Engineered ferritin nanoparticles for biomedical applications: tailoring the external and internal surfaces for enhanced functionality

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Ferritin, a naturally occurring iron storage protein, has acquired significant attention as a versatile and promising tool for a wide range of biomedical applications, owing to its inherent biocompatibility and unique characteristics. Due to its 24-subunit shell surrounding an internal cavity, ferritin offers an excellent platform for several biomedical purposes including drug delivery. Its hollow sphere architecture allows for modifications of both the external surface, creating new binding sites for ligands, antibodies, or other targeting moieties, as well as the internal cavity, facilitating the encapsulation of diverse therapeutic cargoes. The outer surface can be genetically engineered, for instance, by adding therapeutic peptides to the N-terminus of each subunit. This approach aims to overcome limitations associated with the therapeutic use of free peptides, such as rapid renal clearance and reduced bioavailability. Additionally, the multivalent effect provided by the 24-mer ferritin structure enhances the therapeutic potential of these peptides. An example of this application involves investigating peptides that can interfere with the interaction between the SARS-CoV-2 Spike protein and the ACE2 receptor, potentially offering therapeutic benefits for countering viral infections. Similarly, the internal surface of ferritin can be engineered by fine-tuning its polarity to enhance the encapsulation efficiency of molecules with different properties. For example, the introduction of a few hydrophobic amino acid residues per subunit can render the protein cage suitable for encapsulating hydrophobic anticancer drugs, such as ellipticine. This modification ensures effective drug loading, protection against premature drug release, and controlled drug release kinetics. Ferritin's versatility, along with the possibility of being modified both externally and internally, holds promise for advancing drug delivery systems and addressing various biomedical challenges. By tailoring the surface and the internal cavity of ferritin nanoparticles, efficient and targeted therapies can be designed for a variety of diseases and conditions.