Allogeneic Naïve B Cells as a Novel Cell Therapy Candidate for Regenerative Medicine

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Cell-based approaches to regenerative medicine in the form of stem cell or progenitor cell therapies have been explored for more than 40 years as a method of restoring tissue integrity and improving functional outcomes. Unfortunately, a scalable approach that can successfully advance through FDA review for commercial application has yet to be developed.

Naïve B cells are mature immune cells that have not yet differentiated into memory or effector antibody-generating B cells. Unlike stem cells, they are abundant and accessible, making up 60-70% of the B cells in human peripheral blood (over 5% of the white cells in circulation). Naïve B cells have traditionally been considered a transitional cell type with limited functional roles in the body.

We demonstrated that, when allogeneic naïve B cells are placed into an injured tissue or infused intravenously in the context of CNS injury or Amyotrophic Lateral Sclerosis (ALS), respectively, they have the capacity to induce immune-regulatory, anti-inflammatory and neuroprotective—Regain—effects via multimodal mechanisms. Our findings suggest that naïve B cells are capable of accelerating recovery from injury and promoting functional improvement, including neuroregeneration, within injured tissue. Further, preclinical studies in mouse models of traumatic brain injury, intracranial hemorrhage (ICH) and ALS as well as initial first-in-human studies in two patients with ALS have demonstrated safety and potential to alter a subject's immune profile, elicit neuroprotection, and positively impact function.

We have established a GMP-ready process of isolating up to a billion naïve B cells and potentially multiple doses could be obtained from a single donor leukapheresis. We have stored naïve B cells in a clinical-grade formulation for months in a -80°C freezer while preserving viability and potency. We are currently proceeding towards Phase I studies in the treatment of ICH and ALS. Furthermore, we are exploring novel non-genetic and genetic approaches to augment the Regain functionality of isolated naïve B cells.