Materials Science-2013

OMICS Group Conferences
Accelerating Scientific Discovery

2nd International Conference and Exhibition on
Materials Science & Engineering

October 7-9, 2013 Hampton Inn Tropicana, Las Vegas, USA

Structured PEGs for manipulation of biological macromolecules

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Abstract

Polyethylene glycol (PEG) is one of the most popular water-soluble organic compounds, which has been widely used for biological and medicinal applications. We have been interested in structured PEGs, non-linear PEG analogues having specific two or three-dimensional molecular shapes, with the expectation that these molecules would have distinctive physical or chemical characteristics compared to the conventional linear PEGs. In order to develop structured PEGs having two- or three-dimensional molecular shapes, we have investigated synthetic methods to connect several tetraethylene glycol (TEGs) units with pentaerythritol. This molecular design strategy also enables to obtain PEG analogues in a monodisperse form, which can be a significant advantage over the intrinsically polydisperse conventional PEGs, to allow precise evaluation of their properties at a molecular level. As the first example of the structured PEG, we have developed macrocyclic triangle PEG (**1**) that consists of three TEG and pentaerythritol units, respectively. Interestingly, this triangle molecule exhibits hydrophilicity/hydrophobicity switching at lower temperature than the linear PEG with a comparable molecular weight. Furthermore, **1** effectively suppressed thermal aggregation of lysozyme even after 30-min heating at 90 ºC, while lysozyme alone tends to denature around 80 ºC to give precipitates. After the heating, lysozyme showed nearly 80% of the residual activity at 20 ºC. CD and NMR spectroscopic studies revealed that, in the presence of **1**, the higher-order structures of lysozyme are preserved at high temperatures, whereby the native conformation is recovered after cooling. In contrast, the linear PEGs have no such features.

Biography

Kazushi Kinbara has completed his PhD in 1996 from the University of Tokyo. In 2008, he was promoted to Professor of the Institute of Multidisciplinary Research for Advanced Materials, Tohoku University. His research interests include (1) development of biomimetic molecules, (2) supramolecular chemistry of macromolecules, and (3) protein engineering.