Quantification of TDP-43 in lymphoblasts from ALS patients and their exovesicles with QD-based multiplexing approach

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Amyotrophic Lateral Sclerosis (ALS) is a lethal neurodegenerative disease characterized a progresive loss of motor neurons, that yields muscle tone waste leading to paralysis. Currently, drug development is hampered due to the heterogeneity of the disease and the lack of knowledge of the mechanism triggering selective motor neuron death. TDP-43 is the main affected protein in ALS. Physiologically, TDP-43 is located at the nucleus, and in ALS, it is found aggregated in the cytoplasm. [1].

Molecular profiling is an innovative powerful technology for unravelling complex molecular pathways that underlie physiological and pathological processes. Quantum dots (QDs) are luminescent nanoparticles with a high potential to become promising tools to detect molecular mechanisms at the subcellular level enabling multiplexing applications.[2]

After studying QD penetration properties in lymphoblasts derived from patients, we determined that the nuclear penetration of antibody-conjugated QDs can be controlled [4] and thus an efficient manner to target ALS pathologic TDP-43 has been developed. This enables an automated rapid analysis of TDP-43 and its relation to other ALS key targets by immunofluorescence and the possibility of quantification by flow cytometry. Here we implement this methodology and study ALS pathology in this model derived from patients and its modulation upon drug treatment, as an approach towards personalized medicine in ALS starting from patient derived models. Finally we use these nanoparticles to phenotype exovesicles in our model of ALS.

References

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Figures

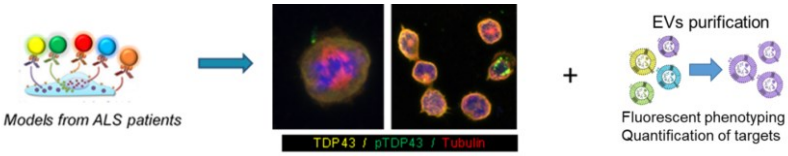

Figure 1: QDs multiplexing in lymphoblast from ALS patients targeting TDP-43 and analysis and phenotype of their exovesicles.