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Autologous neural cell therapy reverses a dementia syndrome in older pet dogs

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Dementia currently affects 50 million individuals worldwide, with projections of 130 million by the year 2050. Due to limited progress in medical management dementia remains an incurable and fatal disorder. The underlying clinic-pathologic issue in early Alzheimer's dementia is mass neuronal loss in the hippocampus. Repopulation by exogenous neural precursors is a promising therapeutic strategy but has yet to reach clinical trial. One of the major challenges has been poor translational fidelity between rodents and humans. We have therefore focused on Canine Cognitive Dysfunction (CCD), a neurodegenerative disorder in older pet dogs with many parallels to human Alzheimer's and dementia. Dogs with CCD display amnesia, spatial disorientation and agitation and express neurodegeneration alongside Alzheimer pathology. To date, we have produced >50 genetically non-modified neural precursor cell lines from adult canine skin, termed SKNs. These are highly homogenous in culture, rate-limited by virtue of low number of maximal cell doublings and differentiate almost exclusively into neurons, endogenously up-regulating neuronal specification genes. We show that canine SKN transplantation into the aged rodent hippocampus is safe and leads to widespread neuronal engraftment. Donor cells become electro-physiologically active and integrate synaptically into host neuronal circuitry. Moreover, we observe rescue of hippocampal-dependent place recognition memory deficits, with exploration ratio restored to levels equivalent with young rats. Accordingly, we are now assessing the safety and efficacy of our SKN therapy in a world-first therapeutic trial to treat dementia in a higher-order animal model. We can report that 18-months following MRI-guided intra-hippocampal injection of autogenic SKNs, two consecutive patients demonstrate stable and clinically meaningful improvement in CCD signs, such that they are functionally cured. These results are paralleled by dramatic improvements on objective spatial memory testing. These exciting early trial results indicate that SKN therapy can, in-principle reverse a naturalistic dementia-like syndrome.

Biography

Thomas Duncan is a Postdoctoral Researcher at the University of Sydney, Australia. His background is in histology, cell biology and regenerative medicine. At the University of Sydney, he manages Australia's first Canine Brain Bank and leads research into the neuropathology of canine dementia and the development of an autologous cell therapy for human Alzheimer's disease. He is a Lecturer at the University of Sydney of Neuroscience, Regenerative Medicine and Human Anatomy and Histology.

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