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A Quest for Bio-Orthogonal Transition Metal Catalysis in Living Cells

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The development of transition metal catalyzed reaction is an emerging and fascinating area of research at the interface of homogenous catalysis and chemical biology. As it is still virtually unexplored but already holds out wide prospects of applications in molecular biology and medicine, it represents a fantastic playground for molecular organometallic chemists.

Our group started recently to be involved in this new field of research and this talk will present our progress in two related projects in the field of *in cellulo* prodrug activation.

Our approach is focused on finding transition metal pre-catalysts for which activation will occur after internationalization in the cell through bioactivation. The active complex will then be able to catalyze the uncaging on either a fluorophore or an active drug. We have found two families of complexes based on Iridium and Palladium which can be activated by biological co-factors and catalyze simple reactions such as double bond reduction and allylic substitution. In the case of the palladium pre-catalysts, the activation proved to be oxygen-dependent and the first example of a selectivity toward hypoxic cells for the corresponding catalysts was found. Here, we will report the methodology for catalysts optimization and the mechanism of the bioactivation, which finally led to the activation of a cytotoxic prodrug in cancer cells.

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