Title	Isolation of exosomes for drug delivery applications
Keywords (up to 5)	Mesenchymal stem cell, exosome, drug delivery
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Abstract	Stem cell therapy is applied in the management of difficult-to-treat or yet incurable diseases, although the therapeutic administration of living cells bears several risks. Stem cell-derived exosomes are prospective candidates to substitute cell-based therapies, as the safety concerns associated with living cells can be eliminated and their intrinsic therapeutic efficacy can be further improved by drug encapsulation. Therefore, this project aims at establishing a platform technology for the drug loading of stem cell exosomes. First, a well-defined isolation method needs to be optimized and validated to ensure a constant high quality exosome production. Thereafter, a loading method for the efficient encapsulation of anti-inflammatory drugs will be developed and the efficacy of drug-loaded exosomes will be tested in relevant *in vitro* and *in vivo* models. Exosomes derived from human bone marrow mesenchymal stem cells were isolated by ultracentrifugation and size exclusion chromatography and subsequently characterized following the recommendations of the International Society for Extracellular Vesicles. Briefly, particle size, concentration and morphology were analyzed by nanoparticle tracking analysis and electron microscopy. The total protein amount was quantified by bicinchoninic acid assay and exosomal and contamination markers were analyzed by western blot. The integrity of the exosomes was indirectly assessed by measuring the activity of a constitutive enzyme present on their surface. Ultracentrifugation was found to be superior to size exclusion chromatography as it provided enzymatically-active and intact exosomes with high yield and purity in a reproducible manner. Upon optimization of the ultracentrifugation protocol, it was found that the culturing time and centrifugal force were significantly influencing exosome yield and integrity. In conclusion, a robust isolation and characterization protocol for stem cell exosomes was set up. Further steps will consist in using these exosomes as natural drug delivery systems. This work was financially supported by the ETH research grant ETH-10 16-1.
References	1. Théry C, Amigorena S, Raposo G, Clayton A. *Current Protocols in Cell Biology* (2006). 3.22.1-3.22.29. 2. Luan X, Sansanaphongpricha K, Myers I, Chen H, Yuan H, Sun D. *Acta Pharmacologica Sinica* (2017). 754-763.