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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 \rightarrow high capacity for the complexation of other metal ions



hTf/2N

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



Complexation of Cm(III) with transferrin

Experiment conditions ensure exclusive complexation of Cm(III) at the Cterminal binding site

Cm(III) emission spectra upon increasing pH

Species distribution

Complexation of Cm(III) with hTf/2N

Species distribution

Species	τ [μs]	n(H ₂ O)	logK	ΔH [kJ/mol]	∆S [J/mol∙K]
Cm(III) transferrin species I	129	4.2	-	41	-
Cm(III) transferrin species II	221	2.1	8,1	118	548

Influence of carbonate on the complexation reaction

- 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:
 - $\Delta H = 257 \text{ kJ/mol}$
 - $\Delta S = 981 \text{ J/mol} \cdot K \rightarrow \text{endothermic}$ and entropy-driven reaction

Complexation at physiological conditions

- pH 7.4, T = 37° C, 150 mM NaCl, c(Carbonat)_{tot} = 25 mM
- N-Lobe:
 - No relevance at physiological conditions
 - Cm(III) carbonate species are formed exclusively
- C-Lobe:

hTf/2N

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

15% Cm(III) Tf II; 85% Cm(III) carbonate species

Conclusion:

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

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