Cadmium Exchange with Zinc in the Non-Classical Zinc Finger Protein Tristetraprolin

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Background

- Tristetraprolin (TTP) is a zinc-finger protein that requires Zn^{2+} for proper function
- TTP dysregulation is linked to cancer and rheumatoid arthritis
- Cadmium is a proinflammatory carcinogen that may cause TTP dysregulation

Lessons Learned

- Slow infusion rate (50-100 nL/min) and 30 µm diameter emitter tip was required to achieve stable spray
- H_2O:MeOH:ACN:IPA and 6% HNO_3 washes between infusions to remove residual metals

Brandis JEP, Zalesak S, et al. (2021) *Inorg.*

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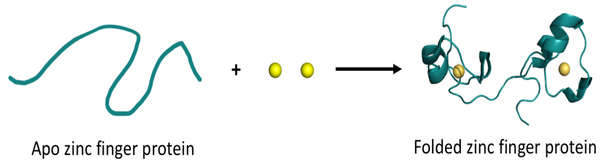
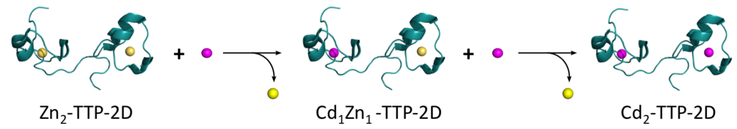
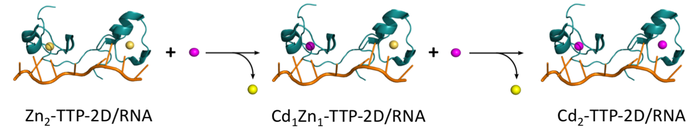
TTP requires Zn^{2+} for proper function



How does toxic Cd^{2+} interact with Zn_2-TTP?



Zn_2-TTP-2D + Cd competitive titration

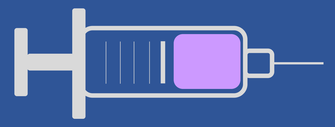


Zn_2-TTP-2D/RNA + Cd competitive titration

Cd^{2+} Can Exchange with Zn^{2+} in Zinc-Finger Protein TTP

<u>Without</u> Affecting TTP Binding to its Target RNA

Direct Infusion

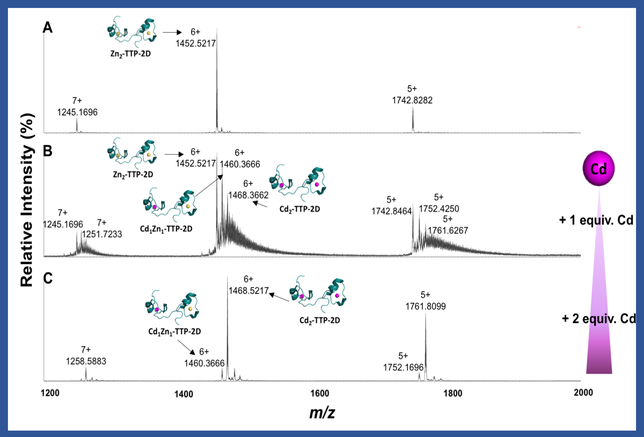


Buffer: 10 mM NH_4OAc

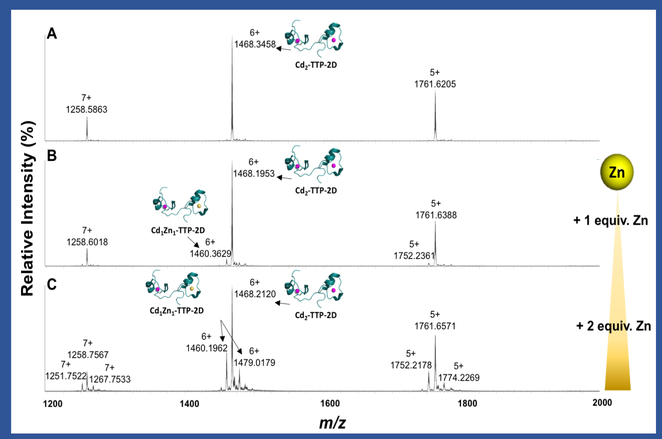
Waters Synapt G2S

nanoESI

Zn^{2+}TTP Plus Cd^{2+}



Cd^{2+}TTP Plus Zn^{2+}



Zn^{2+}TTP-RNA Plus Cd^{2+}