Persons with spinal cord injury (SCI) endure life-long functional struggles due to limited or no movement or control of their affected limbs. Spinal injury often results in partial sparing of residual neural pathways to motor neurons that enable some return of limb movement. Although reorganization and strengthening of these preserved networks may occur after injury, restoring function remains frustratingly limited. Thus, there is an overwhelming need for targeted therapies that may guide the reorganization of these spared pathways toward functionally meaningful recovery.

One promising strategy to augment motor recovery is to induce neuroplasticity via repetitive exposures to modest bouts of low oxygen (acute intermittent hypoxia, AIH). Rodent models of SCI demonstrate that AIH elicits remarkable respiratory and non-respiratory motor plasticity, which appears pronounced when repetitive (up to 7 consecutive days) AIH pairs with motor training (e.g., breathing, locomotor training). Detailed mechanistic studies show that up-regulation of brain-derived neurotrophic factor (BDNF) along the spinal cord plays an important role in this plasticity. Several clinical studies support the possibility of repetitive AIH with motor training as a combinatorial approach to enhance motor recovery in humans with SCI. Despite these exciting findings, essential questions about the clinical translation of AIH remain. The purpose of this presentation is to introduce an automated pressure-swing delivery system for administering AIH safely and to discuss the potential impact of several confounding factors that may undermine AIH efficacy. Understanding the extent to and the mechanisms by which neural pathways may contribute to the enduring effects of AIH on motor recovery is crucial to the success (or failure) of AIH as an adjuvant to SCI rehabilitation.