Off-the-Shelf CAR-T Therapy-using Hybrid NPs: Physicochemical Characterization

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Abstract

Ixaka (previously Rexgenero France) is a preclinical stage biotech company developing off-the-shelf and universal chimeric antigen receptor (CAR)-T therapy allowing in vivo targeting and transduction of T-cells.
Ixaka is producing bald-lentivectors lacking the VSV-G immunogenic protein which are later encapsulated in targeting ligand incorporated biodegradable, oligo-peptide modified poly(beta amino ester)s to obtain T-cell targeting hybrid nanoparticles (NPs). Further, these hybrid NPs are used as therapeutic agents to generate in vivo CAR-T therapy.

In the field of nanomedicine, physicochemical properties of nano-sized materials play a significant role on the in vivo fate of nanomaterials. Moreover, particle size and particle size distribution (PSD) are defined as the key parameters by health agencies for the manufacturing quality as well as the safety and efficacity of nano-sized particles. Therefore, a multispectral nanoparticle tracking analyzer (NTA), Viewsizer 3000 (HORIBA) was used as a high resolution, single particle analysis technique to determine PSD, particle concentration and the aggregation profile of both lentiviral vectors as starting material and hybrid NPs, as a final drug product. In addition, electrophoretic mobility of the NPs is also considered as one of the critical physicochemical parameters for in vivo fate of nanoparticles. Hence, electrophoretic mobility of the particles was determined using electrophoretic light scattering (ELS) measurements with a SZ-100Z2, Horiba instrument. Furthermore, ELS measurements allowed us to confirm the presence of the polymer coating on the hybrid NPs. Importantly, these analyses required very low amounts of bioproducts in their native form (without filtration or additional sample treatment). Consistent product specifications could be generated across several batches in time-efficient manner (NTA run takes 20 min - ELS run completed within 2 min).

All together our results confirm the power of HORIBA solutions for in process control during manufacturing but also for regulatory compliant characterization of lentivector/nanomedicine-based gene therapy products.

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