Charge specific CdSe/ZnS quantum dots enhance amyloid fibrillization of human insulin protein in physiological conditions

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CdSe/ZnS quantum dots (QD) are a unique nanomaterial capable of absorbing light in the UV-visible region and converting it through photoluminescence into emission in a narrow spectral region determined by their size. This photo property, the relatively small size of QD, the tenability of the QD surface chemistry and their superior photostability, as compared to conventional fluorescent dyes, make QD one of the perfect candidates for *in vivo*, *ex vivo*, and *in vitro* fluorescence labeling in biomedicine (1).

Recent studies have demonstrated the capacity of QD and other nanoparticles to interact with biomolecules *in vitro* and *in vivo*, forming the so-called hybrid materials in biological fluids. Furthermore these publications show the capacity of nanomaterials to act on the structure of surrounding biomolecules and to destabilize or to stabilize their structure under physiological conditions. It is known that some biomolecules called amyloid-prone proteins have a tendency to form pathologic fibers *in vivo* when their structure is destabilized (2). Conflicting results have underlined the capacity of different types of nanoparticles to enhance or reduce the speed of amyloid fiber formation without been able to clearly explain the mechanism responsible for these observation (3-5).

Thanks to the state-of-the-art CIC nanoGUNE Consolider platform of colloidal chemistry and surface chemistry we have been able to develop new, more stable and usable QD which have allowed us to identify the parameters involved in amyloid fiber formation and to create a general theory able to explain the results obtained previously by other research teams with different nanoparticles. The research work performed within this project includes:

- Synthesis of high quality Cd/Se core / ZnS shell hydrophobic QD of various well-defined sizes (6)
- Development of state-of-the-art solubilisation techniques for QD guaranteeing the aqueous stability and functionality of QD
- Development of surface chemistry techniques allowing to precisely modify the chemical function displayed at the surface of QD
- Creation of a characterization platform allowing the time-course analysis of rheological and photoluminescent properties of QD in various environmental conditions
- Analysis of the effect of QD presence on the kinetics of human insulin for various sizes of QD displaying various chemical functions at their surface.
- Identification of the environmental impact on *in vitro* QD-enhanced insulin fibrillization phenomenon
- Analysis of the effect of QD surface charge pattern on insulin fibrillization dynamics and identification of the optimum surface charge distribution/density for kinetic enhancement

References

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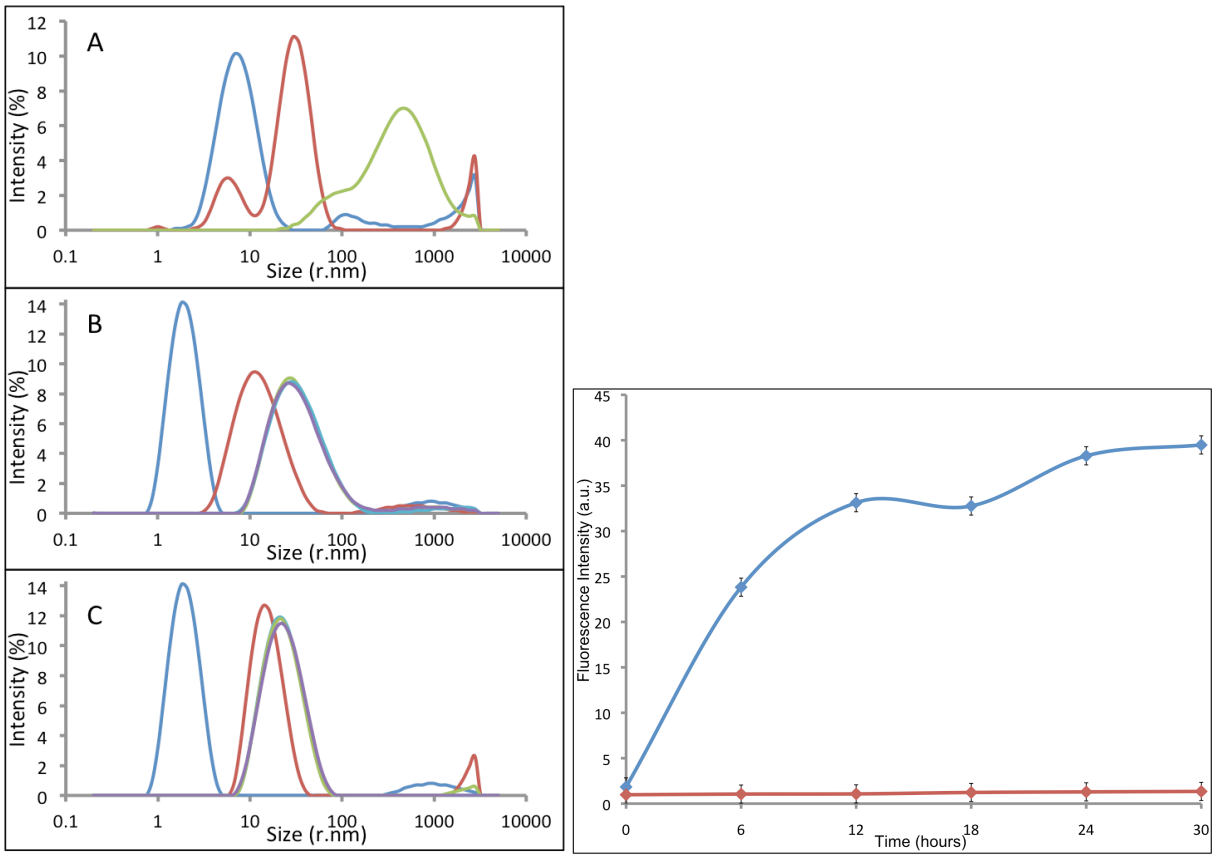
Figures



Legend:

Figure 1: Rheologic analysis of human insulin fibrillization in presence of QD presenting different chemical function at their surface.

Figure 2: Amylid specific time-course fluorescence assay of human insulin in presence (blue) or absence (red) of QD with specific chemical function surface distribution.