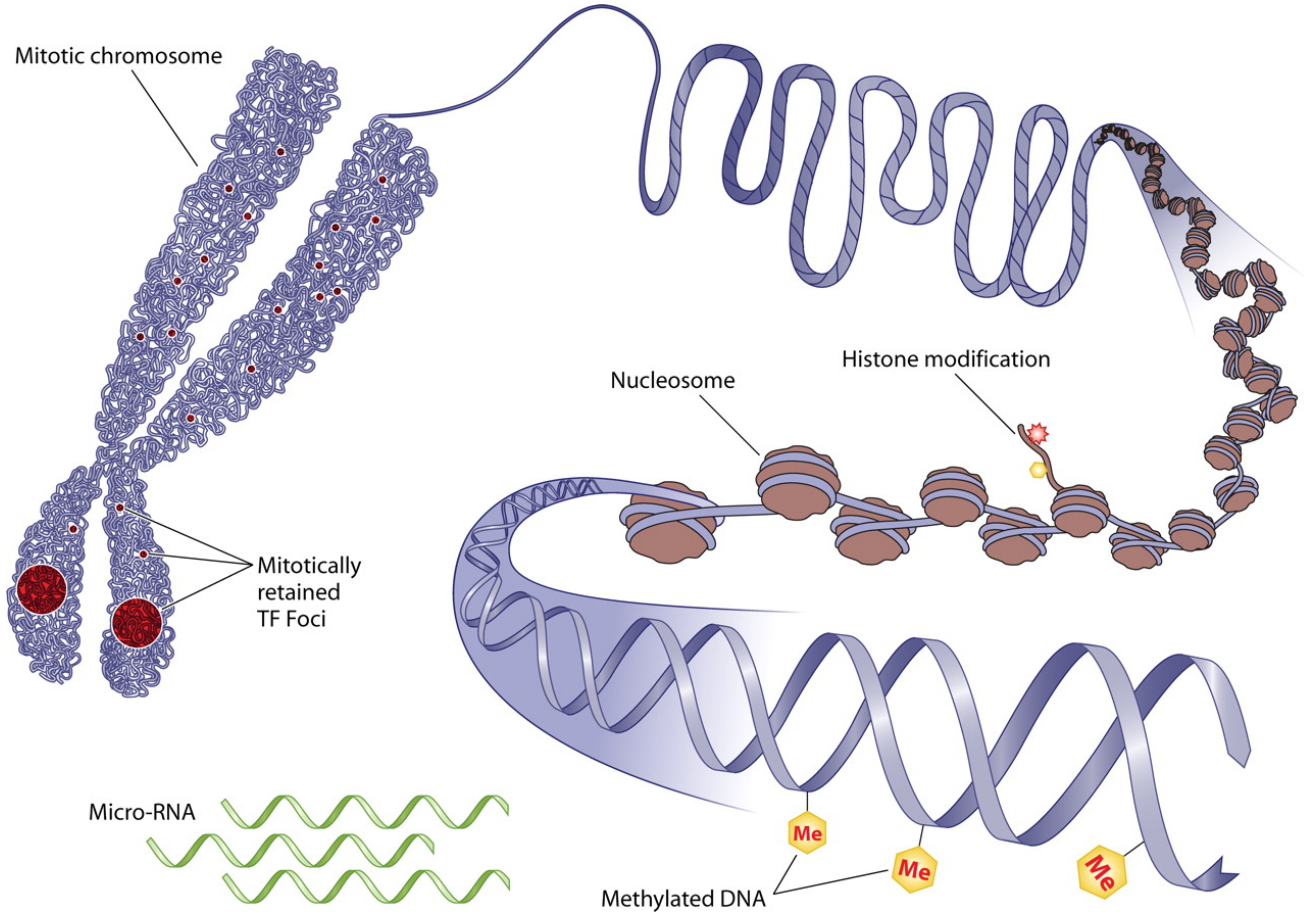
EPIGENETICS, STEM CELL-DERIVED NEURONS AND PD

Implications for disease modelling

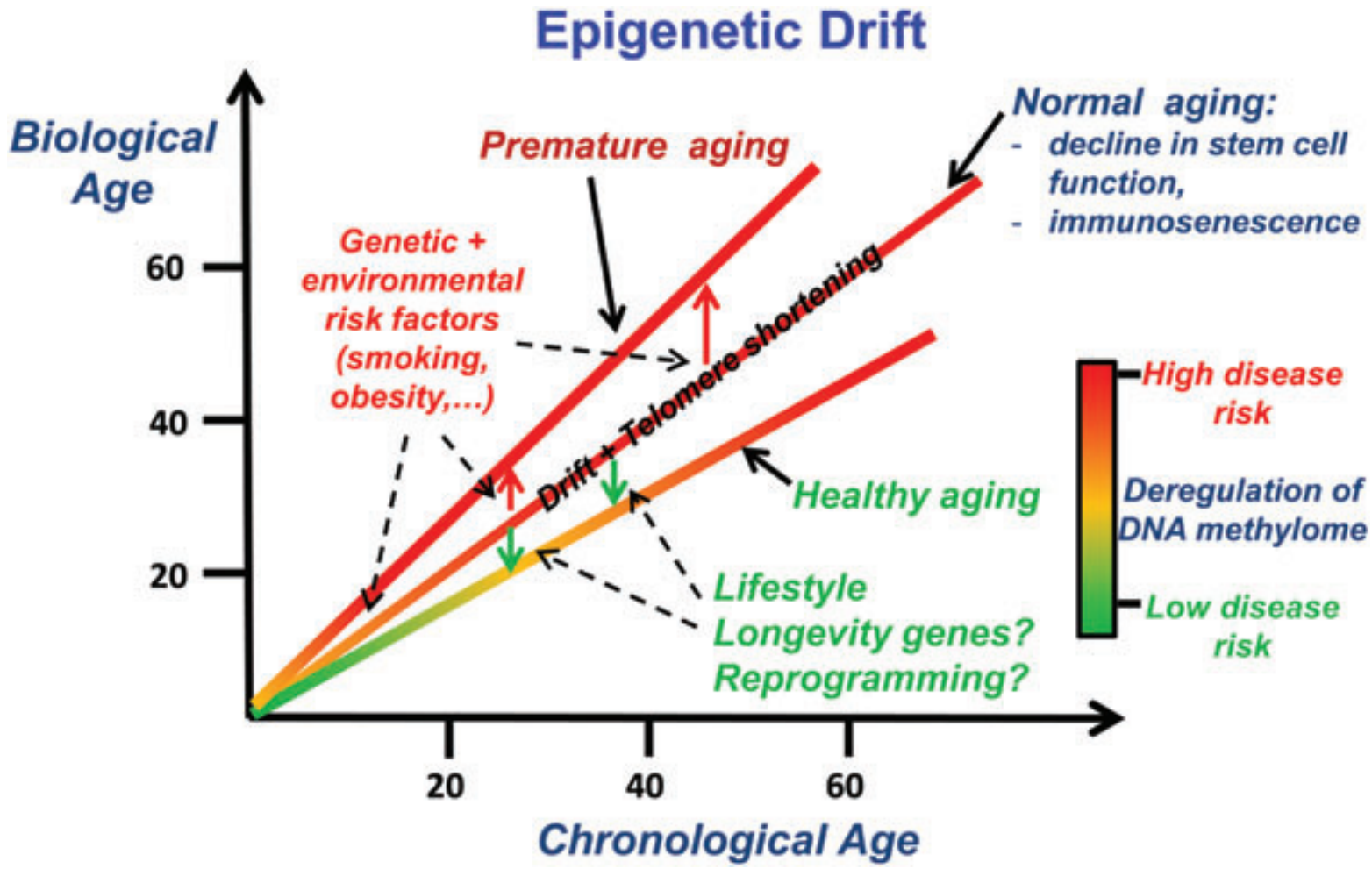
Searching for the cause of iPD

Maybe epigenetics?



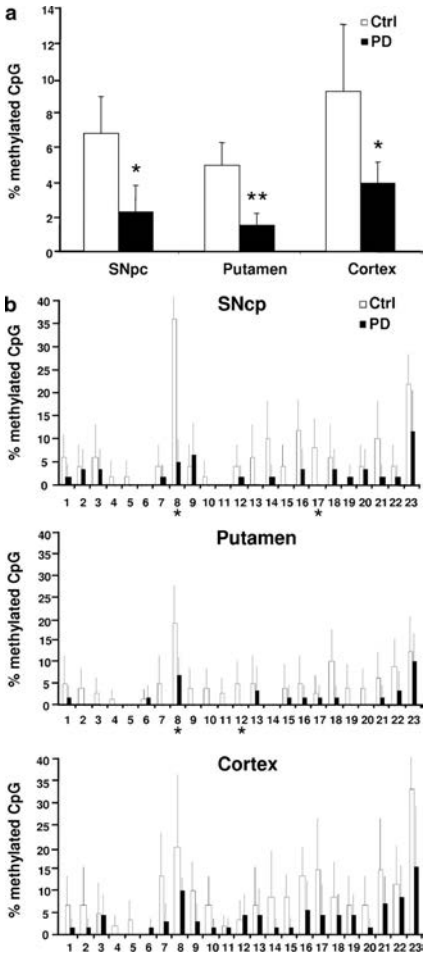
Sayyed K. Zaidi et al. Mol. Cell. Biol. 2010;30:4758-4766

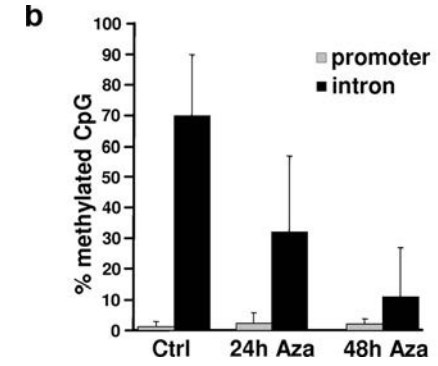
Epigenetic drift

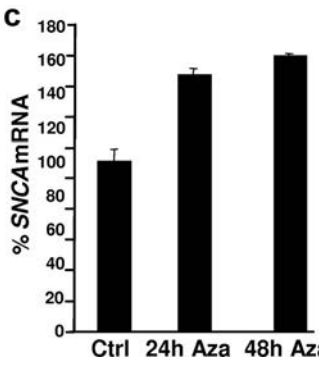


Teschendorff et al., Human Molecular Genetics, 2013, Vol. 22, Review Issue 1

Methylation Regulates Alpha-Synuclein Expression and Is Decreased in Parkinson's Disease Patients' Brains

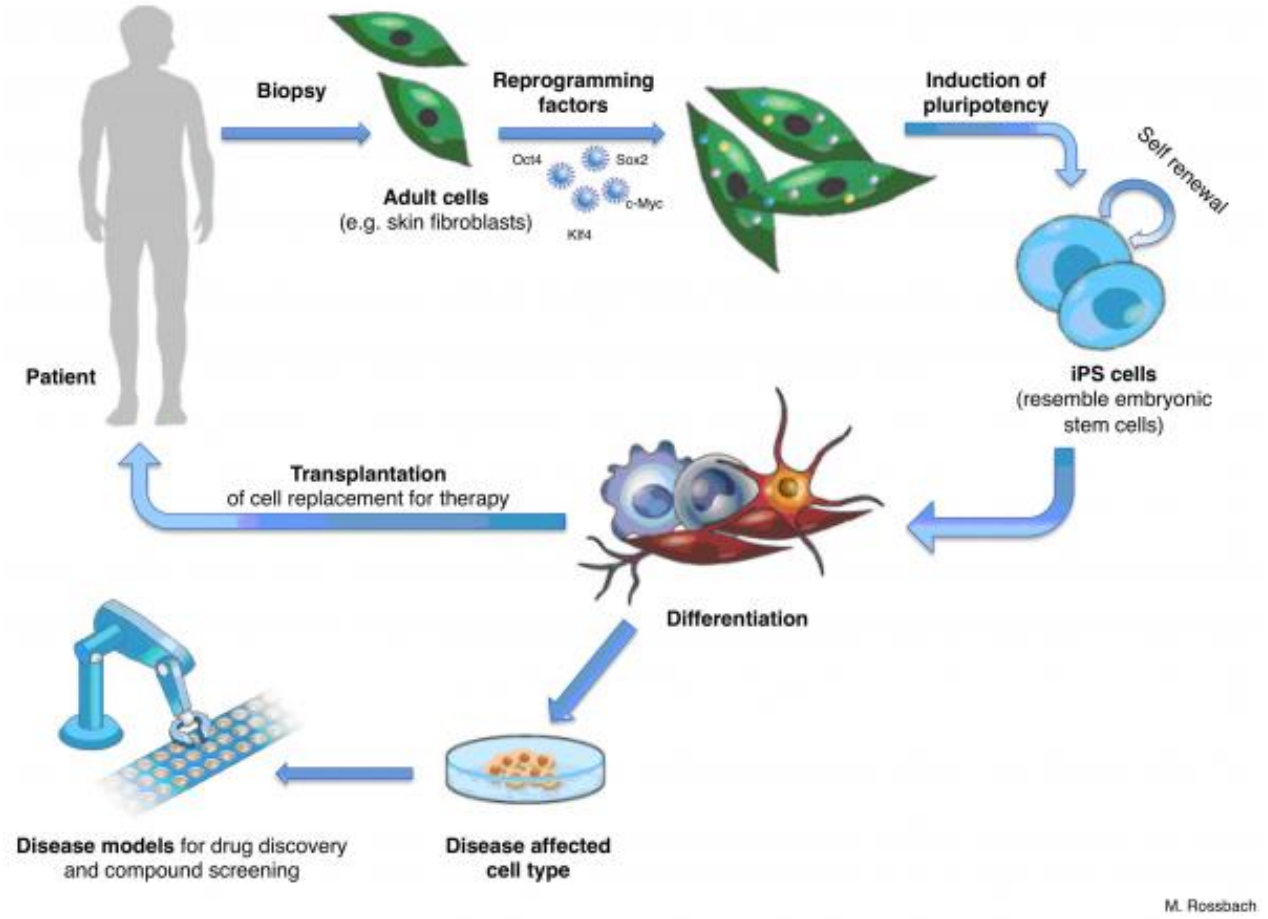






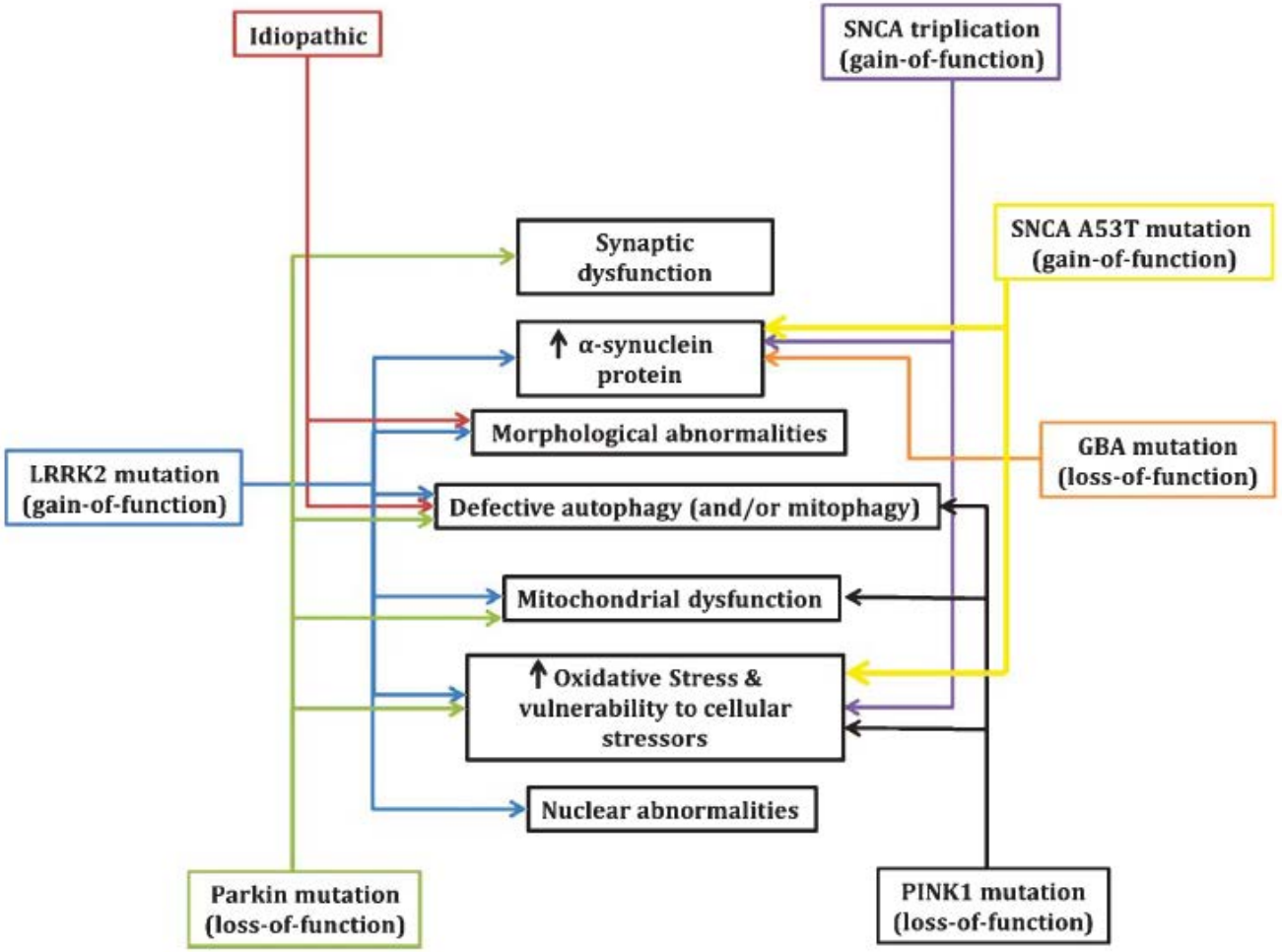
Jowaed et al. The Journal of Neuroscience, May 5, 2010 30(18):6355-6359

What about iPSC-derived patient-specific neurons?



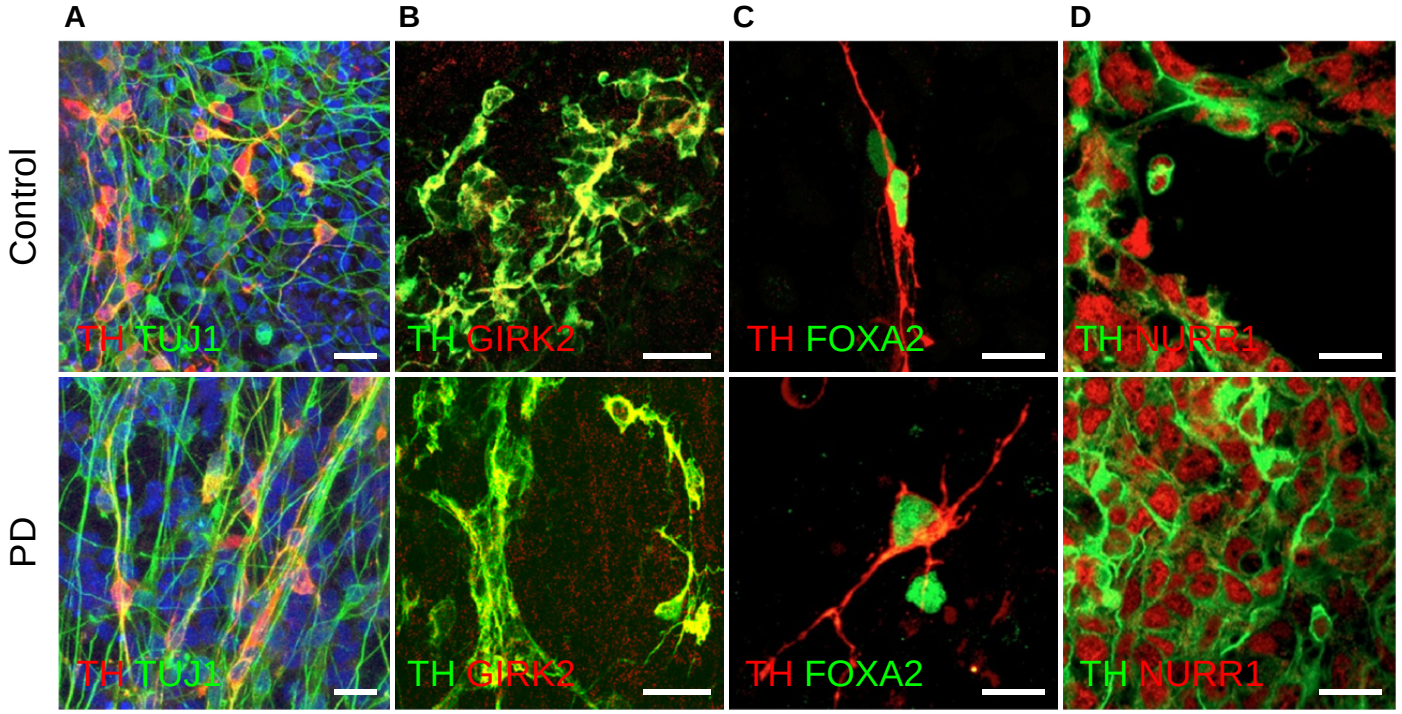
M. Rossbach, Factsheet EuroStemCell 5.10.2010

iPSC models of PD



Jacobs, Journal of Parkinson's Disease 4 (2014) 15-27

Aberrant epigenome in iPSC-derived dopaminergic neurons from Parkinson's disease patients



Fernández-Santiago et al. EMBO Mol Med. 2015 Dec; 7(12): 1529–1546.

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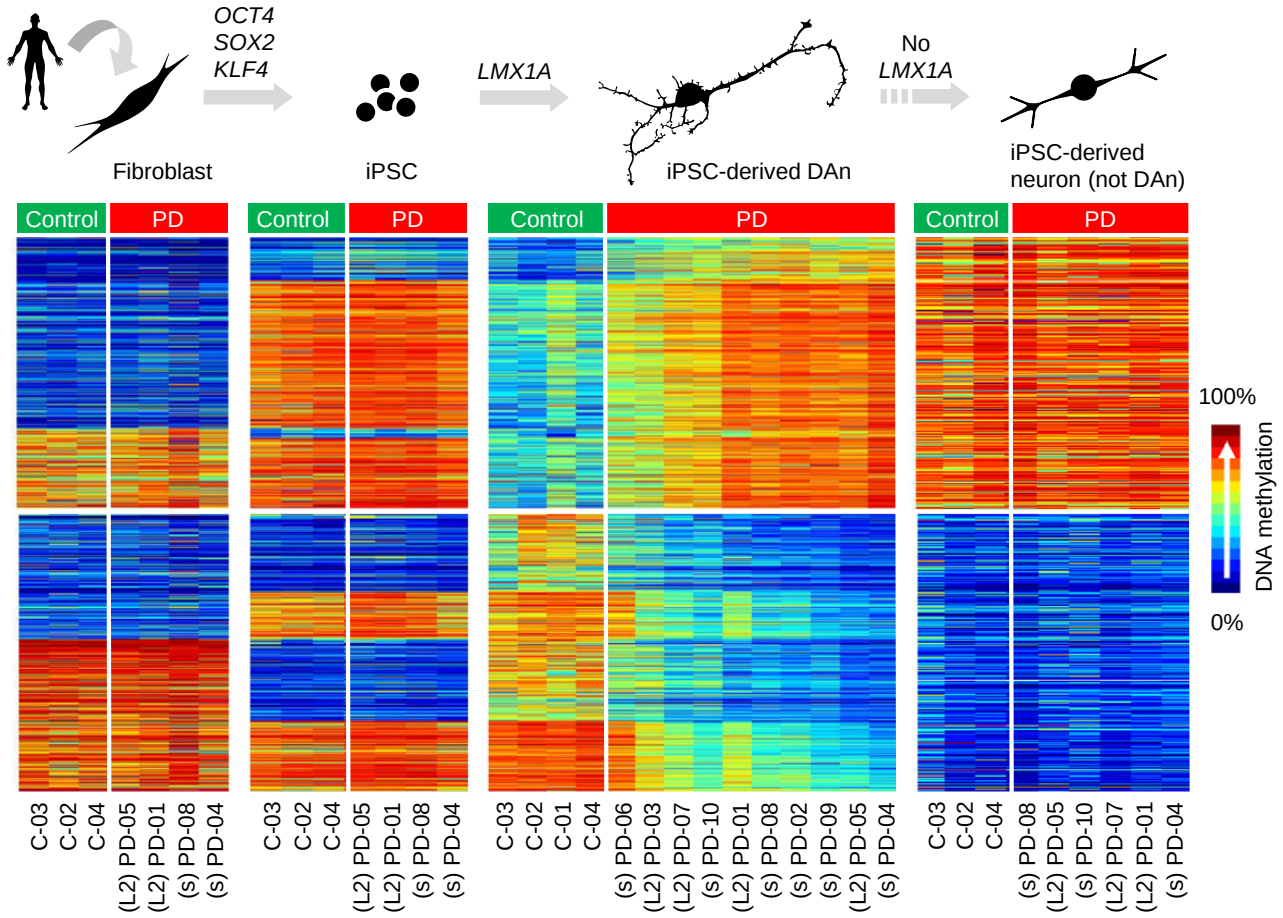
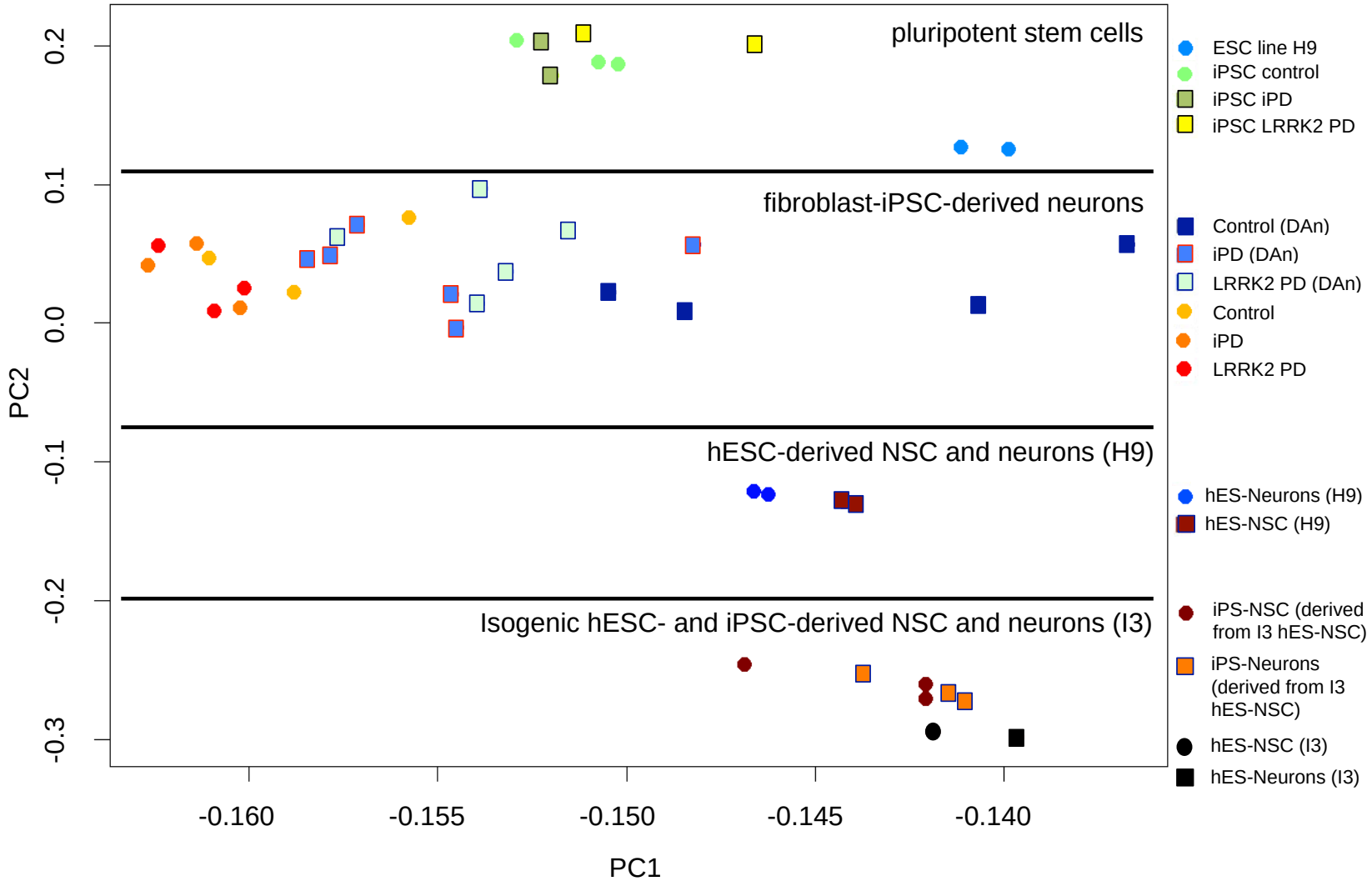


Fernández-Santiago et al. EMBO Mol Med. 2015 Dec; 7(12): 1529–1546.

Variability of DNA methylation patterns in iPSC- and ESC-derived neurons

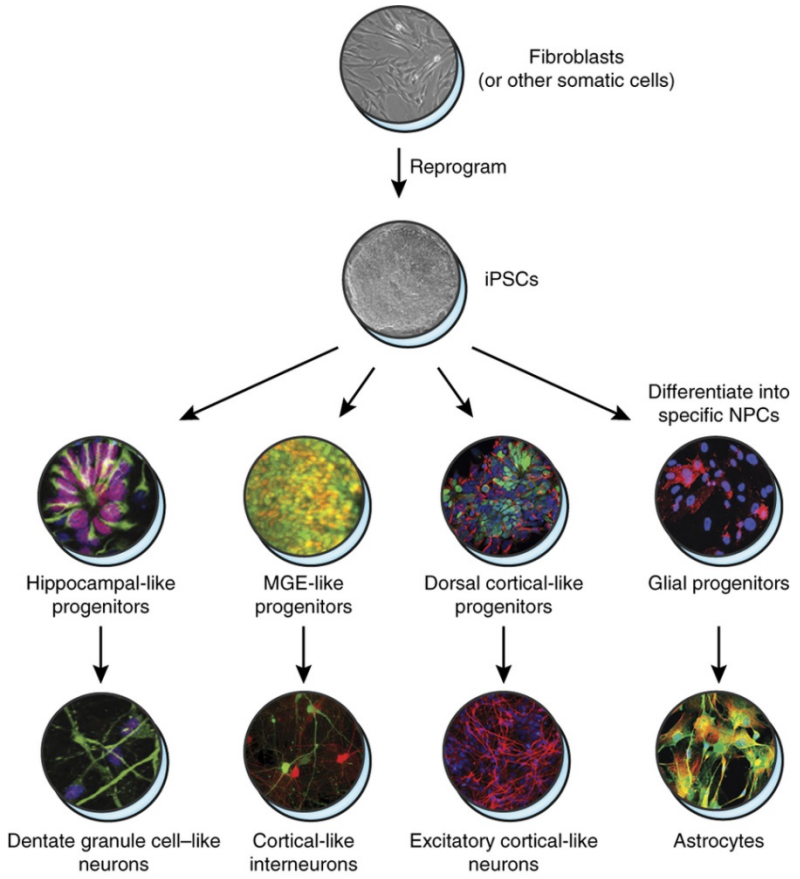


Caveats

(1) Reprogramming-associated epigenetic differences

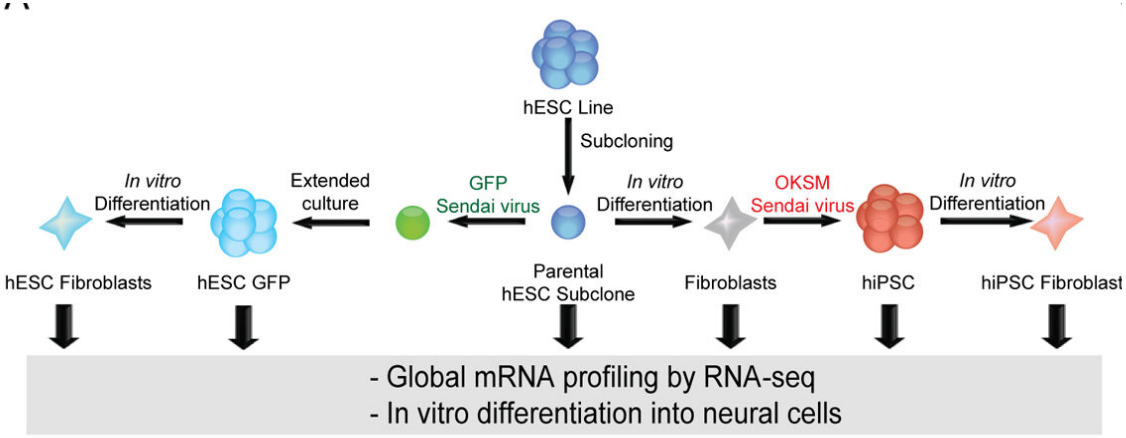
(2) Rejuvenation of iPSC-derived cells

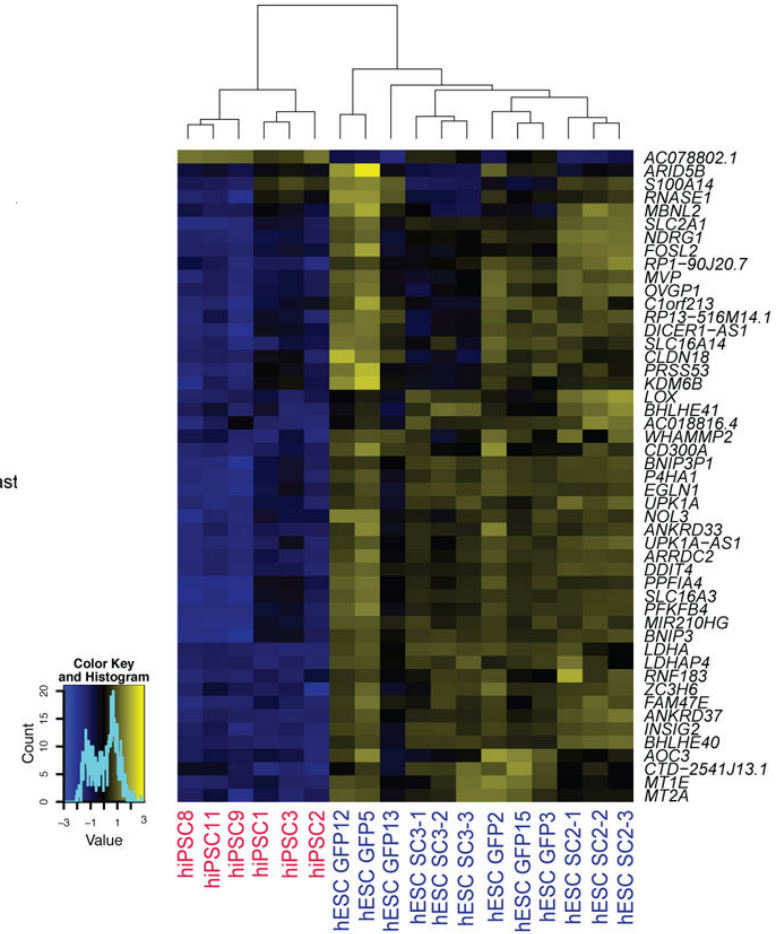
(3) *In vitro* vs. native neurons



Parent and Anderson Nature Neuroscience 18, 360–366 (2015) doi:10.1038/nn.3944

Reprogramming does not lead to an aberrant gene expression pattern





Choi, Jiho et al. Nature biotechnology 33.11 (2015): 1173–1181.

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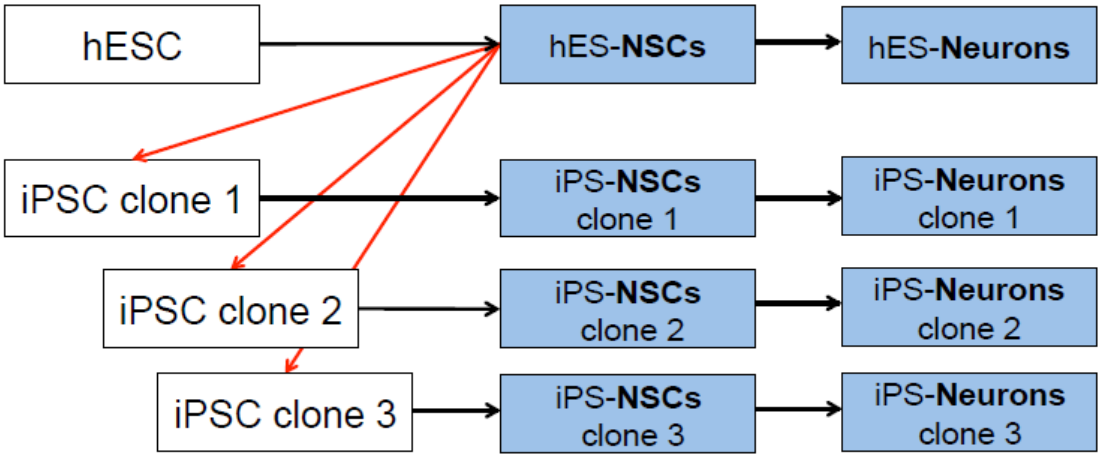
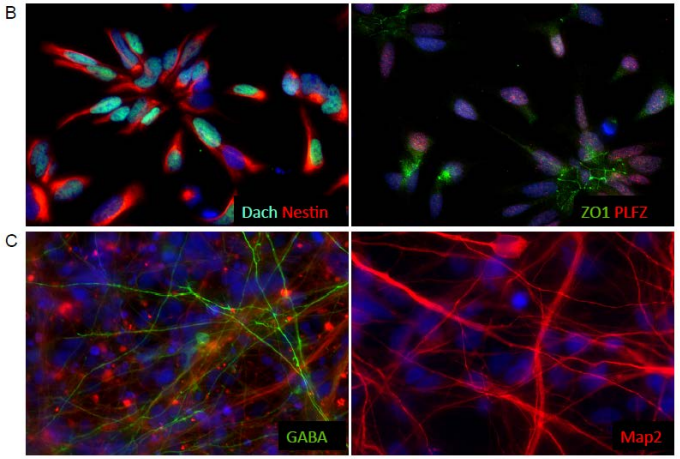
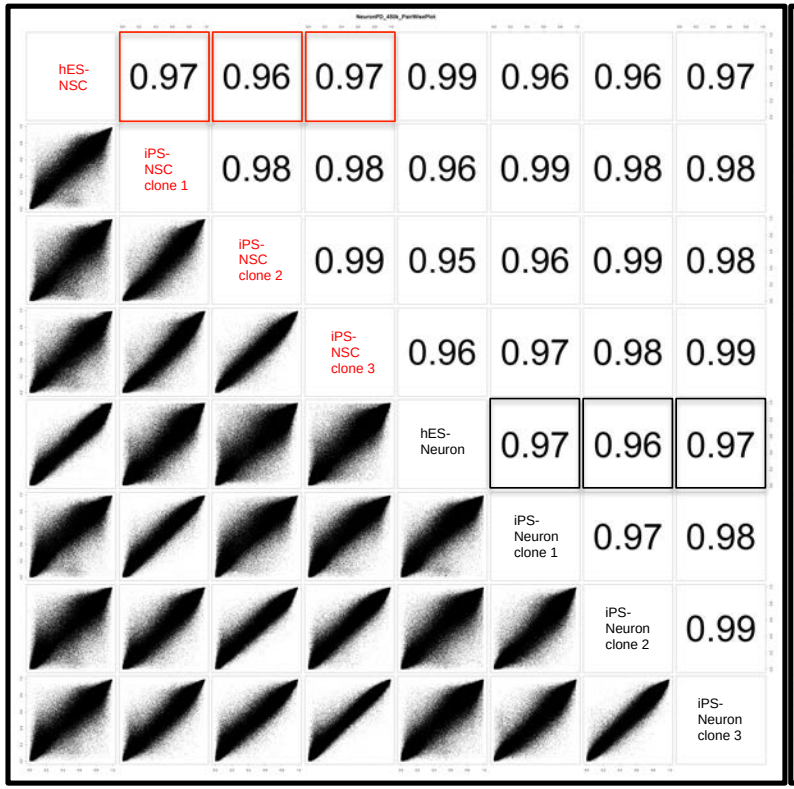


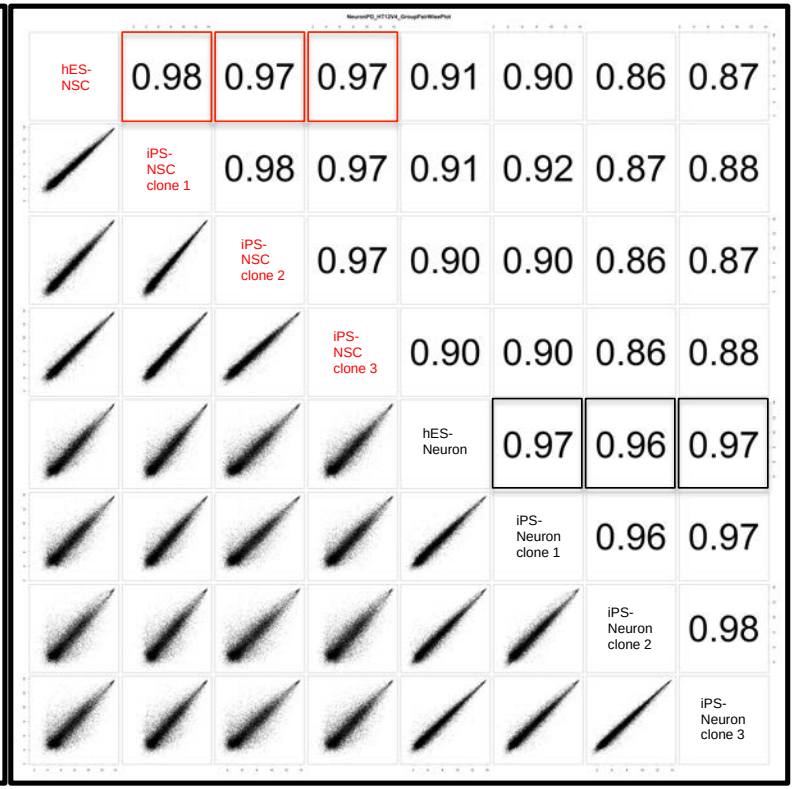


Reprogramming does not lead to an aberrant epigenome

genome-wide DNA methylation (450K, Illumina)



genome-wide expression levels (HT-12 v4, Illumina)



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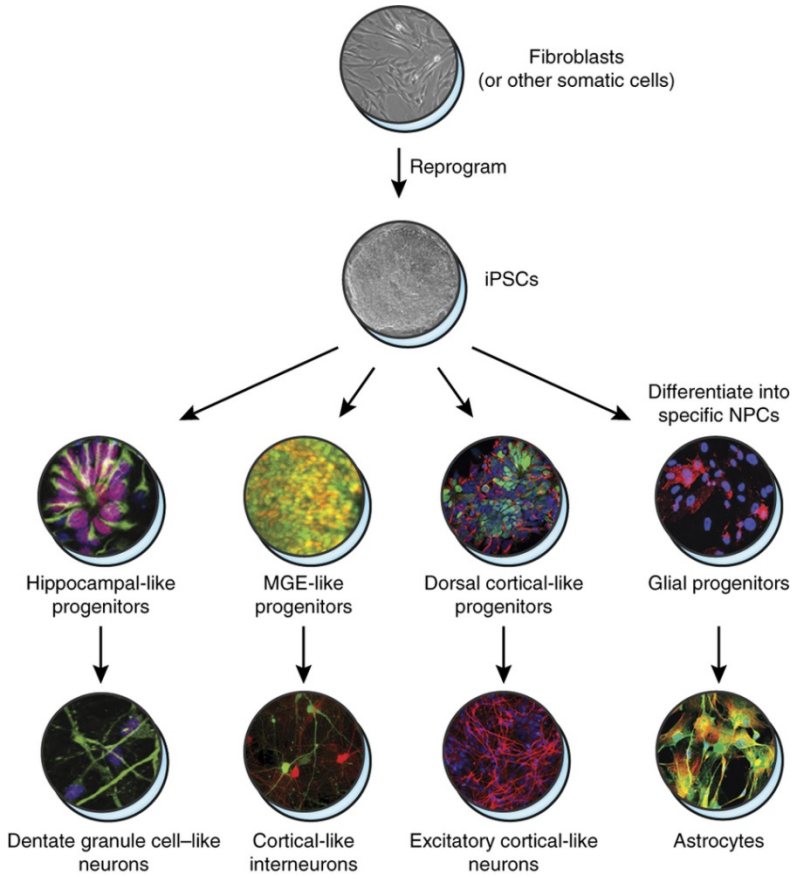

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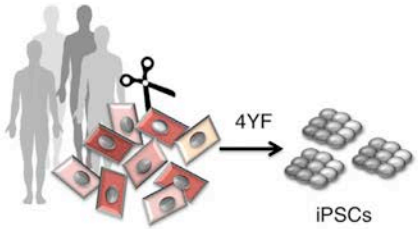
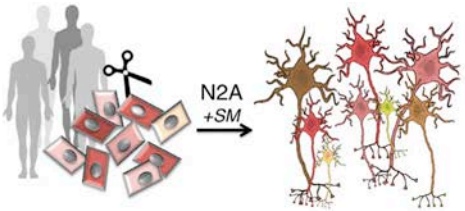
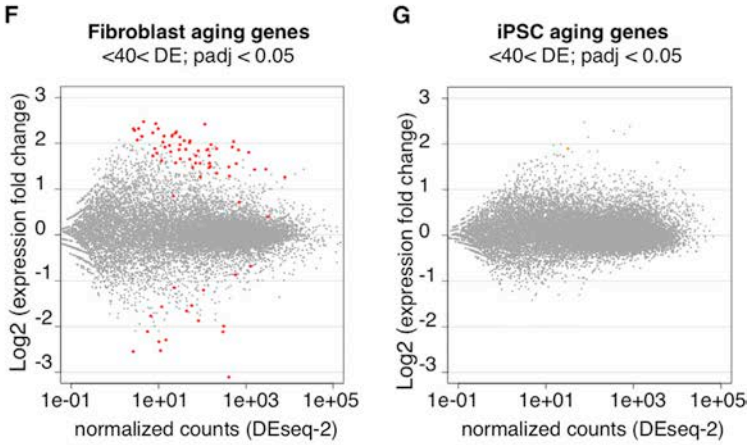
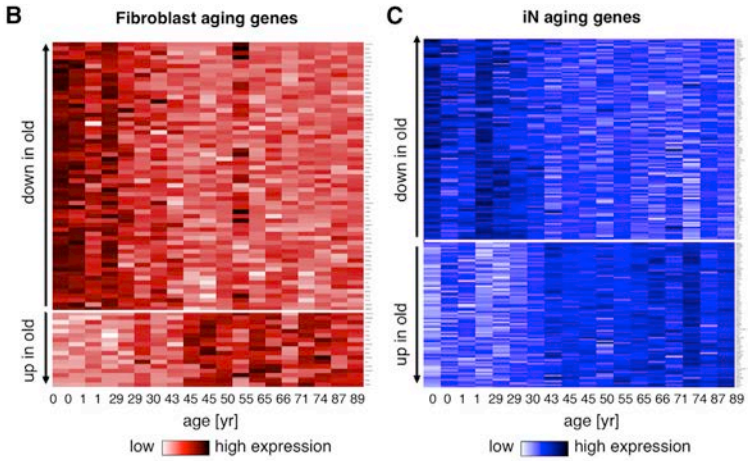
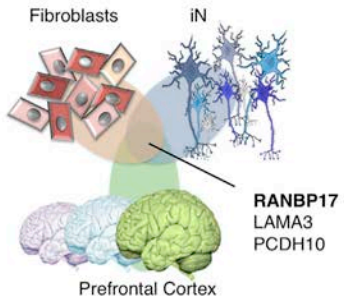
iPSC-derived Neurons vs. iN





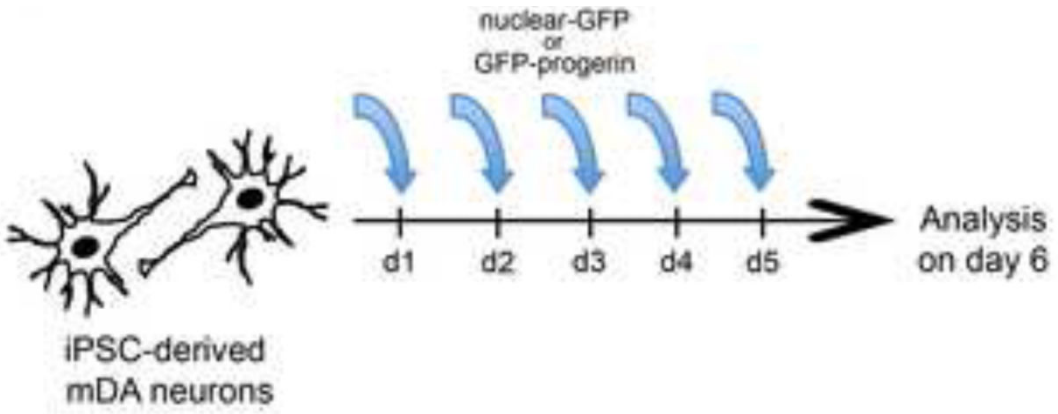






Mertens et al., Cell Stem Cell, Volume 17, Issue 6, 3 December 2015, Pages 705-718

Generating aged iPSC-derived neurons



Miller et al. Cell Stem Cell. 2013 Dec 5; 13(6): 691-705

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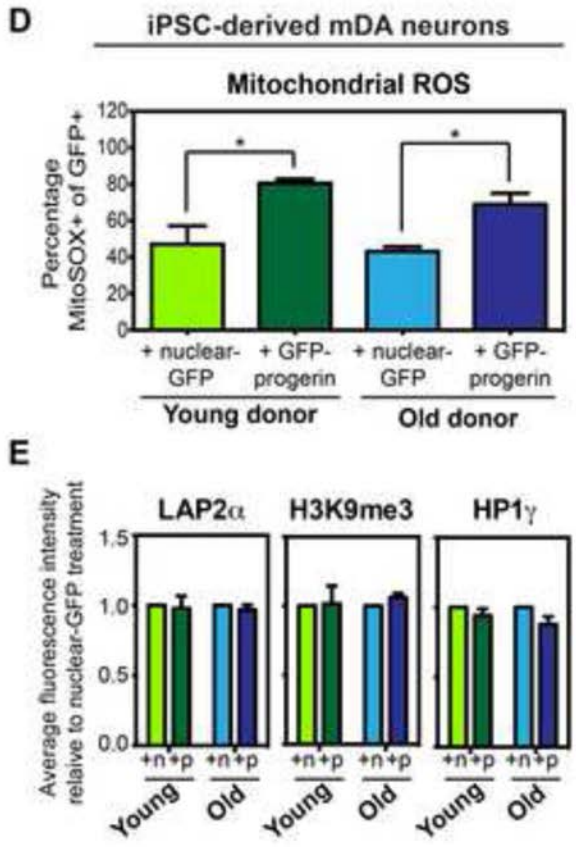

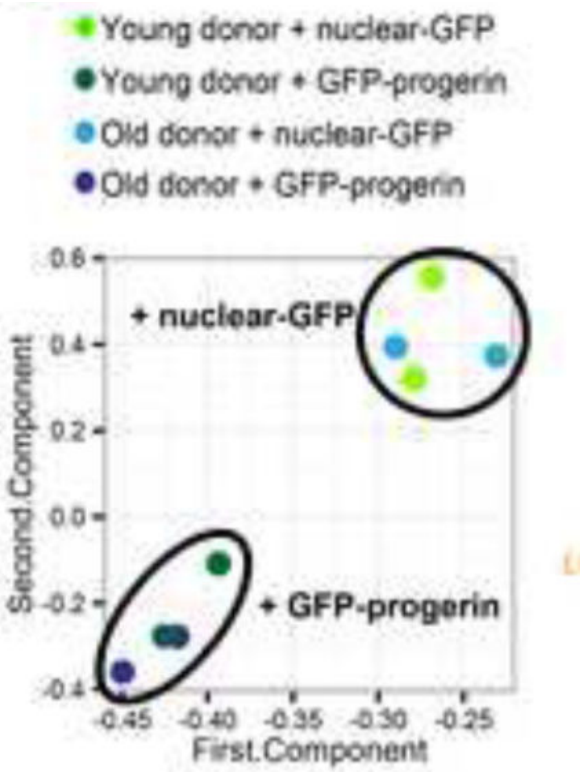

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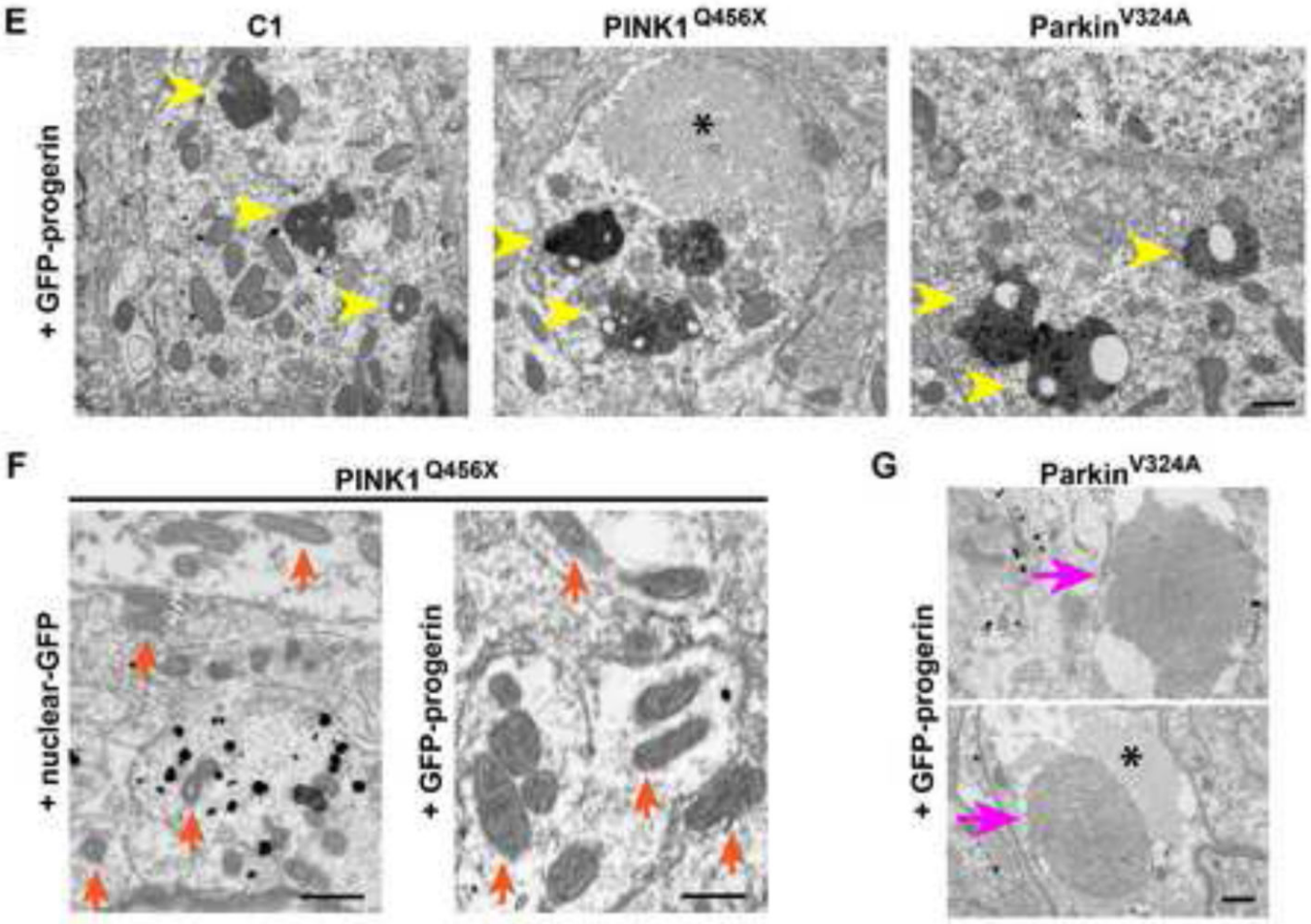

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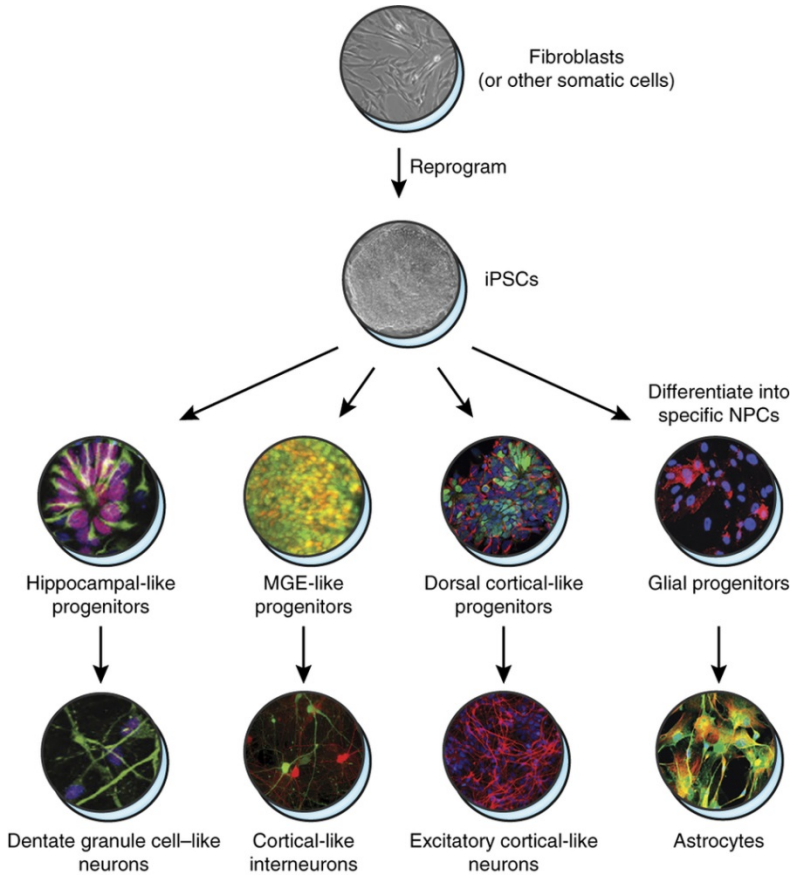

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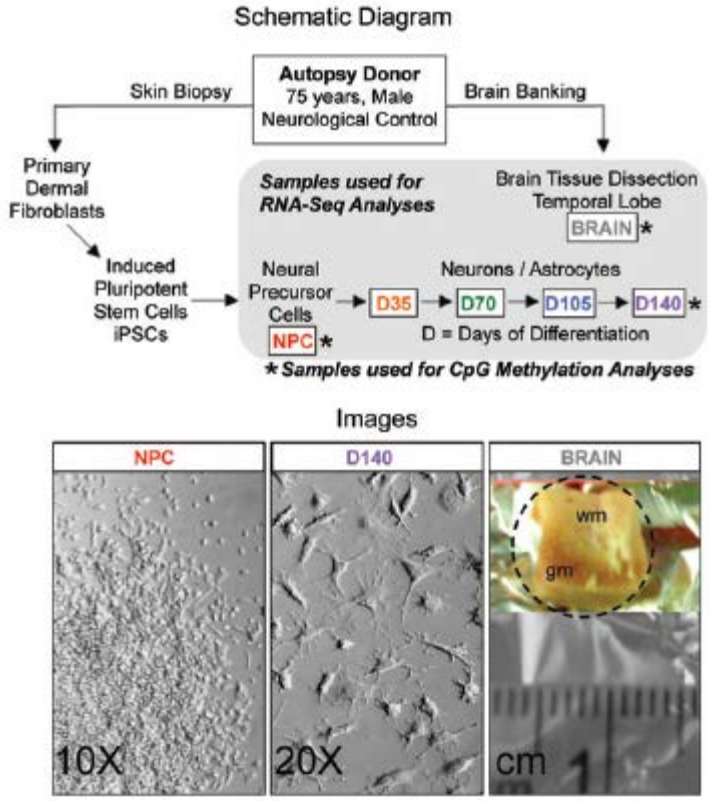

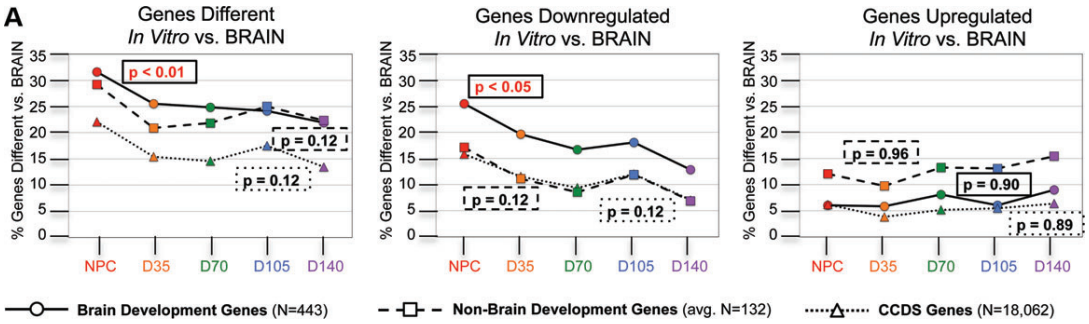

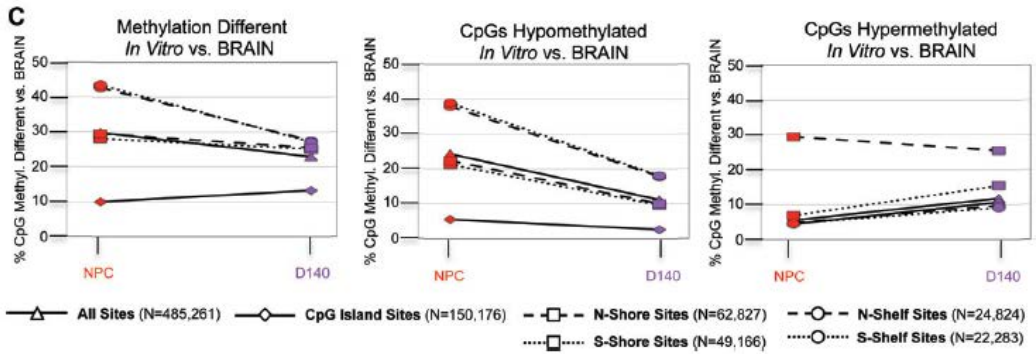

Hjelm et al. Hum. Mol. Genet. (2013) 22 (17): 3534-3546. doi: 10.1093/hmg/ddt208

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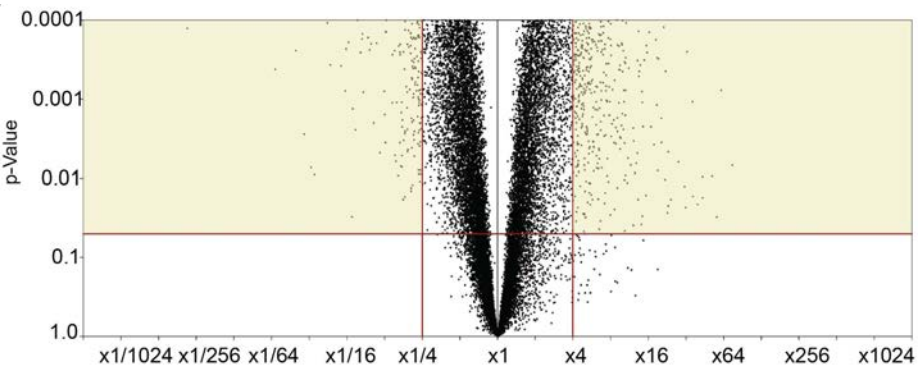

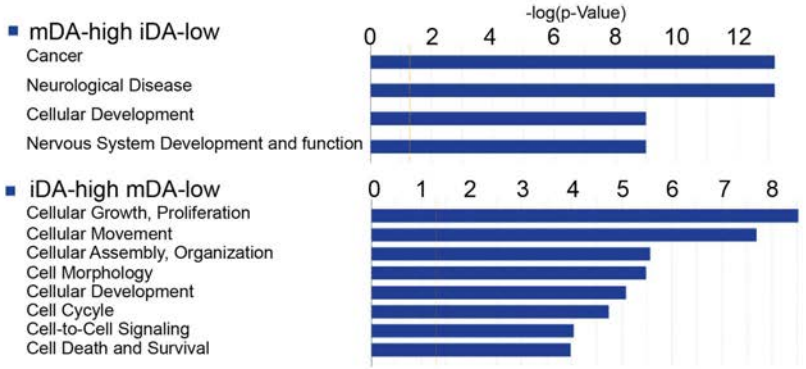

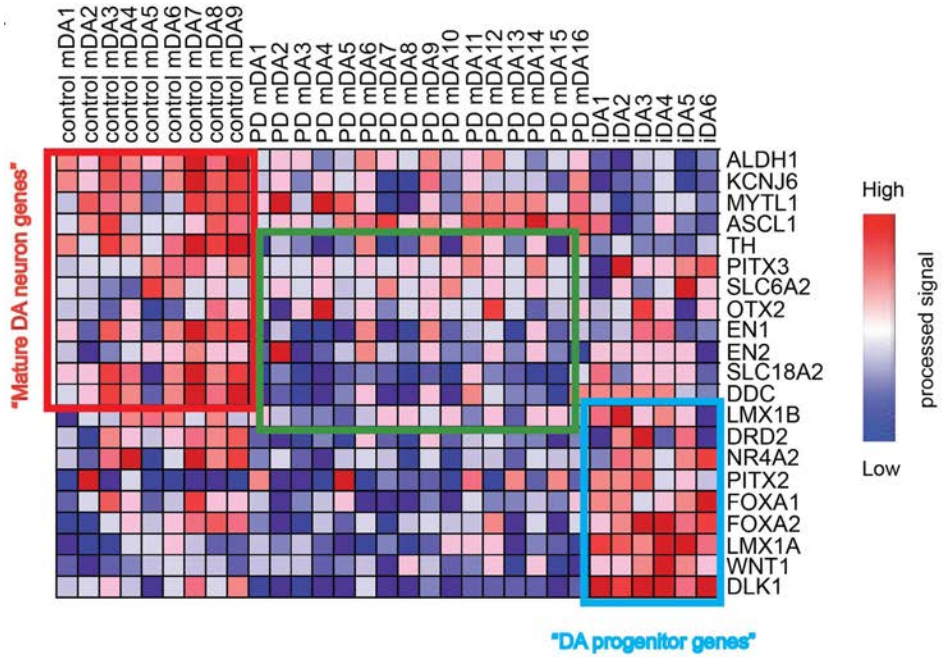

Xia et al., Scientific Reports volume 6, Article number: 20270 (2016)
doi:10.1038/srep20270

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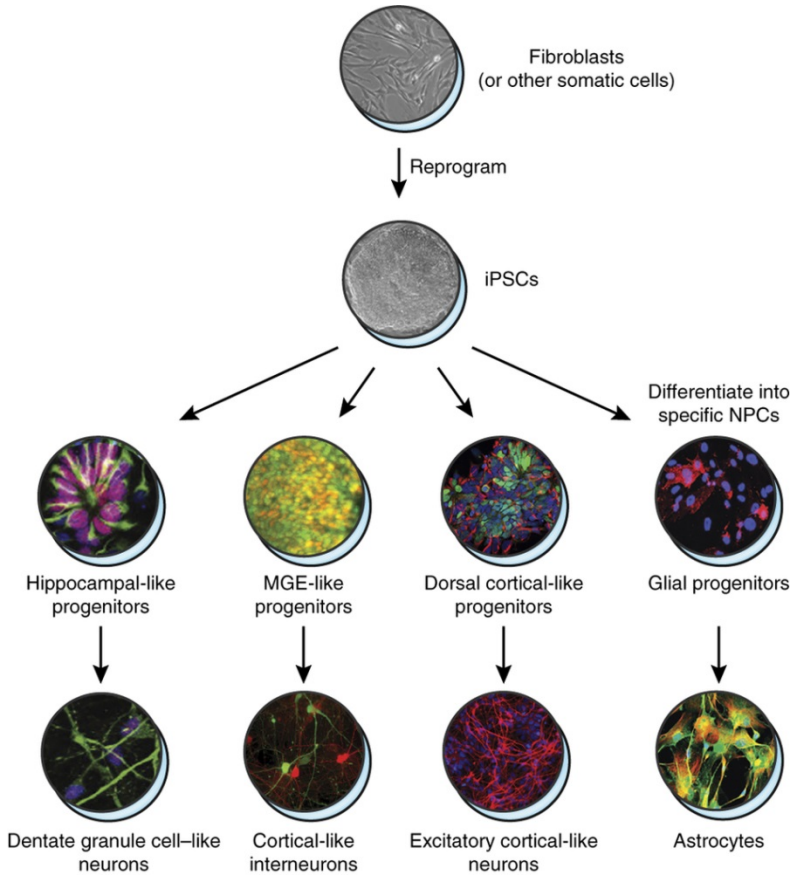

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The way is the goal – but where are we going?