FERRITIN-BASED HYBRIDS FOR VACCINES, DRUG DELIVERY AND IMAGING PLATFORMS

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Ferritin is a 24-subunit protein nanocage that combines high stability, biocompatibility, and a well-defined hollow architecture, making it an attractive platform for recombinant vaccines, targeted drug delivery, and multimodal imaging. In this contribution, we summarize recent progress in ferritin-based hybrid nanoparticles, i.e. cages assembled from distinct ferritin subunits or subunit-conjugates that enable modular control of surface occupancy, ligand density, cargo loading, and circulation properties [1], [2]. Natural heteropolymers, including mammalian H/L ferritins and several non-mammalian hybrids, show that successful cage formation depends not only on sequence identity but also on conserved structural form factor and conformational flexibility of the protomers. Engineered hybrids extend this principle to multifunctional systems for mosaic vaccines, theranostic carriers, and neutron capture therapy.

Special attention will be paid to structural studies by small-angle scattering. Time-resolved SAXS has shown that ferritin reassembly proceeds through folded dimeric and higher oligomeric intermediates and is strongly influenced by electrostatic screening and solution conditions [3]. Complementary SAXS/SANS studies of apoferritin provide low-resolution shell parameters, reveal concentration-dependent interparticle effects, and offer a convenient benchmark for validating hollow-cage integrity in solution. For hybrid ferritins, these approaches are especially valuable because they allow one to verify whether antigen fusion, PEGylation, peptide targeting, or cargo encapsulation preserves the cage geometry. In addition, SANS at pulsed neutron sources such as YuMO/IBR-2 is well suited for the analysis of ferritin-based supramolecular assemblies because ferritin behaves as a structurally well-defined hollow shell with characteristic scattering features. Thus, SAXS/SANS can serve not only as mechanistic tools for studying self-assembly, but also as a practical layer of structural quality control for biomedical ferritin constructs [4].

Finally, we conclude that ferritin hybrids are among the most promising modular protein nanoplatforms for immunology and theranostics, and that their further translation will depend on combining rational subunit engineering with routine SAXS/SANS characterization of assembly pathways, cage integrity, and structural heterogeneity.

The study was supported by the Ministry of Science and Higher Education of the Russian Federation (agreement 075–03–2026-305, project FSMG-2025-0003).

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