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Effect of glycation on amyloid aggregation and cytotoxicity

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Abstract

Neurodegenerative diseases are associated with misfolding and deposition of specific proteins, either intra or extracellularly in the nervous system. Advanced glycation end products (AGEs) originate from different molecular species that become glycated after exposure to sugars. Several proteins implicated in neurodegenerative diseases have been found to be glycated *in vivo* and the extent of glycation is related to the pathologies of the patients. Although it is now accepted that there is a direct correlation between AGEs formation and the development of neurodegenerative diseases, several questions still remain unanswered: whether glycation is the triggering event or just an additional factor acting on the aggregation pathway. To this concern, in the present study we have investigated the effect of glycation on the aggregation pathway of the amyloidogenic W7FW14F apomyoglobin. Although this protein has not been related to any amyloid disease, it represents a good model to resemble proteins that intrinsically evolve toward the formation of amyloid aggregates in physiological conditions. We show that D-ribose, but not D-glucose, rapidly induces the W7FW14F apomyoglobin to generate AGEs in a time-dependent manner and protein ribosylation is likely to involve lysine residues on the polypeptide chain. Ribosylation strongly affects its aggregation kinetics producing amyloid fibrils within few days. Cytotoxicity of the glycated aggregates has also been tested using a cell viability assay. These results open new perspectives for AGEs biological role as they can be considered not only a triggering factor in amyloidosis but also a player in later stages of the aggregation process.

Biography

Clara Iannuzzi obtained a degree in Chemistry at University Federico II of Naples (Italy) in 2002 and a PhD in Cellular Biochemistry at Seconda Università di Napoli (Italy) in 2006. Between 2006 and 2012 she held a Career Development fellowship at MRC-National Institute for Medical Research in London (UK). At present she is Researcher at Seconda Università di Napoli and Associate Researcher at CNR- Institute of Protein Biochemistry (Naples, Italy). She has published many research papers on peer-reviewed journals in the field of biochemistry and molecular biophysics.

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