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Human MuStem cells_impact on adaptive and innate immunity : definition of immunomodulatory properties of a cell-based therapy candidate for Duchenne Muscular Dystrophy
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Abstract:(300-400 words)
Despite great improvements in stem cell transplantation, allogeneic strategy is highly limited by graft rejection. Immunosuppressive regimen can improve graft survival but are involved in strong secondary effect such as lymphoma or cardiac failure. Recently, several teams demonstrated the immunosuppressive ability of mesenchymal stem cells (English et al., 2013; Prockop et al., 2012) by acting on a large numbers of immune cell partners, not only in adaptive immune system but also in the innate one, mainly by soluble factors. This ability should be clearly an advantage in the treatment of neuromuscular disorders such as Duchenne Muscular Dystrophy by decrease the immunosuppressive regimen given to the patient, enhance stem cell graft in allogeneic recipient and acting on chronic inflammation that characterizes DMD tissues and negatively impacts the muscle regenerative potential. In our lab, we isolated a population of muscle derived-stem cells, that we called cMuStem cells, initially from healthy dog muscle tissue. We made the proof of concept of the systemic efficiency of this cells in the dystrophic animal model, the Golden Retriever Muscular Dystrophy (GRMD) dog (Rouger et al., 2011; Robriquet et al., 2015). Recently, in the lab, we succeed in isolated and characterized the same population from human muscle tissue, that we called hMuStem cells. It's a composite population composed of both mesenchymal-perivascular and myogenic cells, that display important proliferation capacity, oligopotency and the ability to fuse with muscle fibers in vivo. In this study, we tried to determine if hMuStem cells display immunosuppressive capacity in vitro. Interestingly, our preliminary data show the ability of hMuStem cells from different donors to modulate allogeneic T cell proliferation and to express immunomodulatory molecules such as prostaglandin-E2, indoleamin-2,3-deoxygenase-1, Heme oxygenase-1 and inducible nitric-oxide synthase-1. Finally, our data suggest that hMuStem cells are also able to interact with the complement system by inhibiting complement-mediated lysis of erythrocytes. This effect seems to be mediated by factor H, an alternative inhibitory complement pathway. Overall, our study is critical for the understanding of the interaction between MuStem cells and the immune system, as well as the design of safe and efficient allogeneic stem cell-based therapy for the treatment of muscle dystrophies.
Biography:(within 300-200 words)
Judith LORANT is in last year of PhD, in a French laboratory in Nantes, UMR 703 PAnTHER. Her thesis is devoted to identify and characterized a population of human muscle derived-stem cell population, called MuStem cells, and especially to determine if this population display immunomodulatory properties, such as mesenchymal stem cells.