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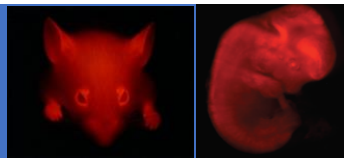
Conditional reprogrammable mouse lines for stem cell, regeneration and aging research



Reference No.: INV-2022004

Mouse Lines Available for Licensing:

1. ROSA26-rtTA-IRES-EGFP
2. ROSA26-rtTA(neo)

The present animal model would be of particular interest not only to researchers interested in studying the reprogramming process and the rejuvenation effect of the limited activation of the reprogramming transgenes, but also to pharmaceutical and biotechnology companies targeting aging, developing, screening, and testing new therapeutic agents for the treatment of degenerative diseases.

Description:

Doxycycline (On/Off) inducible reprogramming Yamanaka factor transgenic cells or animals – designated as secondary (2°) reprogramming systems – provide excellent experimental tools for studying the variances in cellular reprogramming outcomes due to different *in vitro* and *in vivo* environments. To make such studies less cumbersome, we developed two novel transgenic mouse lines that are appropriately efficient to induce successful mass-reprogramming in their somatic cell types.

The lines also include reporter genes enabling easy, Green Fluorescent Protein readout of endogenous Oct4 activation (indicative of pluripotency), and mCherry for reprogramming transgene expression. Notably, somatic cells derived from various foetal and adult tissues from these secondary mouse lines gave rise to efficient and rapid reprogramming, with transgene independent iPSC colonies emerging as early as one week after induction.

These mouse lines are available in two different flavours: (1) the rtTA part of the doxycycline inducible system which is ubiquitously expressed; and (2) the rtTA, which is Cre recombinase excision conditionally expressed. The latter allows activation of the reprogramming in cells defined by Cre recombinase expression specificity both *ex vivo* and *in vivo* in the mouse.

Technology:

The inventors at Sinai Health System developed the transgenic mouse lines using transposon mediated random insertion of a single copy of the reprograming transgenes and the Oct4 promoter driven EGFP transgene. The rtTA on the other hand was targeted to the ubiquitously expressed Rosa26 locus of the mouse.

Availability:

1. Jackson Laboratory

   ROSA26-rtTA-IRES-EGFP (**JAX Stock Number** 005670)
   ROSA26-rtTA(neo) (**JAX Stock Number** 031012)

2. Directly via the Nagy Lab at Sinai Health System (please contact: hanna@lunenfeld.ca)

Publication:

Judith Elbaz, Mira C. Puri1, … and Andras Nagy (2022) Highly efficient reprogrammable mouse lines with integrated reporters to track the route to pluripotency. PNAS 2022 Vol. 119 No. 49. https://doi.org/10.1073/pnas.2207824119

Shakiba, N., Fahmy, A., Jayakumaran, G., McGibbon, S., David, L., Trcka, D., Elbaz, J., Puri, M.C., Nagy, A., Kooy, D. van der, et al. (2019). Cell competition during reprogramming gives rise to dominant clones. Sci New York N Y *364*. https://doi.org/10.1126/science.aan0925.

Opportunity:

Non-exclusive license is available

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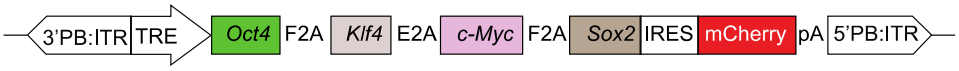
Appendix

Transgene structures:

1. Reprogramming transgene:



2. Endogenous Oct4 expression reporter

3. Cre conditional rtTA expressing constract in the Rosa26 locus