Mesenchymal stem/stromal cell-derived extracellular vesicles, a potential new tool in regenerative medicinemonoliths

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Human mesenchymal stem/stromal cells (MSCs) represent a promising tool in regenerative medicine. Up to now, more than 1,000 NIH-registered clinical trials investigated their immunomodulatory and pro-regenerative therapeutic potential in various diseases, including graft-versus-host disease (GvHD) and ischemic stroke. Despite controversial reports regarding their efficacy, MSCs exert their beneficial effects in a paracrine manner rather than by cell replacement. In this context, extracellular vesicles (EVs) have been identified to execute the MSCs' therapeutic effects. Indeed, we observed beneficial therapeutic impacts of MSC-EVs in an acute GvHD patient, and showed at the example of an ischemic stroke model that systemically administered MSC-EVs and their parental MSCs induce neurological recovery comparably. Since MSC-EVs also mediate therapeutic activities in various other disease models without containing self-replicating capabilities, they are envisioned as next generation cell-free stem cell products in regenerative medicine.
It is our goal to optimize the MSC-EV production strategy in a scaled, GMP compliant manner and to set up an appropriate quality assurance platform to translate MSC-EVs into the clinics. One of the most challenging aspects in translating MSC-EVs into the clinics is the occurrence and recording of product heterogeneity. Currently, it is one of our most important missions to set up a strategy allowing to reduce product heterogeneity to a minimum, and to set up functional in vitro assays reliably predicting the therapeutic activity of given MSC-EV samples.