Optimization of Albumin-Ru artificial metalloenzyme for improved stability and activity

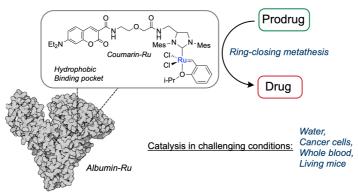
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Aqueous olefin metathesis plays an important role in modern organic and bioorganic chemistry. Hoveyda-Grubbs 2nd generation (HGII) catalysts are viewed as water-tolerant and widely used for proteins modification, stapled peptide synthesis and etc. However, most of these reactions require stoichiometric or even excess amount of catalyst to obtain desired products. Thus, reaction conditions for aqueous olefin metathesis still needs to be optimized.

One of the outstanding approaches for catalyst activity improvement is development of artificial metalloenzyme (ArM). Recently, we reported an efficient ArM based on human serum albumin bound with HGII-type abiotic cofactor.¹⁻³ This enzyme has a remarkable stability in water, biological media (cell media, whole mice blood) and was applied for anticancer therapy via *in vivo* drug synthesis. However, number of successful substrates found to be limited, and several attractive compounds cannot be used with our ArM due to the low catalytic activity.

In this meeting, we will present the easy way for optimization of HGII-type cofactor structure, which leads to a remarkable improvement in activity of the ArM in reaction with various olefins.



S. Eda, I. Nasibullin, K. Vong, N. Kudo, M. Yoshida, A. Kurbangalieva, K. Tanaka, *Nat. Catal.* 2019, 2, 780.
K. Vong, S. Eda, Y. Kadota, I. Nasibullin, T. Wakatake, S. Yokoshima, K. Shirasu, K. Tanaka, *Nat. Commun.* 2019, 10, 5746.
I. Nasibullin, I. Smirnov, P. Ahmadi, K. Vong, A. Kurbangalieva, K. Tanaka, *Nat. Commun.* 2022, 13, 39.