

GP.04

Smart human neural stem cells to degrade scar and optimize regeneration after traumatic cervical spinal cord injury

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Background: Human induced pluripotent stem cell-derived neural stem cells (hiPS-NSCs) represent an exciting therapeutic approach for traumatically spinal cord injury (SCI). Unfortunately, most patients are in the chronic injury phase where a dense perilesional chondroitin sulfate proteoglycan (CSPG) scar significantly hinders regeneration. CSPG-degrading enzymes can enhance NSC-mediated recovery, however, nonspecific intrathecal administration causes off-target effects. We aimed to genetically engineer hiPS-NSCs to express a scar-degrading ENZYME into their local environment to enhance functional recovery. **Methods:** A bicistronic scar-degrading ENZYME and RFP reporter vector was non-virally integrated into hiPS-NSCs and monoclonalized. ENZYME activity was assessed by WST-1 and DMMB biochemical assays and an *in vitro* CSPG spot assay with hiPS-NSC-derived neurons. To assess *in vivo* efficacy, T-cell deficient rats (N=60) with chronic (8wk) C6-7 SCIs were randomized to receive (1)SMaRT cells, (2)hiPS-NSCs, (3)vehicle, or (4)sham surgery. **Results:** SMaRT cells retained key hiPS-NSC characteristics while stably expressing ENZYME. The expressed ENZYME could appropriately degrade *in vitro* and *ex vivo* CSPGs. While blinded neurobehavioural and immunohistochemical assessments are ongoing at 40wks post-injury, an interim analysis demonstrated human cells extending remarkably long ($\geq 20,000\mu\text{m}$) axons along host white matter tracts. **Conclusions:** This work provides exciting proof-of-concept data that genetically-engineered SMaRT cells can degrade CSPGs and human NSCs can extend long-distance processes in chronic SCI.

GP.05

The risk of malignancy after stereotactic radiosurgery

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Background: A major concern of patients undergoing Gamma Knife radiosurgery (GKS) for benign tumors and other conditions is the risk of a separate secondary malignancy or malignant transformation. The incidence of radiosurgery-associated malignancy based on long-term follow-up remains unknown. **Methods:** We conducted a population-based cohort study to estimate the incidence rate of both malignant transformation and a separate radiation-associated malignancy in patients undergoing GKS from 1987 to 2016 at 5 centers. **Results:** 11 527 patients underwent radiosurgery for meningioma (n=3261), arteriovenous malformation (n=2868), trigeminal neuralgia (n=1982), vestibular schwannoma (n=1957), pituitary adenoma (n=1193), other (n=266). The follow-up time ranged from 0.3 to 23.8 years. Four cases of malignant transformation and 3 new malignant brain tumors were reported, two of which were not within the irradiated field. The incidence of malignant transformation was 6.6 per 100 000 patient-years and of new malignancy, either locally or distant, was 5 in 100 000 patient-years. These risks are not higher than

the Central Brain Tumor Registry of the United States derived annual incidence rate of all primary malignant CNS tumors of 7.15 per 100 000. **Conclusions:** Physicians can safely counsel patients that the risk of malignancy after stereotactic radiosurgery remains extremely low, even at long-term follow-up of greater than 10 years.

CNS CHAIR'S SELECT ABSTRACTS

A.01

Parkinson's disease prognosis by early motor subtypes

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Background: Studies of autopsy-confirmed cases suggest that Parkinson's disease (PD) prognosis can be predicted using motor symptom severity at first visit. We evaluated the association between motor symptom subtype at first visit and severity at eight years disease duration among clinically-diagnosed cases at the Saskatchewan Movement Disorder Program. **Methods:** Retrospective data review identified 374 patients with first visit within three years of symptom onset, a clinical diagnosis of idiopathic PD, and a follow-up visit eight years after symptom onset. Subtypes were grouped as tremor-dominant (TD) if tremor was greater than rigidity and bradykinesia, akinetic-rigid (AR) if rigidity or bradykinesia was greater than tremor, and mixed (MX) if patient was neither TD nor AR based on assessment of all four limbs. Primary outcome was disease severity as measured by Hoehn & Yahr score at eight years after symptom onset. **Results:** The most common subtype was AR (n=164) followed by MX (n=156). TD was least common (n=54). There was no significant difference between subtypes in H&Y scores at eight years disease duration. **Conclusions:** These findings suggest that early PD prognosis cannot be predicted based on motor symptoms in all four limbs at first visit. Earlier studies had longer follow-up and future studies will examine progression at longer periods of disease duration.

A.02

Long-term outcomes in the management of central neuropathic pain syndromes

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Background: Central neuropathic pain syndromes are a result of central nervous system injury, most commonly related to stroke, spinal cord injury, or multiple sclerosis. These syndromes are much less common than peripheral etiologies, with less known regarding optimal treatment. The objective of this study was to determine the long-term clinical effectiveness of the management of central relative to peripheral neuropathic pain at tertiary pain centers. **Methods:** Patients diagnosed with central (n=79) and peripheral (n=710) neuropathic pain were identified from a prospective observational cohort from seven Canadian tertiary centers. Data regarding patient