

Apoferritin structure and technological potential

Název:

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Datum: 7. 03. 2014

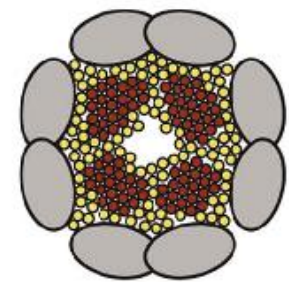
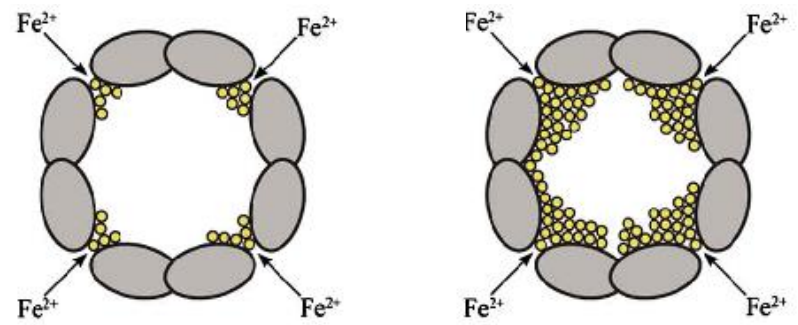
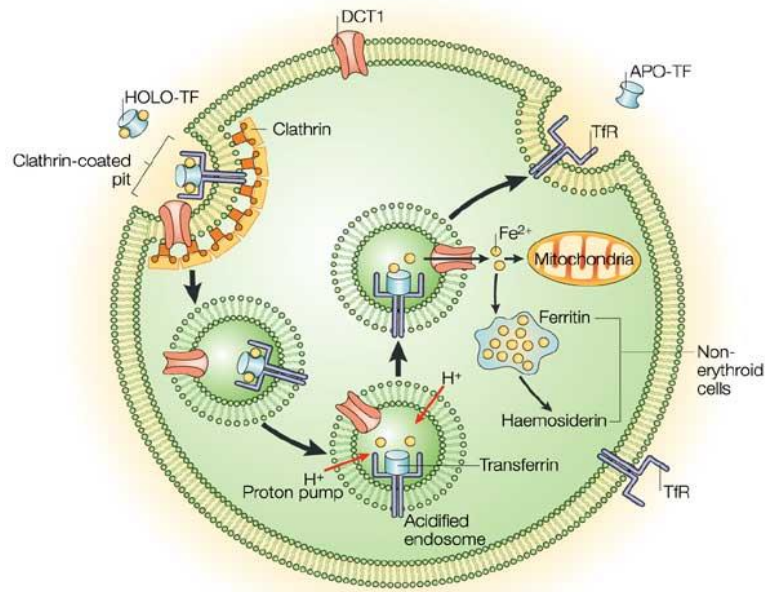
Reg.č.projektu: CZ.1.07/2.3.00/20.0148

Název projektu: Mezinárodní spolupráce v oblasti "in vivo" zobrazovacích technik

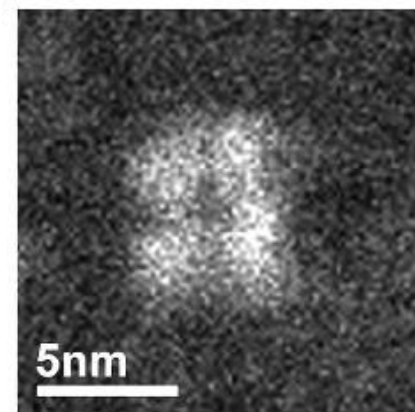


Ferritins

- Ubiquitous, intracellular proteins,
- Iron storage and detoxifying molecule in most organisms throughout evolution.



- Fe^{2+} coordinated to O and OH
- Fe^{3+} in ferrihydrite crystal structure
- Protein shell sub-unit

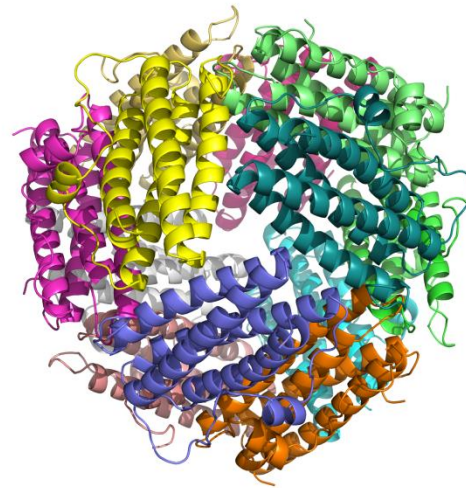
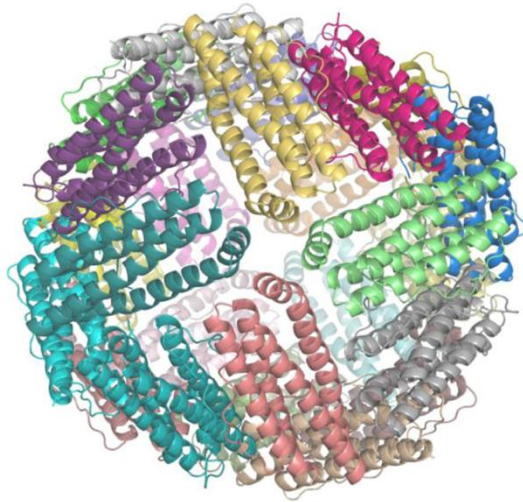
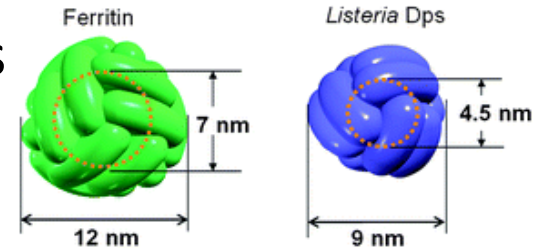


Rouault *et al.* *Nature Reviews Neuroscience*, 14 (8), 2013.

Ferritin proteins superfamily



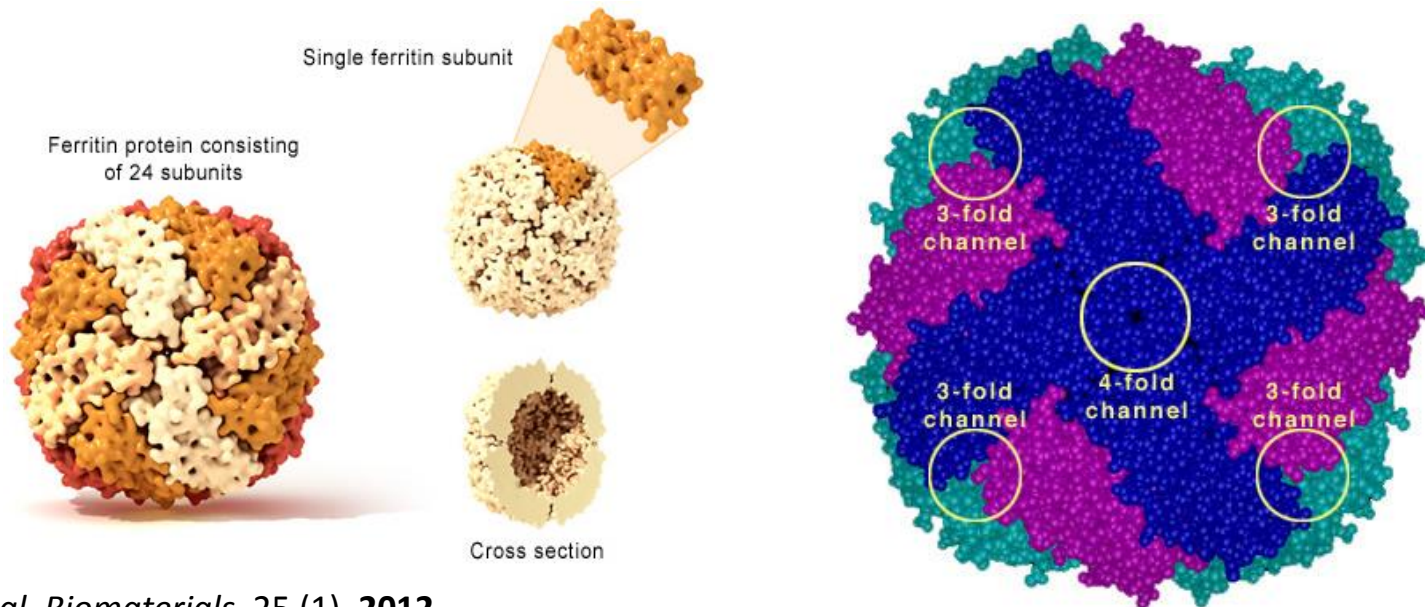
- Classical ferritins (FRTs),
 - The bacterioferritins (BFRs),
 - The DNA-binding proteins from starved cells (DPSs) – Miniferritin
- Maxiferritins



Bou-Abdalah *et al.* *Journal of American Chemical Society*, 130 (52), 2008.

Structure

- 24 (12) subunits – spherical cage-shaped protein shell folded in a bundle of four α -helices,
- Two types of subunits *H*-; and *L*-type (53 % sequence identity).



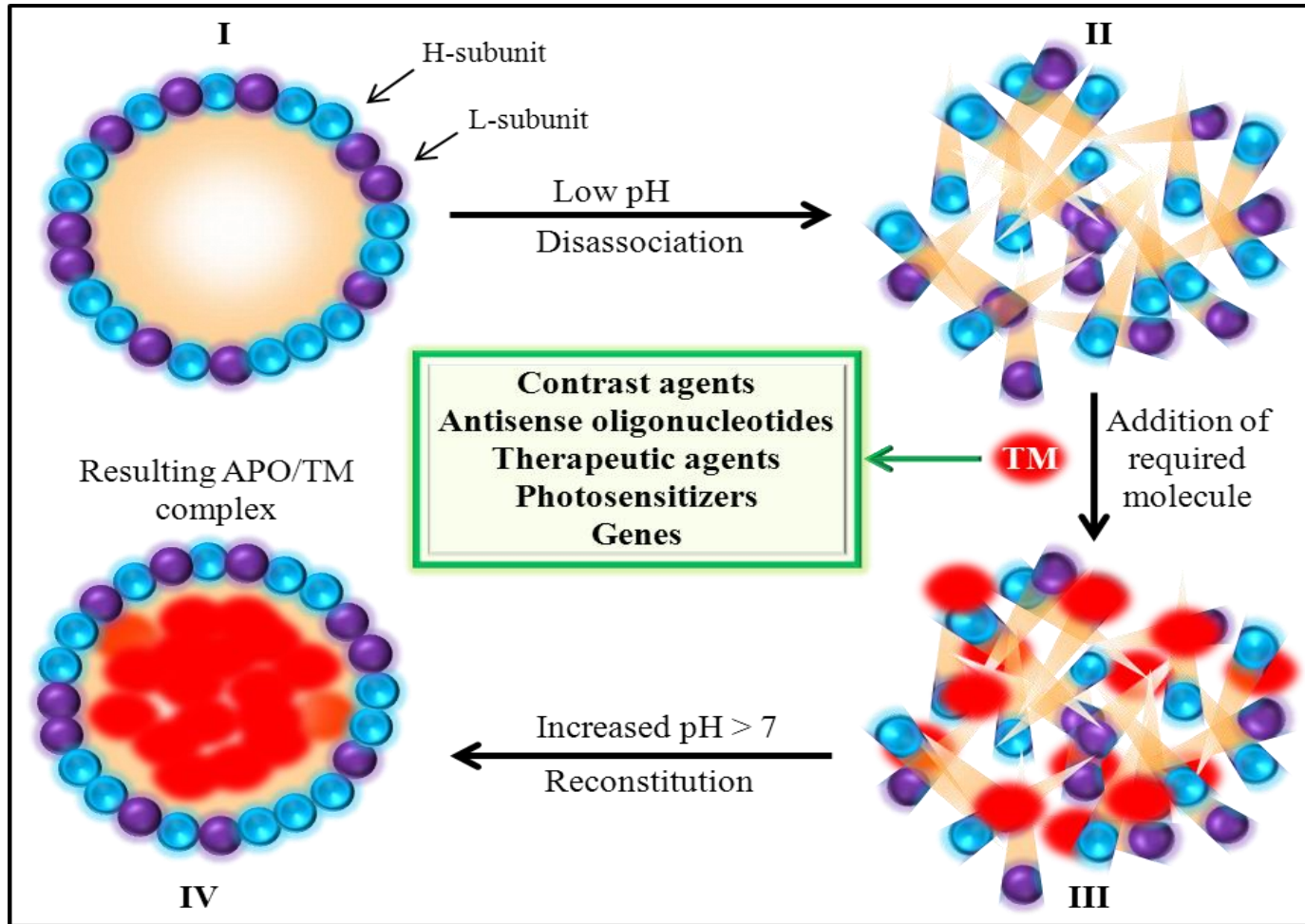
Tian *et al. Biomaterials*, 25 (1), 2012.

Structure



- Cavity with the inner and outer diameters 7-8; 12-13 nm,
- pH-dependent **SELF-ASSEMBLY** ability !!!
- Low pH (< 4) – reversible disassociation into all of 24 subunits.
- Increased pH (> 7) – reconstitution.
- Below pH 0.8 aggregation due to irreversible denaturation.

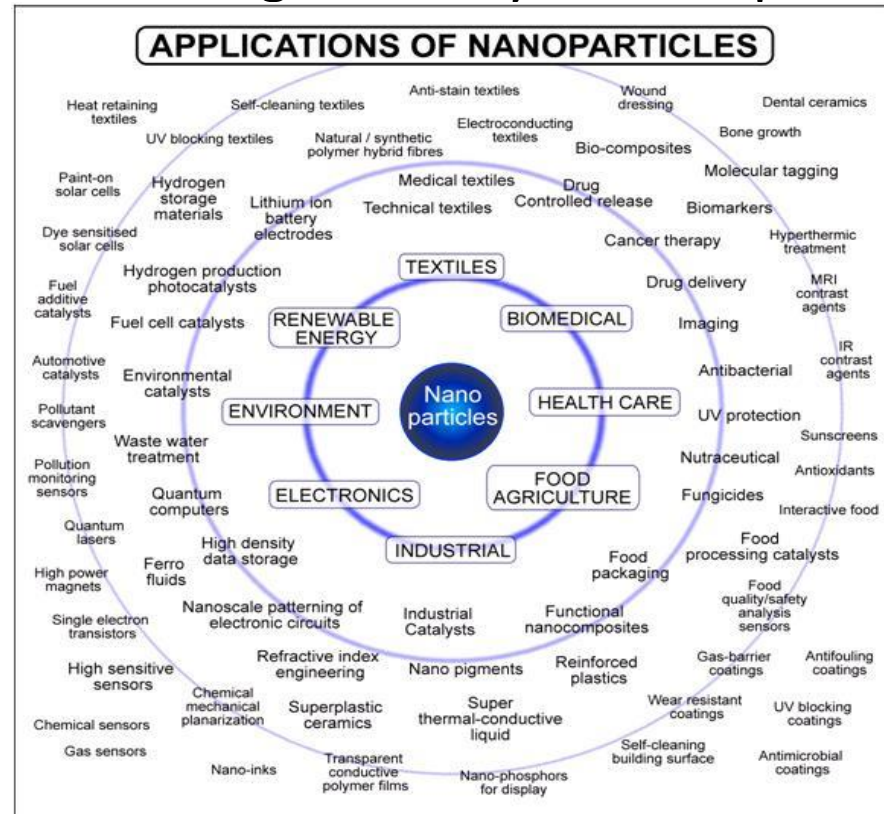
Self-assembly



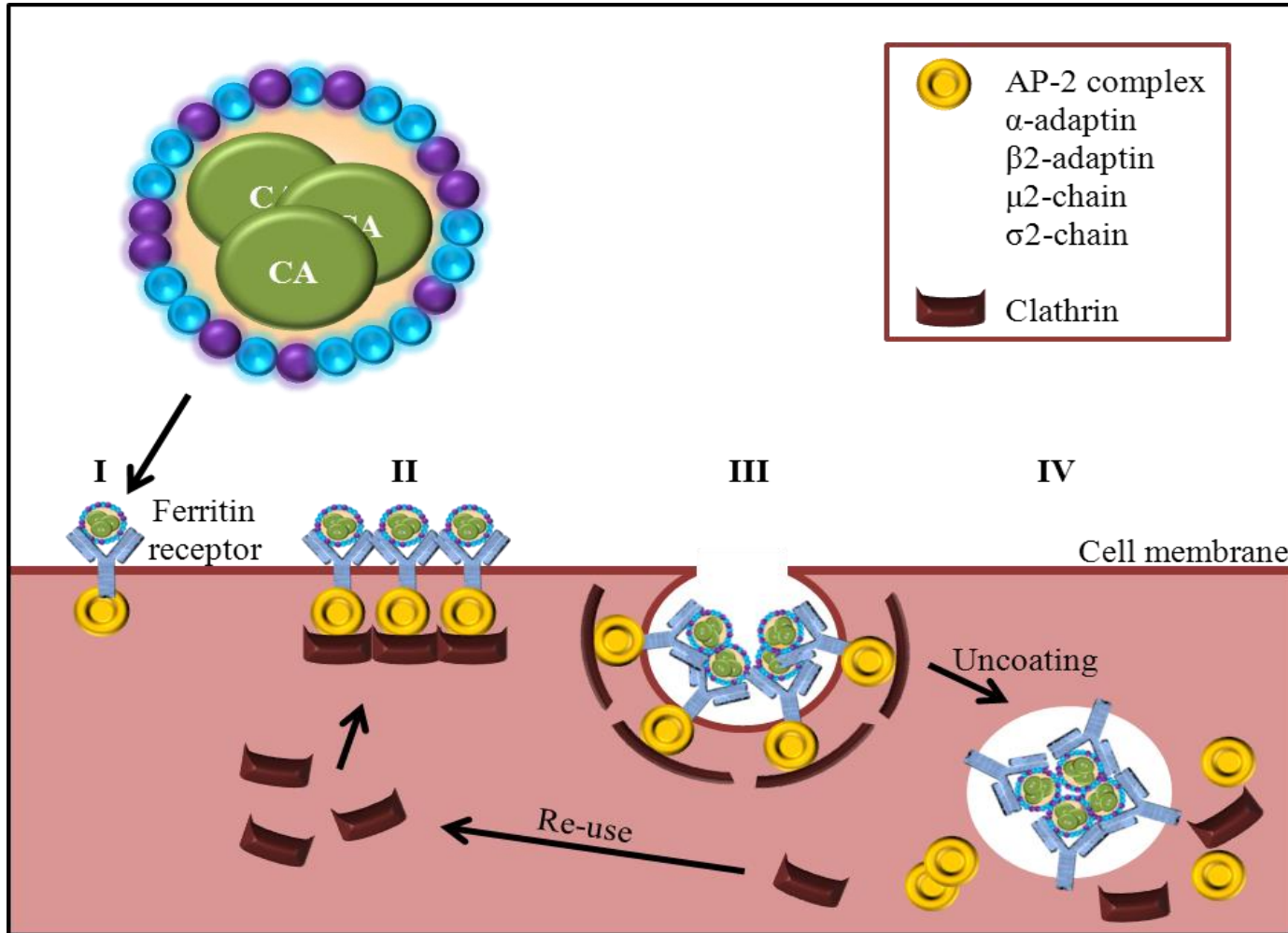
Why apoferritin?



- Nanotoxicology,
- Delivery systems requirements - biodegradability, biocompatibility and non-toxicity,
- Potential to be modified,
- Size-uniformity.



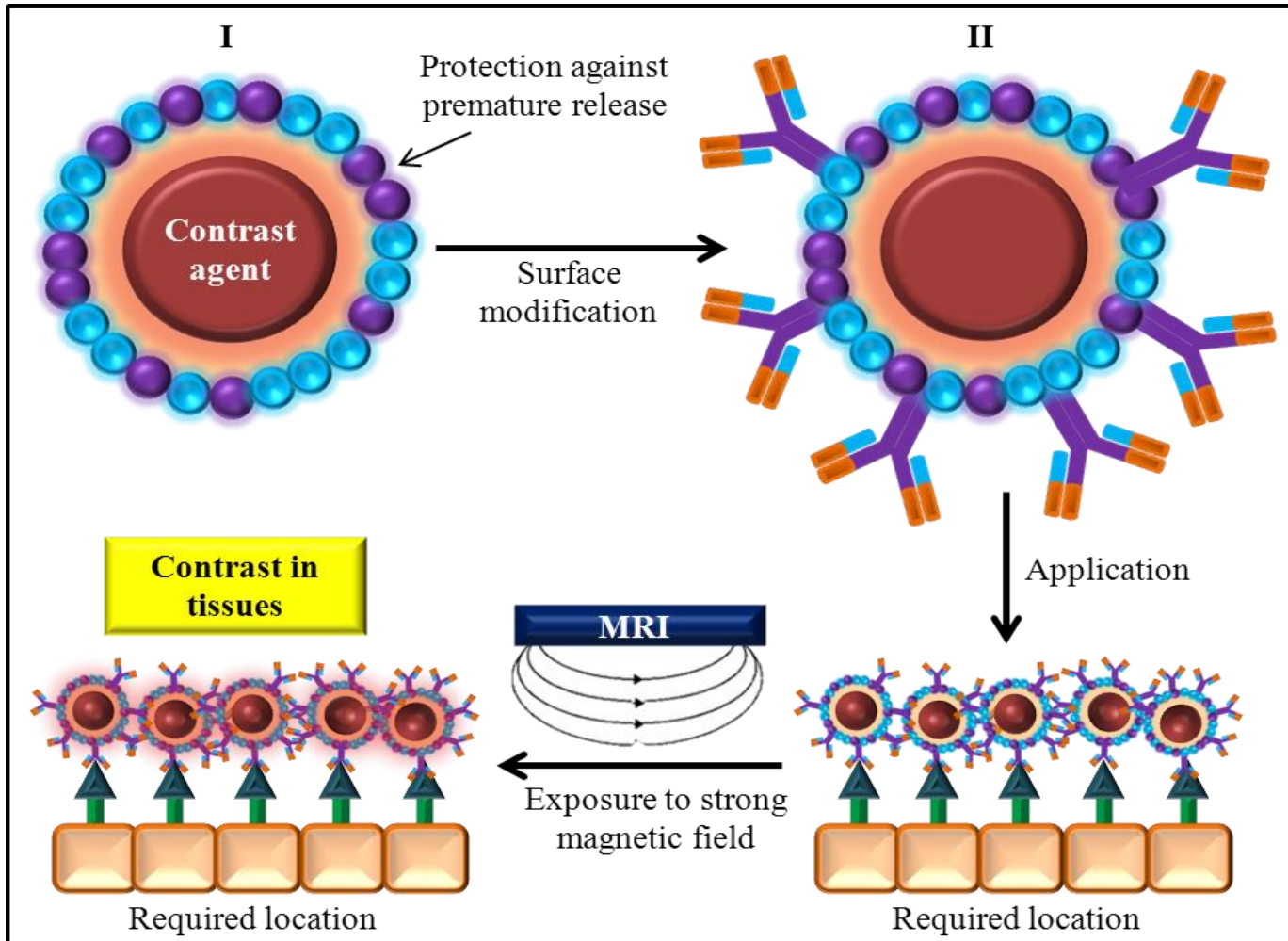
Delivery



Cargo	Complex	Application	Apo ferritin effect
Doxorubicin	APO-DOX	-	Encapsulation concept
Doxorubicin	APO-DOX	-	Drug leakage elimination
Doxorubicin	MPs@APO-DOX	-	Encapsulation and modification through MPs
Cis-; carboplatin	APO-cis-; carPt	-	Improvement of drugs toxicity profiles
Cis-; oxali-; carboplatin	APO-cis-; oxali-; carPt	PC12	Enhancement of platinum-based drugs uptake
Daunorubicin	APO-DNR-PLAA	-	Modification to improve the drug encapsulation
Curcumin, Gadolinium	APO-Cur-Gd	Mice with thioacetamide-induced hepatitis	Enhancement of Cur and Gd stability and bioavailability
5-fluorouracil	APO-AuNPs-5-FU	HepG2	Chemosensitization, decrease of drug IC ₅₀
X	pG, H-tags@APO-X	Capan-1	Possibility to be modified with Abs, or NPs to be selective
PbS Quantum dots	APO-PbSQDs	CRC	Platform for theranostics – imaging and treatment
X	APO-BIBA-PNIPAAm-DMIAAm	-	Surface modification to provide specificity
Doxorubicin	APOfilm-DOX	-	Controlable drug delivery and release
Haemagglutinin	APO-HA	Ferrets	Immunization of control animals towards H1N1 virus challenge

APO - apoferritin; **DOX** - Doxorubicin; **MPs** - Magnetic particles; **PC12** - Rat pheochromocytoma cell line; **PLAA** - Poly-L-aspartic acid; **Cur** - Curcumin; **Gd** - Gadolinium; **5-FU** - 5-fluorouracil; **AuNPs** - Gold nanoparticles; **HepG2** - Liver hepatocellular cells; **X** - No cargo defined; **pG** - Protein G; **H-tags** - His-tags; **Capan-1** - Human pancreatic ductal adenocarcinoma cell line; **Abs** - Antibodies; **NPs** – Nanoparticles; **PbS** – Lead(II) sulphide; **QDs** – Quantum dots; **CRC** – colorectal carcinoma cells; **BIBA** - 2-bromo-isobutyric acid; **PNIPAAm** - Poly(*N*-isopropyl acrylamide); **DMIAAm** - 2-(dimethyl maleinimido)-*N*-ethyl-acrylamide; **APOfilm** – Apoferritin mesoporous film; **HA** – Haemagglutinin.

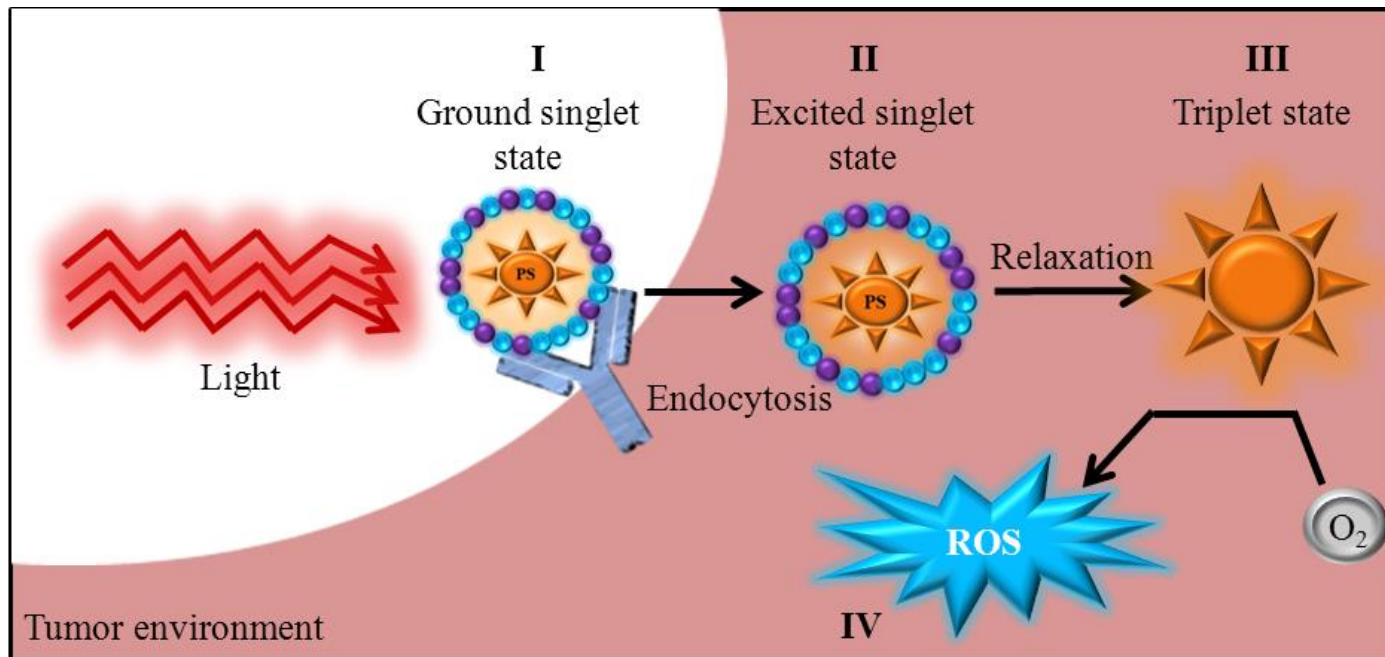
MRI



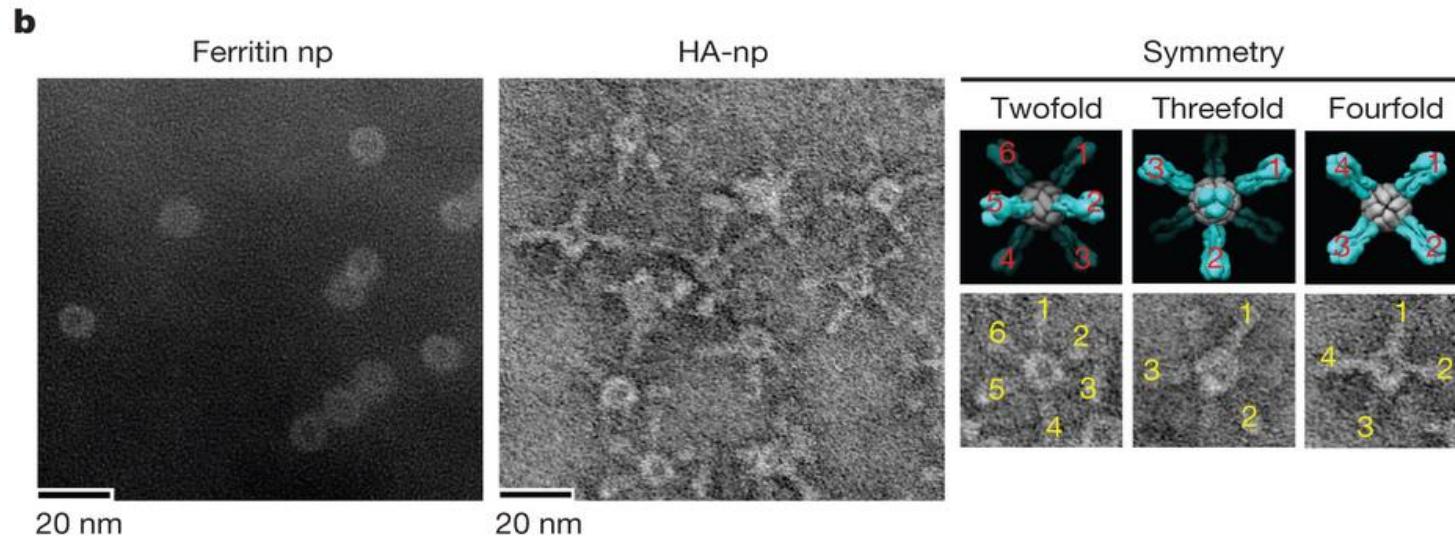
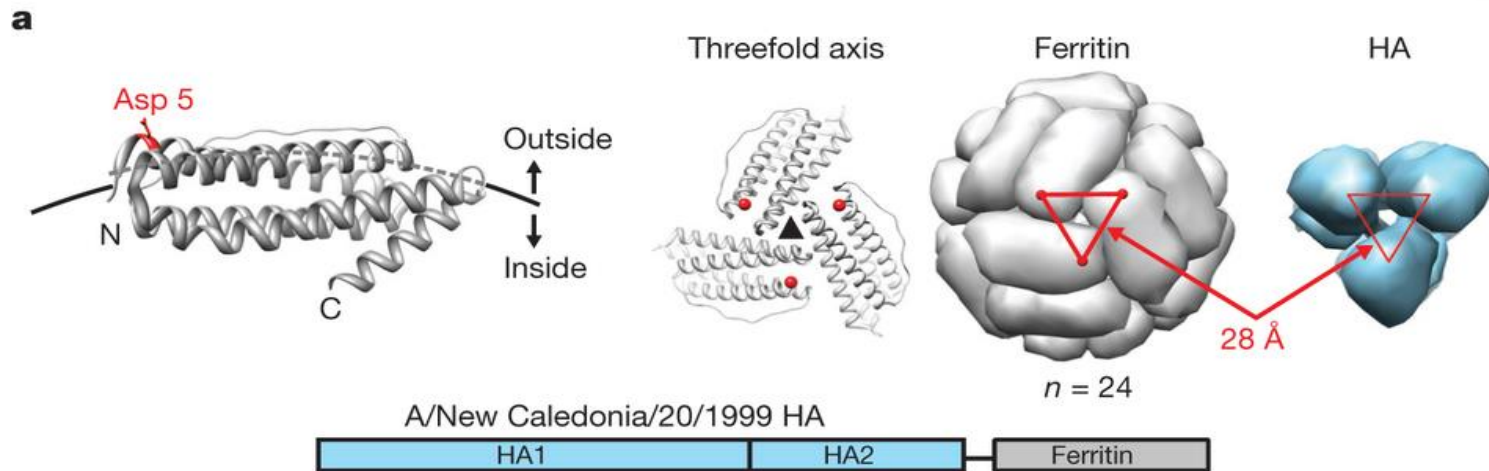
Photodynamic therapy



- Cargo – photosensitisers (PSs),
- Photon excitation to singlet state – relaxation – triplet state.



Immunization

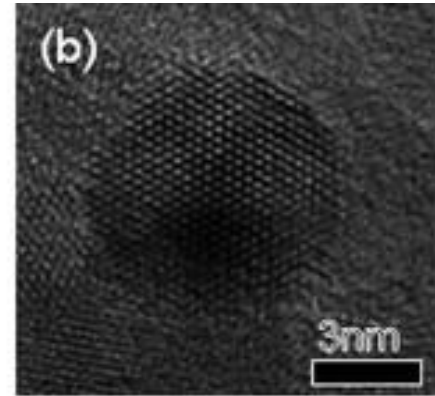
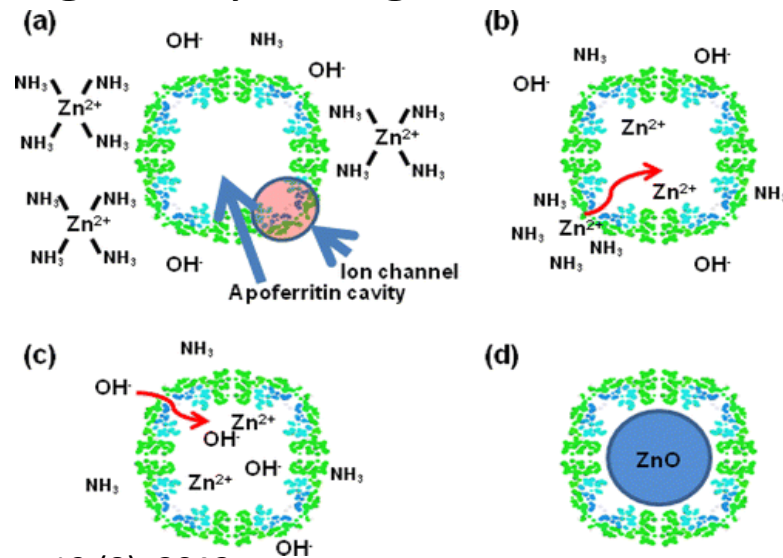


Kanekiyo *et al.* *Nature*, 499 (7456), 2013.

Apo ferritin as a reactor

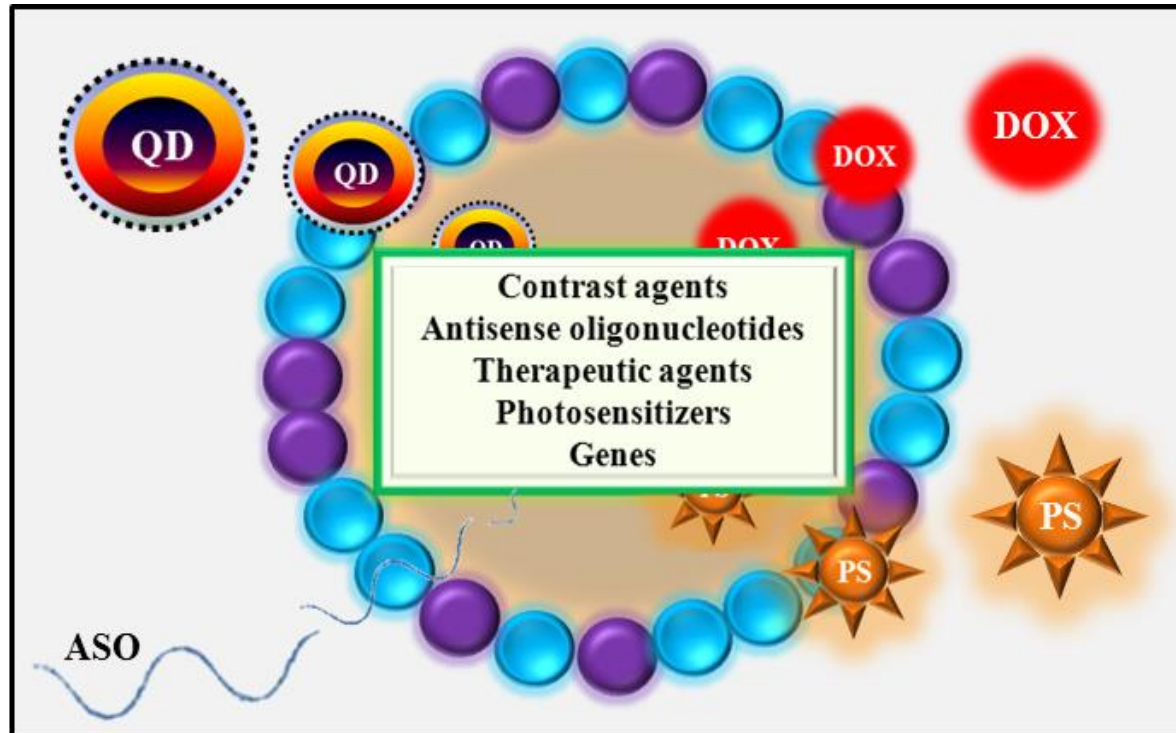


- Bioorganic nanocomposites synthesis – consistent size, shape and monodispersion,
- Ions are oxidized at negatively charged amino acid areas on the inner surface



Suzumoto *et al.* *Crystal Growth and Design*, 12 (8), 2012.

Conclusion

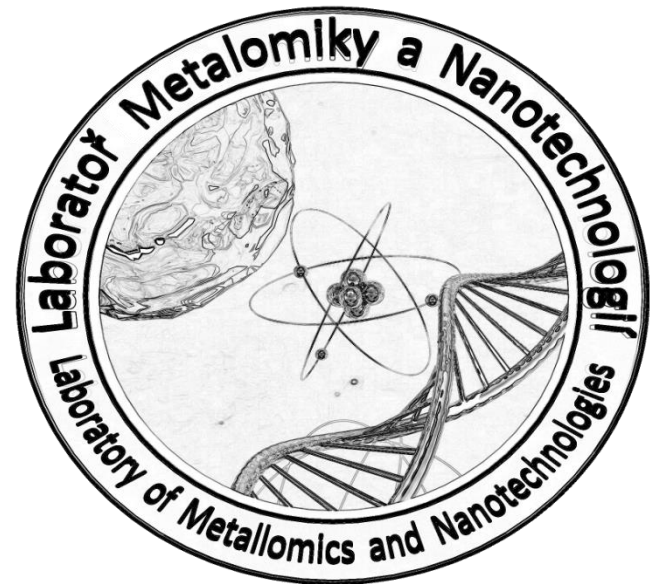


Acknowledgements



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"in vivo" zobrazovacích technik

CZ.1.07/2.3.00/20.0148



Thank you for your attention



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