Biomimetic Synthesis of Functionalized Silica Particles

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Biomimetic methods for the synthesis of nanomaterials are attractive because they are especially mild and allow for incorporation of otherwise sensitive functional biomolecules. Biomimetic synthesis of silica particles can be accomplished by use of silaffin peptides that originally derive from proteins involved in silica deposition in the cell walls of diatoms [1]. Among silaffin peptides, the peptide R5 is particularly effective in precipitation of ordered silica particles from a solution of silicic acid at room temperature and neutral pH [2]. Use of R5 has enabled efficient encapsulation of bio-active substrates within the inner matrices of silica particles and resulted in syntheses of biologically functional silica materials [3]. In order to accomplish this, R5 peptide was linked to small molecules as well as recombinant proteins by using methods such as expressed protein ligation [4, 5]. Nevertheless, the non-covalent nature of the interaction between the cargo and silica means that it is challenging to control the retention and release of the cargo in a precise manner, with certain substrates continuously leaching out of the particles (Fig. 1A). While this property is valuable in some biomedical applications, a stronger covalent conjugation of biomimetic silica would be highly valuable as it would greatly stabilize the conjugated functional groups. Such covalent conjugation could also make it possible to synthesize multifunctional silica particles with functional groups attached both via the silaffin peptide and via the covalent bonds with silica.

We report on a new method of biomimetic synthesis of hybrid silica particles with covalently attached functional groups. The particles have been prepared by use of the R5 peptide at room temperature and neutral pH. The covalent functionalization was accomplished by use of a custom silylated building block [6]. It was possible to modify silica particles covalently in this manner with a fluorescent dye (Fig. 1B). The resulting particles retained spherical morphology and were observable by fluorescence microscopy. Use of these fluorescent particle conjugates enabled visualization of the uptake of silica particles by macrophages derived from the THP-1 cell line.

In addition, we demonstrated that the newly developed method can also be used in order to prepare multi-functional silica particles. It was possible to synthesize particles that have been simultaneously labeled by the cyanine and fluorescein dyes, where the former was loaded together with the R5 peptide and the latter was covalently linked to silica (Fig. 1C). The properties of the resulting materials, such as release kinetics of the cargo dyes, were carefully analyzed by electron and fluorescence microscopies as well as bio-analytical chemistry techniques.

The mild nature of this synthetic approach means that it is potentially applicable for a wide range of functional substrates, including proteins and nucleic acids. The use of this method can, therefore, have a significant impact in bio-medical research, as it enables easy access to hybrid bio-inorganic materials with highly tunable functionalities.

References

[1] N. Kröger, R. Deutzmann, M. Sumper, Science 286 (1999) 1129–1132.
[2] N. Kröger, R. Deutzmann, M. Sumper, J. Biol. Chem. 276 (2001) 26066–26070.
[3] C.C. Lechner, C.F. Becker, Mar. Drugs 13 (2015) 5297–5333.
[4] C.C. Lechner, C.F.W. Becker, Bioorg. Med. Chem. 21 (2013) 3533–3541.
[5] C.C. Lechner, C.F. Becker, Biomater. Sci. 3 (2015) 288–297.
[6] J. Ciccione, T. Jia, J.-L. Coll, K. Parra, M. Amblard, S. Jebors, J. Martinez, A. Mehdi, G. Subra, Chem. Mater. 28 (2016) 885–889.

Figures

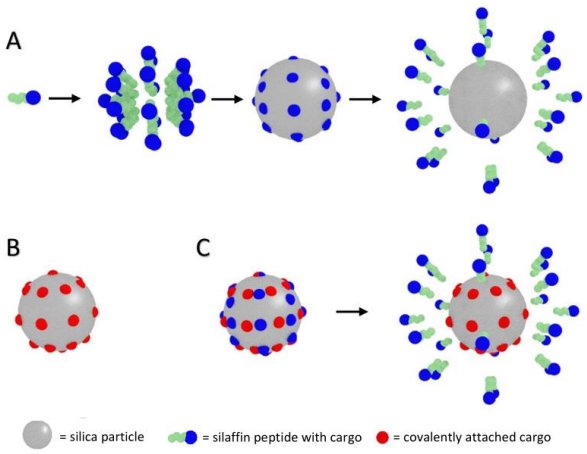

Figure 1. Silica particle fictionalization: A) biomimetic silica particles that release silaffin-cargo; B) silica particle covalently conjugated with cargo; C) multifunctional silica particles that release silaffin cargo but retain covalently attached cargo.