Catalytic olefin metathesis in blood

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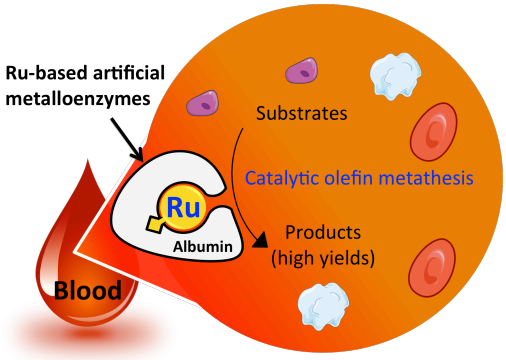
The direct synthesis of drugs in vivo enables drugs to treat diseases without causing side effects in healthy tissues. Transition-metal reactions have been widely explored for uncaging and synthesizing organic compounds in cell culture settings. However, the examples of transition-metal reactions that work in live mammals (in vivo) have been limited because numerous blood cells and metabolites in the bloodstream of the body deactivate transition-metal catalysts.[1]

Artificial metalloenzymes (ArMs) are the result of inserting abiotic-metal complexes into protein scaffolds of interest, which can impart enhanced substrate reactivity to the anchored metal catalysts.[2] Here we report that a robust ArM with a very low loading can catalyze Ru-based olefin metathesis in blood to construct various compounds and a bioactive drug in substantial yields. Moreover, the ArM retained its activity after soaking in blood for 24 h. Such a system offers a new avenue for building various bioactive drugs in vivo, enabling the development of innovative drug therapies without side effects.



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