## **Biohybrid Nanoparticles for Nanomedicine and Sensing**

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Proteins are sequence specific and geometrically defined macromolecules representing the central framework of all biological processes in Nature. Their precise physical architecture and consequent biochemical functions are unique and unrivalled in the synthetic world, providing an impetus for the incorporation of proteins into the development of contemporary hybrid materials. Unlike conventional polymers, their repertoire of chemical functionalities at discrete positions facilitates the grafting of designated synthetic moieties [1] to achieve a nanoscale construct with exceptional macromolecular definition.[2,3] Through these synthetic appendages, supramolecular polypeptides [4] and protein-polymer biohybrids [2,3] can be chemically programmed to possess new and improved physico-chemical properties while simultaneously exhibiting unique biological behavior.

We have designed multifunctional copolymers derived from proteins[2] that possess attractive features such as an accurately known length and a defined number of functional groups at distinct locations within the peptide backbone, low size-dispersity as well as intrinsic biocompatibility. Such copolymers allow the stabilization of various nanoparticles such as quantum dots (QDs) [5,6] or nanodiamonds [7] via multivalent interactions. A pronounced responsiveness of the emission intensity of these nanoparticles was found in the presence of DNA [6] or upon pH [5] changes which is attractive for achieving biocompatible sensors for in vitro and in vivo applications. In addition, multiple drug molecules with different modes of action as well as cell targeting entities were attached based on sophisticated peptide chemistry. Such protein-derived nanoparticles have a great potential for in vivo therapy and pave the way to intelligent vehicles for nanomedicine applications.

- [1] T. Wang, A. Pfisterer, Y. Wu, O. Dumele, M. Lamla, K. Müllen, T. Weil "A Versatile and Bioorthogonal Approach for the Cross-Conjugation of DNA, Proteins and Peptides via the pH Switch", Chem. Sci. 4 (2013) 1889-1894.
- [2] Y. Wu, G. Pramanik, K. Eisele, T. Weil "Controlled synthesis of defined polypeptide copolymers from protein precursors", Biomacromolecules 13, 6 (2012) 1890-1898.
- [3] Y. Wu, S. Ihme, M. Feuring-Buske, K. Eisele, M. Lamla, C. Buske, T. Weil, "Tailored albumin copolymers for high capacity loading and two-step release of doxorubicin with enhanced anti-leukemia activity", Adv. Healthcare Mater. 2, 6 (2013) 884-894.
- [4] M. Yolamanova, F. Arnold, O. Zirafi, J. Müller, D. Sauter, C. Goffinet, M. Reisser, V. Vas, H. Geiger, O. Lunov, T. Simmet, J. Bohne, K. Eisele, C. Meier, T. Weil, K. Schwarz, F. Kirchhoff, J. Münch, "Small amyloidogenic HIV-1 gp120 fragments boost retro-and lentiviral gene transfer" Nature Nanotechnol., 8, 2 (2013) 130-136.
- [5] Y. Wu, S. Chakrabortty, R. A. Gropeanu, J. Wilhelmi, X. Yang, K. S. Er, S. L. Kuan, K. Koynov, Y. Chan, T. Weil, "pH-Responsive Quantum Dots via an Albumin-Polymer Surface Coating" J. Am. Chem Soc. 132, 14, (2010) 5012–5014.
- [6] Y. Wu, K. Eisele, M. Doroshenko, K. Koynov, T. Weil, "A Quantum Dot Photoswitch for DNA Detection, Gene Transfection and Live-Cell Imaging" Small, 8, 22 (2012) 3381–3537.
- [7] A. Ermakova, G. Pramanik, J. Cai, G. Algara-Siller, U. Kaiser, T. Weil, Y. K. Tzeng, H.-C. Chang, L. P. McGuinness, M. B. Plenio, B. Naydenov, F. Jelezko, "Detection of few metallo-protein molecules using color centers in nanodiamonds" Nano Lett. 13, 7 (2013) 3305-3309.

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