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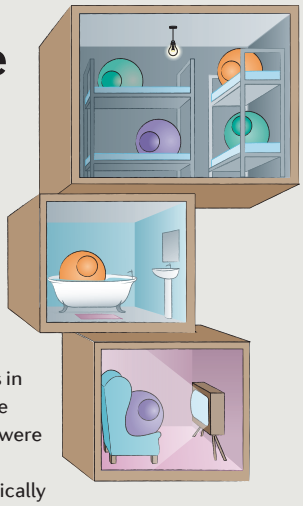
STEM CELLS

Engineering an artificial niche for cell quiescence

Some adult stem cells reside in their tissues in a quiescent state, which is important for their regenerative capacity. Cell culture conditions fail to maintain stem cell quiescence, and thus cells isolated from their *in vivo* niche immediately start proliferating. Now, Rando and colleagues report the development of an artificial niche for muscle stem cells (MuSCs, also known as satellite cells) that preserves their quiescence and increases their potency, that is, their capacity for engraftment and tissue regeneration.

The authors analysed the expression of 39 genes that are important for the myogenic programme in freshly isolated, single quiescent MuSCs compared with MuSCs that were induced to proliferate *in vivo*. This enabled them to identify a molecular signature of quiescent mouse MuSCs that could then be used to screen different culture media for maintaining MuSCs in a quiescent state. Next, they screened for molecules that, when added to the medium, maintained the expression of the quiescence signature. They tested different combinations of compounds with the potential to prevent cell proliferation for 2 days in culture and identified a 'quiescence medium' in which cultured MuSCs were kept very similar to freshly isolated quiescent MuSCs, both morphologically and in terms of gene and cell-surface marker expression profiles.

As quiescent MuSCs usually reside under the basal lamina of muscle fibres, the authors tested whether culturing cells in the quiescent medium on an artificial niche composed of engineered muscle fibres (which recapitulate key properties of native myofibres and the basal lamina) would prolong the quiescent state. Indeed, using a collagen-based microscaffold in the shape of a muscle fibre with a defined degree of elasticity delayed entry into the cell cycle — in these conditions, MuSCs could be maintained in a quiescent state up to 7 days and then efficiently be activated. Importantly, when cells were cultured on this artificial niche, their engraftment capacity was increased and they were able to regenerate muscle fibres when transplanted into injured muscles of mice as well as to self-renew with efficiencies that were similar to freshly isolated MuSCs. Moreover, human MuSCs cultured on the artificial niche also had the capacity for engraftment into injured mouse muscles.



Vicky Summersby/NPG

> "artificial niches should enable ... the maintenance of cells with high potency *in vitro*"

The development of artificial niches should enable not only the maintenance of cells with high potency *in vitro*, thereby greatly enhancing their clinical potential, but also better characterization of the quiescent state, which could be further exploited when manipulating stem cells.

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