Nearly a century ago, the concept of the secondary injury in spinal cord trauma was first proposed to explain the complex cascade of molecular and cellular events leading to widespread neuronal and glial cell death after trauma. In recent years, it has been established that the ependymal region of the adult mammalian spinal cord contains a population of multipotent neural stem/progenitor cells (NSPCs) that are activated after spinal cord injury (SCI) and likely play a key role in endogenous repair and regeneration. How these cells respond to the various components of the secondary injury remains poorly understood. Emerging evidence suggests that many of the biochemical components of the secondary injury cascade which have classically been viewed as deleterious to host neuronal and glial cells may paradoxically trigger NSPC activation, proliferation and differentiation thus challenging our current understanding of secondary injury mechanisms in SCI. Herein, Hachem et al. highlighted new findings describing the response of endogenous NSPCs to spinal cord trauma, redefining the secondary mechanisms of SCI through the lens of the endogenous population of stem/progenitor cells. Moreover, they outlined how these insights can fuel novel stem cell-based therapeutic strategies to repair the injured spinal cord.

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