
화학과 대학원 세미나

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Design of Artificial Metalloproteins Using Flexible Scaffolds

In this talk, I will introduce design approaches for artificial metalloproteins using flexible protein scaffolds and discuss the biochemical lessons that can be learned from designed proteins. Metalloproteins are closely associated with vital functions of living organisms, such as metal homeostasis and enzymatic reactions. Central to the functions of metalloproteins is selective metal coordination; each metalloprotein must pair with its cognate metallocofactor to fulfill its biological role. Without the aid of intracellular regulatory mechanisms, most metalloproteins in heterogeneous environments exhibit low fidelity in metal selectivity. Inherently flexible motions of protein backbones and side chains can disrupt steric selection of the metal ions whose d-orbital electron configurations determine preferred coordination geometries. Accordingly, a large number of metalloproteins have been reported to generally follow the Irving-Williams (IW) series ($Mn^{II} < Fe^{II} < Co^{II} < Ni^{II} < Cu^{II} > Zn^{II}$) in binding affinities between the metal ions and the proteins, thereby losing their intrinsic structural/catalytic functionalities. I will discuss the design strategy and characterization of artificial dimeric proteins that thermodynamically overcome the IW restrictions *in vitro* and *in cellulo*, favoring the binding of lower-IW transition metals over Cu^{II} - the most dominant ion in the IW series. Additionally, I will also present how the flexible dimer scaffold could be systematically applied to new variants with different metal selectivity or enzymatic activity.

References

1. T. S. Choi, F. A. Tezcan, *J. Am. Chem. Soc.*, **2022**, 144, 18090-18100
2. T. S. Choi, F. A. Tezcan, *Nature*, **2022**, 603, 522-527
3. T. S. Choi, F. A. Tezcan, *in preparation*

최 태 수 교수
고려대학교 생명과학부