Design of Synthetic Polymer Nanoparticles That Facilitate Resolubilization and Refolding of Aggregated Proteins

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Denaturation and aggregation of proteins is one of the most serious problems in the utilization of proteins. Therefore, materials that stabilize the native structure of proteins and/or facilitate refolding of denatured proteins are of significant interest. In living cells, protein chaperones facilitate refolding of denatured proteins and/or nascent proteins. However, little has been reported about materials that facilitate resolubilization and refolding of aggregated proteins. [1,2]

In this study, we aimed to design polymer hydrogel nanoparticles (NPs) capable of facilitating resolubilization and refolding of an aggregated protein. Multifunctional acrylamide-based hydrogel NPs were utilized as platform[3]. Lysozyme, a positively charged glycoside hydrolase (isoelectric point = 9.3, molecular weight = 14.3 kDa) was selected as the model substrate protein. NPs with various combinations of functional groups and populations were prepared. Capability of each NP to facilitate resolubilization. NPs designed to interact strongly with denatured lysozyme and relatively weakly with native lysozyme, facilitated resolubilization and refolding of aggregated lysozyme (Figure 1). Such NPs could be prepared by copolymerizing optimized combinations and populations of functional monomers. The refolded lysozyme showed native conformation and enzymatic activity. Eleven grams of aggregated protein was refolded by 1 g of NPs. However, NPs having low affinity to denatured lysozyme and NPs having high affinity to both denatured and native lysozyme showed relatively low facilitation activity. Our results suggest a potential strategy for the design of artificial chaperones with high facilitating activity.

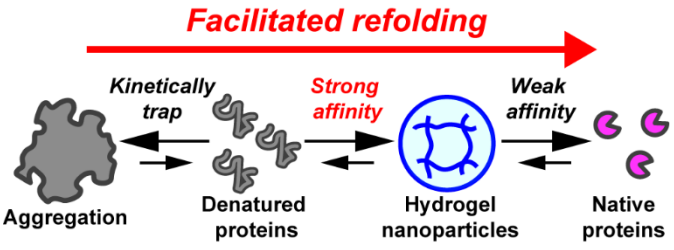

Figure 1. Schematic illustration of facilitated disaggregation by hydrogel nanoparticles

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2) Akiyoshi, K.; Deguchi, S.; Moriguchi, N.; Yamaguchi, S.; Sunamoto, J. Macromolecules 1993, 26, 3062−3068.

3) Hoshino, Y.; Urakami, T.; Kodama, T.; Koide, H.; Oku, N.; Okahata, Y.; Shea, K. J. Small 2009, 5,

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