“Engineering angiogenesis following spinal cord injury: building functional, stable blood vessels and promoting the formation of the blood-spinal cord barrier”

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Abstract:
It is estimated that there are 250,000 people in the U.S. with spinal cord injuries (SCI) and over 2 million worldwide. While, the majority of SCI research has focused on regenerating neural tissue, recovery is correlated with angiogenesis. Furthermore, vessels appear to play an important role in the neural stem cell (NSC) niche and may promote the proliferation, and neuronal differentiation of NSCs. However, inducing angiogenesis following SCI has been challenging since many of the factors and drugs permeabilize the surrounding vessels and can exacerbate injury. Engineering vascular networks could be an alternative to inducing extensive angiogenesis, but it has been challenging to engineer vascular networks that are stable for long times. We sought to determine whether stable, microvascular networks could be engineered using a coculture of primary ECs and NSCs. We isolated primary rat NSCs and primary ECs and cocultured them in a macroporous hydrogel based on poly(L-lysine) (PLL) and poly(ethylene glycol) (PEG). Coculture of primary NPCs and ECs led to stable, functional vessels up to 6 weeks with no signs of clot formation in a subcutaneous model. Moreover, this coculture promoted the formation of microvascular networks in a spinal cord model. The coculture also led to the formation of the blood-spinal cord barrier whereas the controls did not. This lays the groundwork for a new approach to promote recovery and regeneration following injury in the CNS and may provide a new paradigm to understand and treat neurological diseases and disorders in the CNS more broadly.