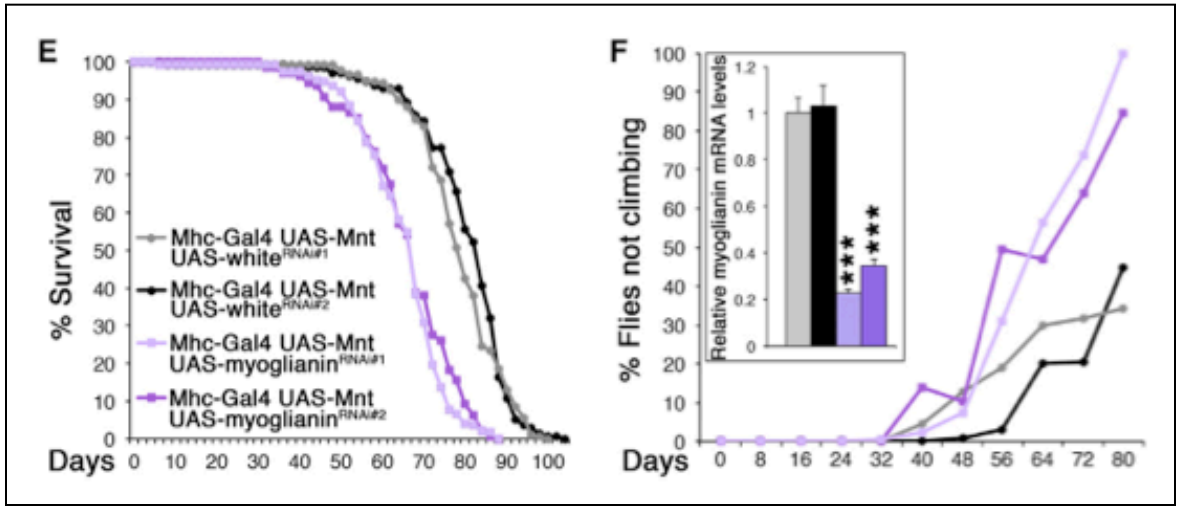

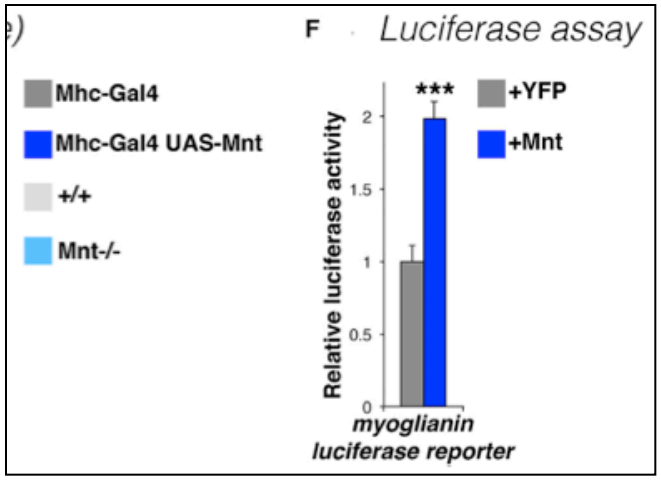

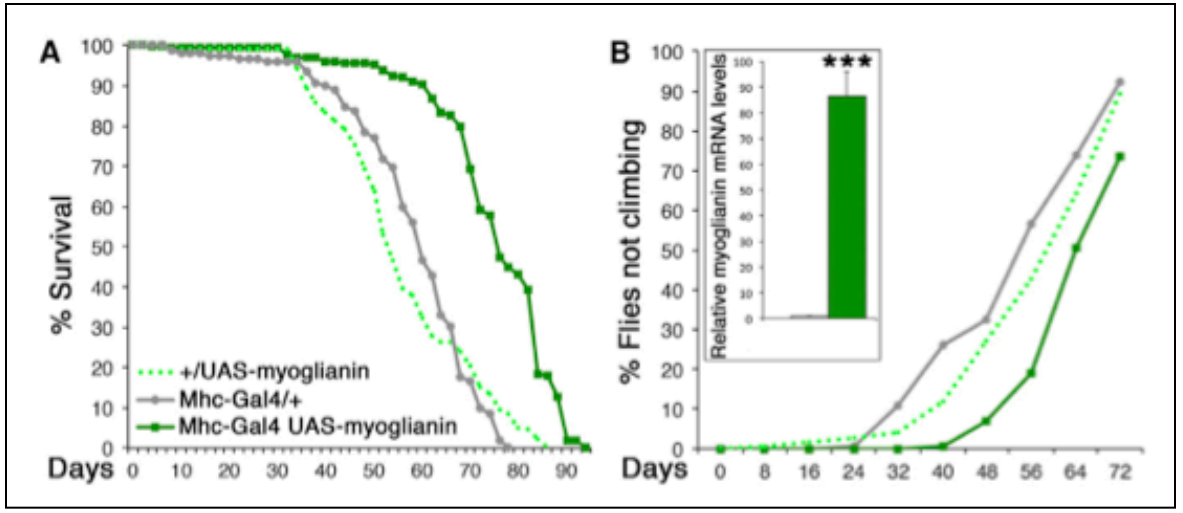

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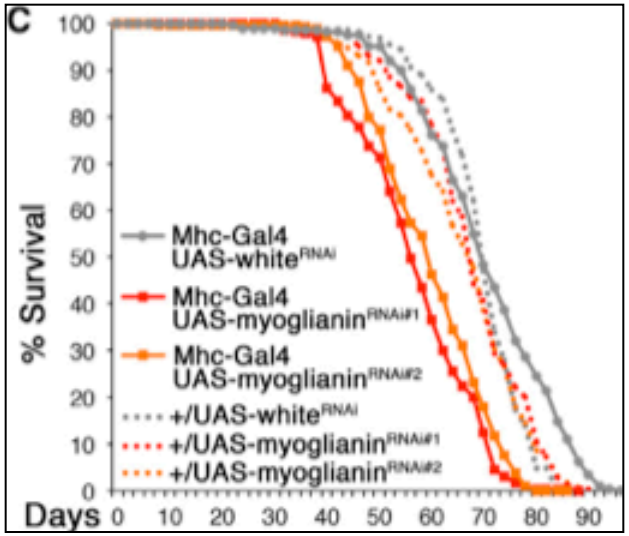

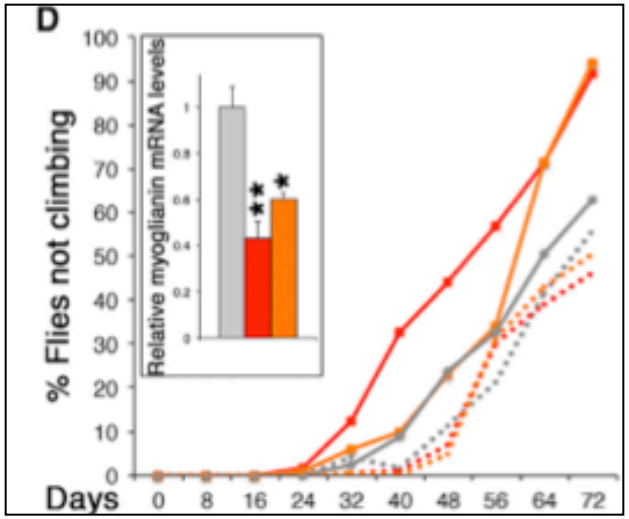

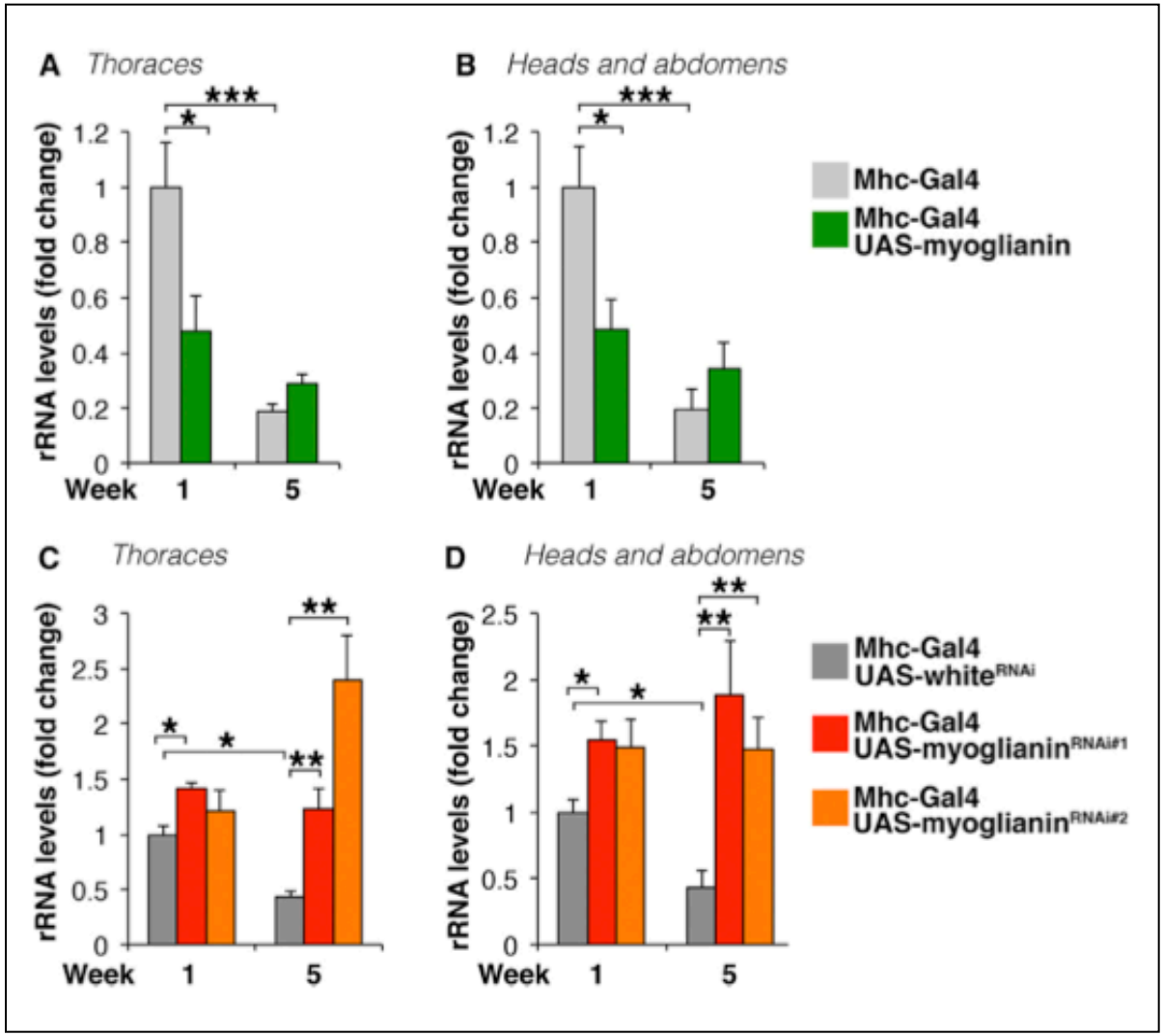

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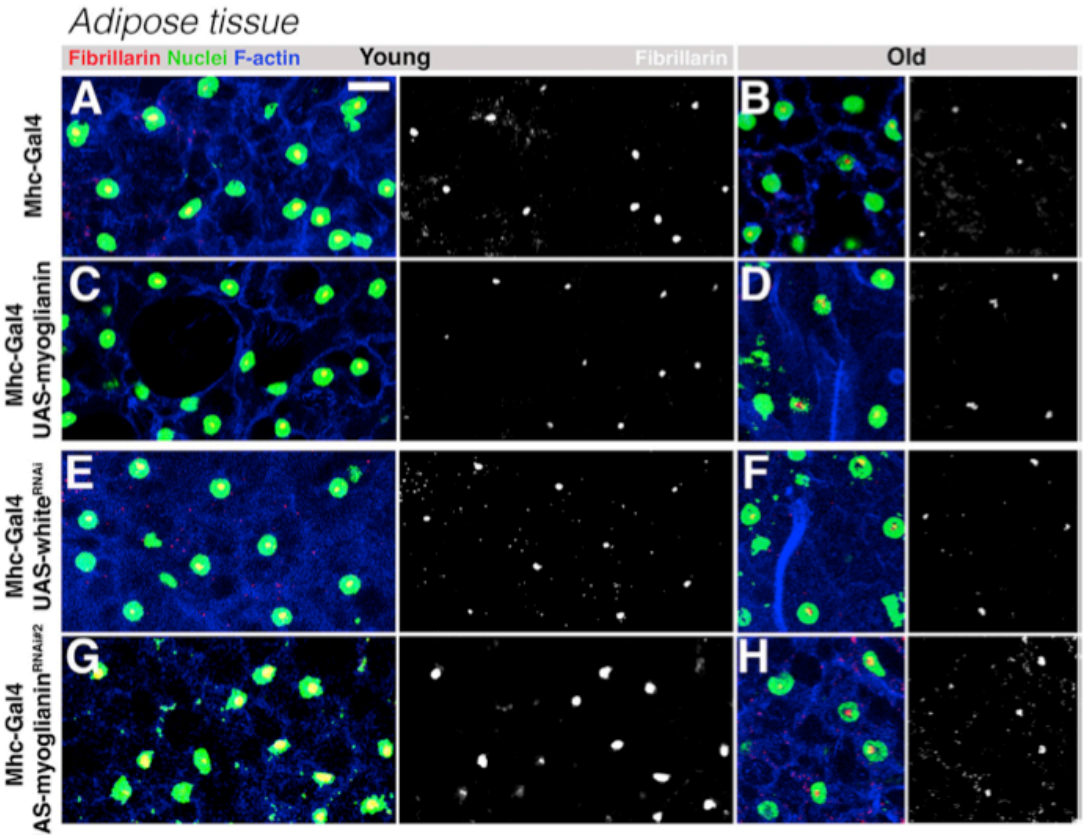
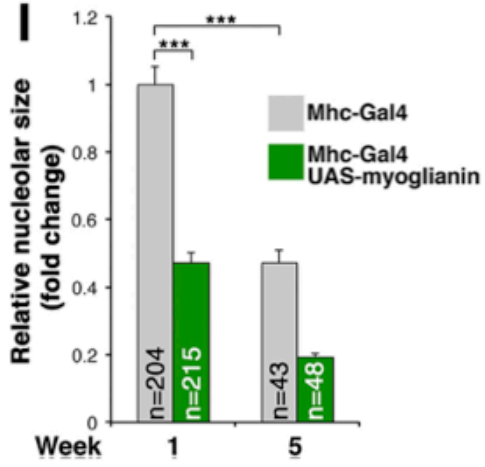
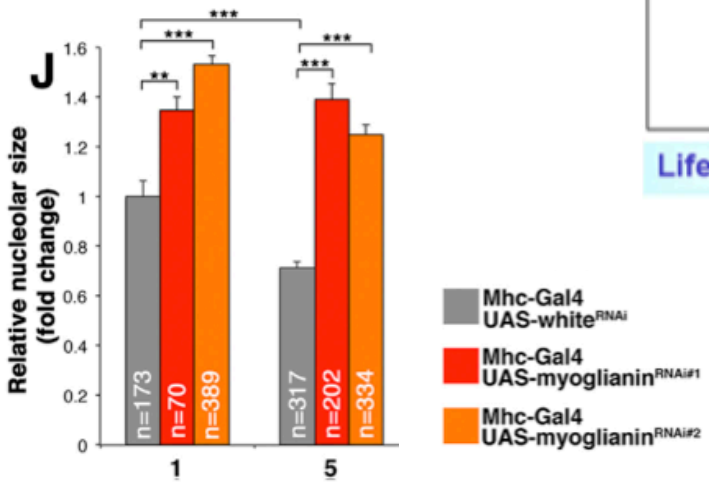
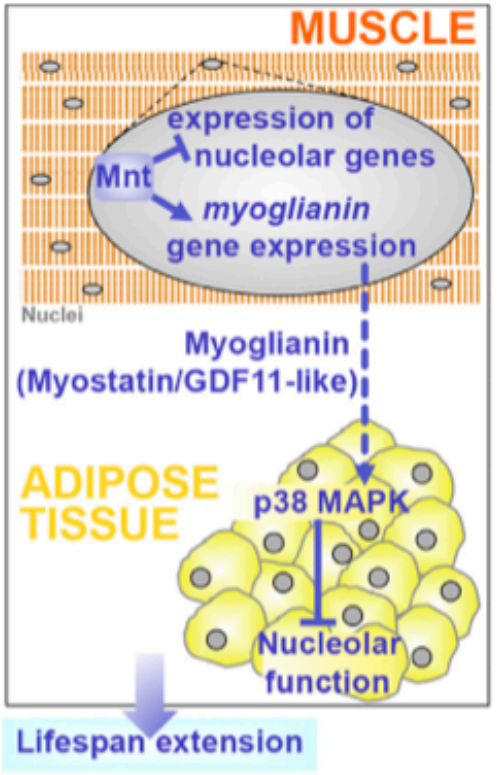
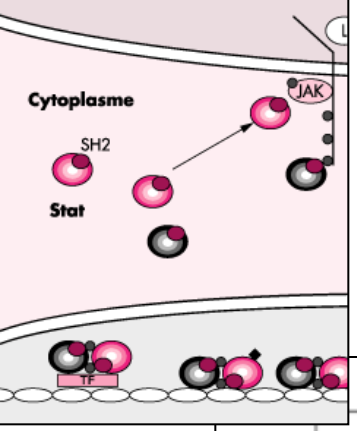






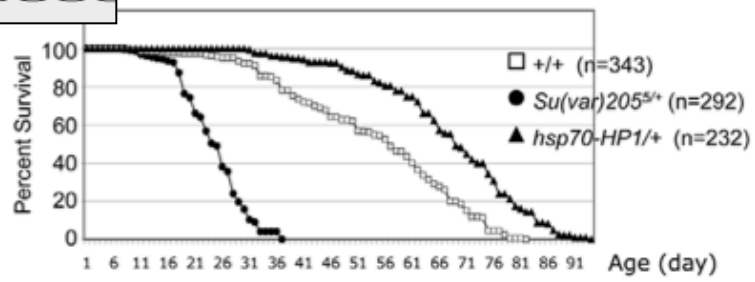




Heterochromatin formation promotes longevity and represses ribosomal RNA synthesis

PLoS Genet
2012 vol. 8 (1) pp. e1002473

Larson K, Yan S, Tsurumi A, Liu J, Zhou J, Gaur K, Guo D, Eickbush T, Li W



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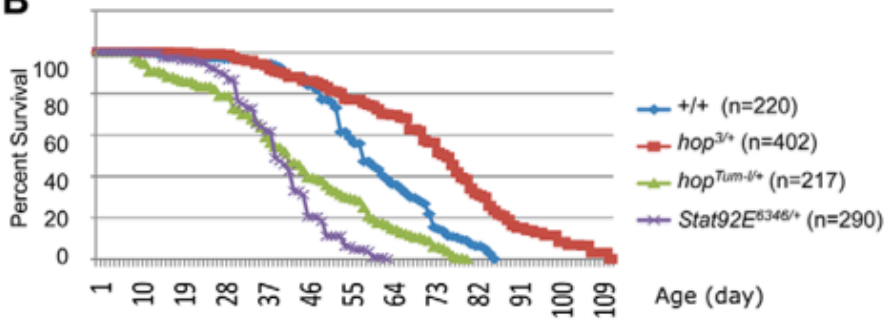

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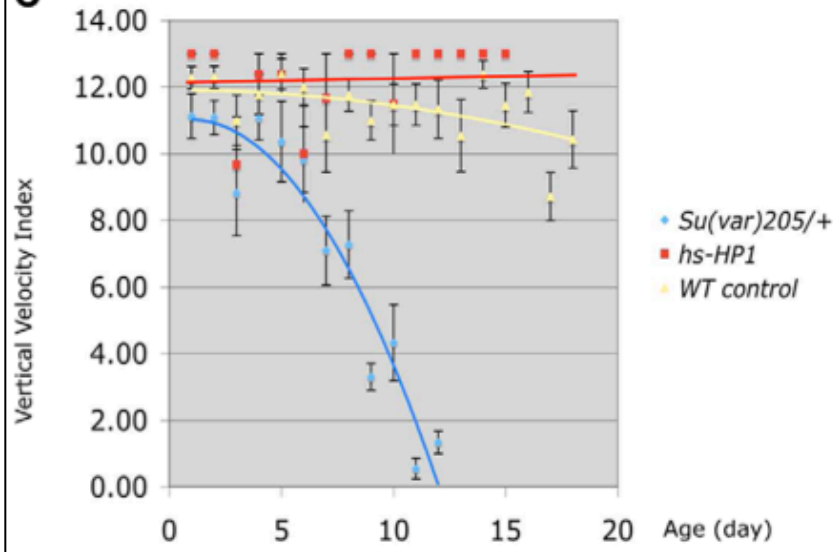

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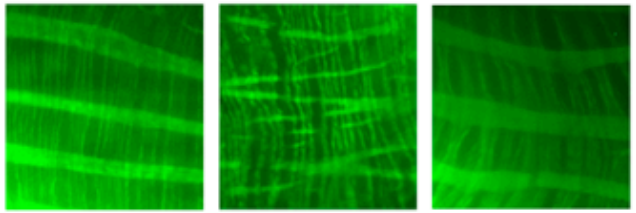

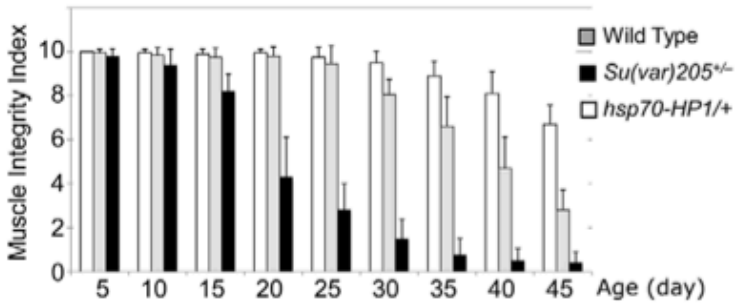

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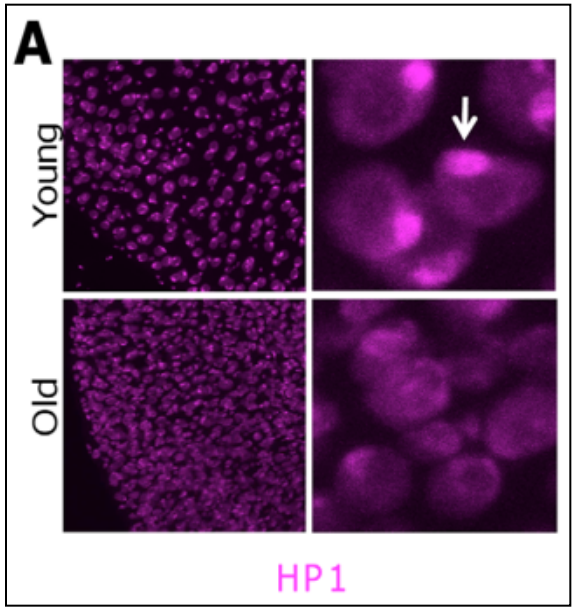

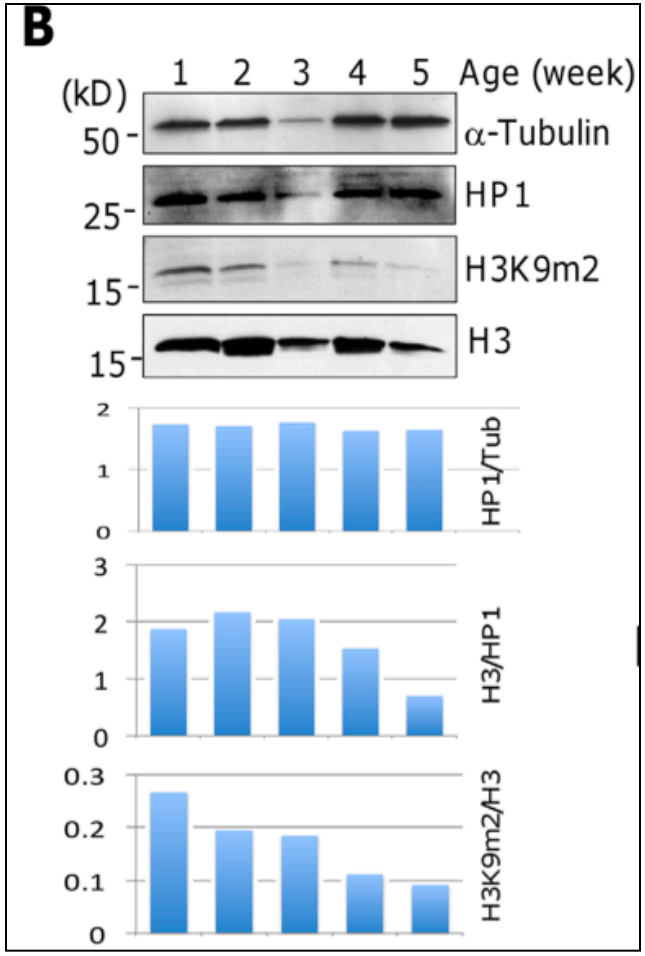

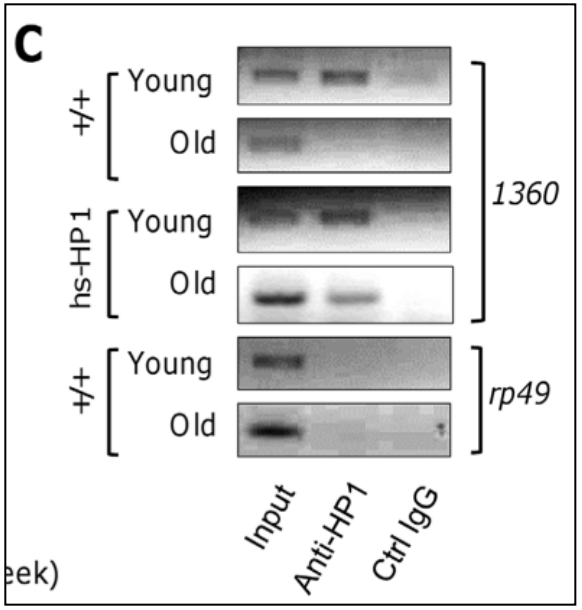

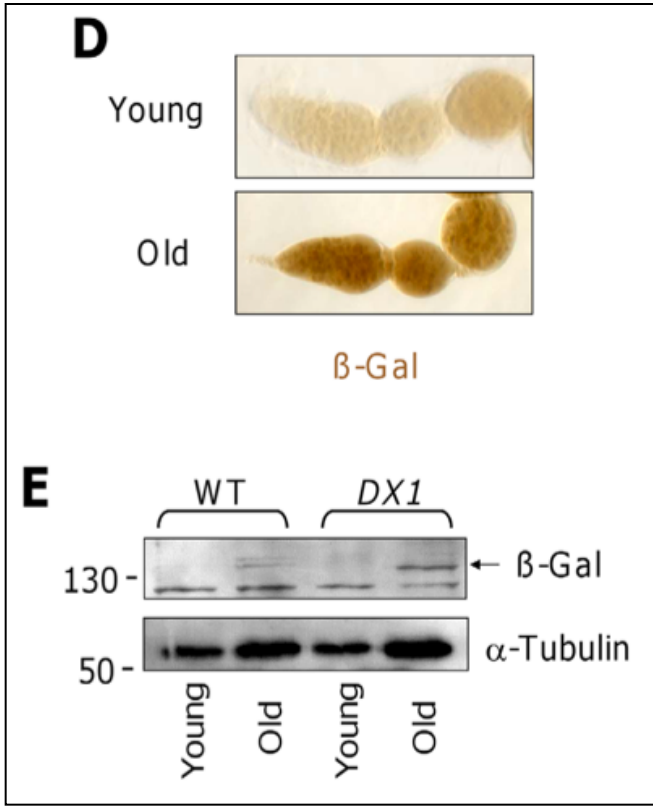

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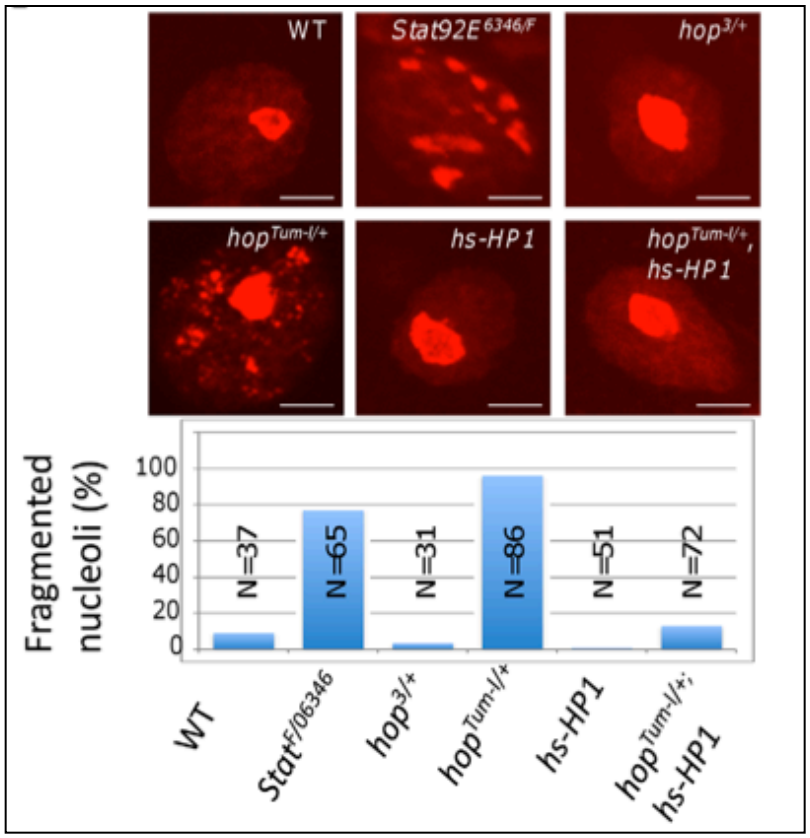

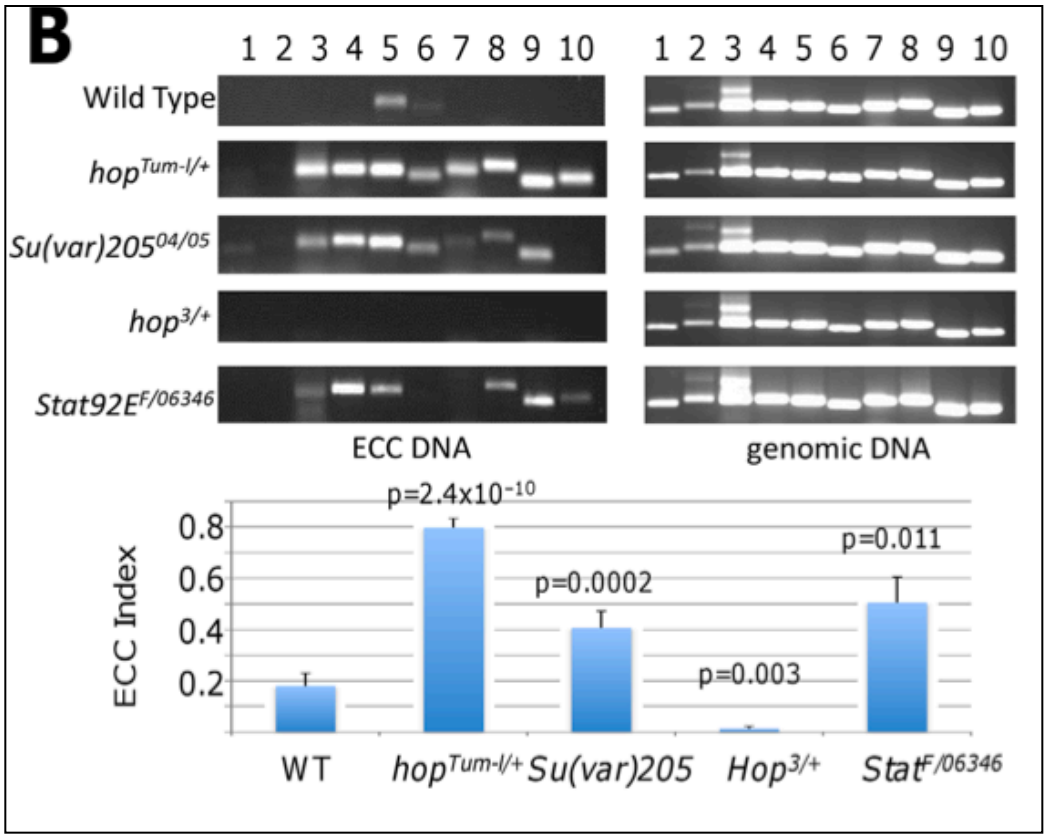

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