

Investigation of the Interaction of Cm(III) with human serum transferrin and hTf/2N

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Introduction

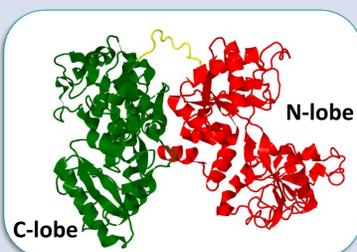
In case of an accidental release of radionuclides to the environment actinides can cause a serious health risk upon incorporation. With regard to the development of potential decontamination therapies, a detailed understanding of the mechanisms of relevant biochemical reactions is required.

Time-Resolved Laser Fluorescence Spectroscopy (TRLFS) studies of Cm(III) with transferrin and hTf/2N

- Multiple information on the number and type of the coordinating ligands can be obtained from the spectroscopic parameters, including shape and position of the emission bands as well as fluorescence lifetimes

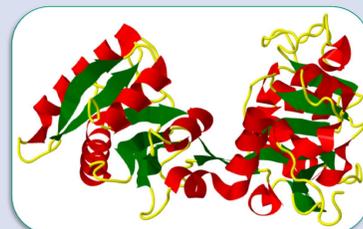
Transferrin

- Iron carrier protein in the blood
- Folded into two similar but not identical lobes housing the metal binding sites
- In vivo*, only 30 % of transferrin is saturated with iron → high capacity for the complexation of other metal ions



hTf/2N

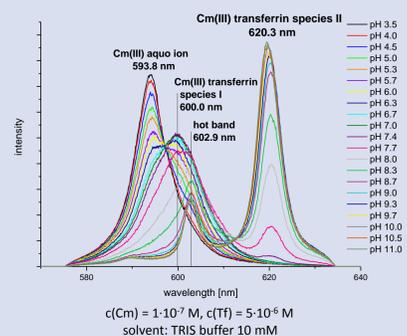
- Recombinant N-lobe of human serum transferrin
- Model for the N-terminal binding site



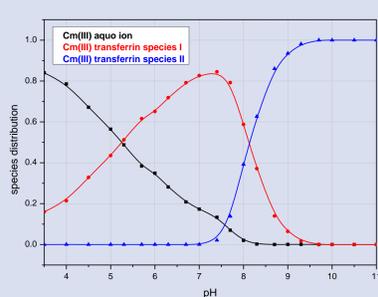
Complexation of Cm(III) with transferrin

- Experiment conditions ensure exclusive complexation of Cm(III) at the C-terminal binding site

Cm(III) emission spectra upon increasing pH



Species distribution



Cm(III) transferrin species I

- pH 6.3 – 7.7
- Nonspecific Cm(III) transferrin species

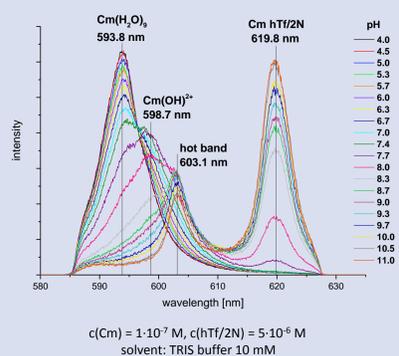
Cm(III) transferrin species II

- pH 7.7 – 11.0
- Complexation of Cm(III) at the C-terminal binding site of transferrin

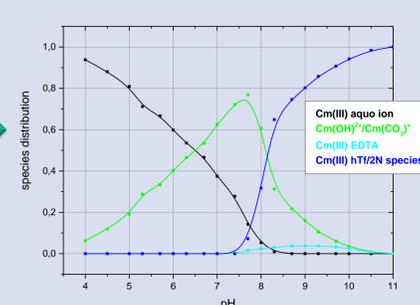
Species	τ [μs]	$n(\text{H}_2\text{O})$	$\log K$	ΔH [kJ/mol]	ΔS [J/mol·K]
Cm(III) transferrin species I	129	4.2	-	41	-
Cm(III) transferrin species II	221	2.1	8,1	118	548

Complexation of Cm(III) with hTf/2N

Cm(III) emission spectra upon increasing pH



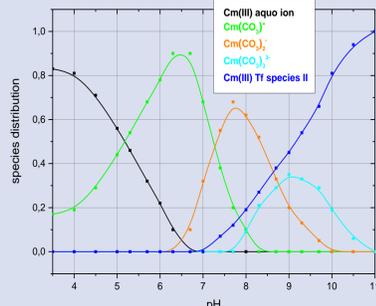
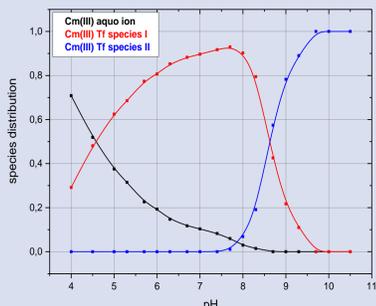
Species distribution



- No formation of a nonspecific Cm(III) hTf/2N species
- Cm(III) hTf/2N species**
 - Complexation of Cm(III) at the N-terminal binding site
 - Corresponds to Cm(III) Transferrin species II
 - $\log K_N = 5.7$
 - Thermodynamics:
 - $\Delta H = 257 \text{ kJ/mol}$
 - $\Delta S = 981 \text{ J/mol}\cdot\text{K} \rightarrow$ endothermic and entropy-driven reaction

Influence of carbonate on the complexation reaction

Transferrin



- ☺ Synergistic effect
- ☹ Competitive ligand

hTf/2N

- No synergistic effect of carbonate
- $c(\text{carbonate})_{\text{tot}} = 25 \text{ mM}$: exclusive formation of Cm(III) carbonate species

Complexation at physiological conditions

- pH 7.4, $T = 37^\circ\text{C}$, 150 mM NaCl, $c(\text{Carbonat})_{\text{tot}} = 25 \text{ mM}$
- N-Lobe:**
 - No relevance at physiological conditions
 - Cm(III) carbonate species are formed exclusively
- C-Lobe:**
 - 15% Cm(III) Tf II; 85% Cm(III) carbonate species

Conclusion:

A complex with Cm(III) bound at the C-terminal binding site and further metal ions coordinated at the N-Lobe might potentially bind to the receptor and be transported into cells via endocytosis