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Mitigating the Aggregation of Human Islet Amyloid Polypeptide with Nanomaterials

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Abstract : Human islet amyloid polypeptide (IAPP) is a hormone associated with glycemic control and type 2 diabetes. Biophysically, the chirality of IAPP fibrils has been little explored with respect to the aggregation and toxicity of the peptide. Biochemically, it remains unclear as for how protein expression in pancreatic beta cells may be altered by cell exposure to the peptide, and how such changes may be mitigated by nanoparticle inhibitors for IAPP aggregation. In this study, we first demonstrated the elimination of the IAPP nucleation phase and shortening of its elongation phase by silica nanoribbons. This accelerated IAPP fibrillization translated to reduced toxicity, especially for the right-handed silica nanoribbons, as revealed by cell viability, helium ion microscopy, as well as zebrafish embryo survival, developmental and behavioral assays. We then examined the proteomes of βTC6 pancreatic beta cells exposed to the three main aggregation states of monomeric, oligomeric and amyloid fibrillar IAPP, and compared that with cellular protein expression modulated by graphene quantum dots (GQDs). A total of 29 proteins were significantly regulated by different forms of IAPP, and the majority of these proteins were nucleotide-binding proteins. A regulatory capacity of GQDs against aberrant protein expression was confirmed. These studies have demonstrated the great potential of employing nanomaterials targeting the mesoscopic enantioselectivity and protein expression dysregulation in pancreatic beta cells.

Keywords : graphene quantum dots, IAPP, silica nanoribbons, protein expression, toxicity
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