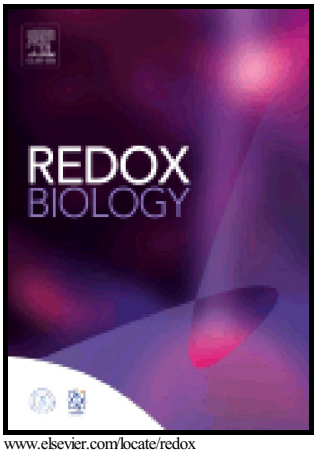

www.elsevier.com/locate/redox

Protein aggregation into insoluble deposits protects from oxidative stress

Anita Carija, Susanna Navarro, Natalia Sanchez de Groot, Salvador Ventura

PII: S2213-2317(17)30125-8
DOI: http://dx.doi.org/10.1016/j.redox.2017.03.027
Reference: REDOX622

To appear in: *Redox Biology*

Cite this article as: Anita Carija, Susanna Navarro, Natalia Sanchez de Groot and Salvador Ventura, Protein aggregation into insoluble deposits protects from oxidative stress, *Redox Biology,* http://dx.doi.org/10.1016/j.redox.2017.03.027

Protein aggregation into insoluble deposits protects from oxidative stress

Anita Carija[a], Susanna Navarro[a], Natalia Sanchez de Groot[b,c], Salvador Ventura[a*]

[a]Institut de Biotecnologia i Biomedicina and Departament de Bioquímica i Biologia Molecular, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Spain

[b]Centre for Genomic Regulation (CRG), The Barcelona Institute for Science and Technology, Dr. Aiguader 88, 08003 Barcelona, Spain

[c]Universitat Pompeu Fabra (UPF), Barcelona, Spain

[*]Correspondence to: Institut de Biotecnologia i de Biomedicina, Parc de Recerca UAB, Mòdul B, Universitat Autònoma de Barcelona, E-08193 Bellaterra, Barcelona. salvador.ventura@uab.es

Abstract

Protein misfolding and aggregation has been associated with the onset of neurodegenerative disorders. Recent studies demonstrate that the aggregation process can result in a high diversity of protein conformational states, however the identity of the specific species responsible for the cellular damage is still unclear. Here, we use yeast as a model to systematically analyse the intracellular effect of expressing 21 variants of the amyloid-ß-peptide, engineered to cover a continuous range of intrinsic aggregation propensities. We demonstrate the existence of a striking negative correlation between the aggregation propensity of a given variant and the oxidative stress it elicits. Interestingly, each variant generates a specific distribution of protein assemblies in the cell. This allowed us to identify the aggregated species that remain diffusely distributed in the cytosol and are unable to coalesce into large protein inclusions as those causing the highest levels of oxidative damage. Overall, our results indicate that the formation of large insoluble aggregates may act as a protective mechanism to avoid cellular oxidative stress.