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Joint Departmental Seminar

By

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Photo-removable protecting groups: Applications in photo-pharmacology

Date: **23 October 2024 (Wednesday)**

Time: **10:30 am – 11:45 am**

Venue: **LI-1410 (1st Floor)**
Li Dak Sum Yip Yio Chin Academic Building
City University of Hong Kong
Tat Chee Avenue, Kowloon Tong

For abstract, please refer to the attached sheet.

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~ All Are Welcome ~

Abstract

The use of photolabile protecting groups (PPGs) has been growing in emphasis for decades, and they nowadays enable cutting-edge results in numerous fields ranging from organic synthesis to biology.1 PPGs are chemical entities that can be conjugated to a biological effector to hide its biological activity, forming a stable so called "caged compound". This conjugate can be simply cleaved by light and therefore, the functionality of the biological effector is restored with the formation of a PPG by-product. The use of UV irradiation (normally within power density between 10−1 and 10−3 W.cm-2) to manipulate the functions of biomolecules or mediate on-demand drug release in living systems via effective photoactivation with very high spatial and temporal control is well-developed and reviewed technique.[1] During the last two decades, the challenge was to overcome the difficulty that only high energy light (i.e. UV, the one damaging biological tissues) can induce photochemical reactions. One strategy to lower phototoxicity within the domain of one-photon excitation process is based on tailoring the caging groups with extended π-conjugation and introducing heteroatoms and functional groups in the ring system. Therefore, blue light-sensitive photoremovable groups have been reported.[2] This later strategy enables new biomedical applications in particular for the treatment of proliferative retinopathy and the development of blue light sensitive caged small gene inducers[3] will be presented in this context.

For more general biomedical applications the development of Red to NIR sensitive systems is highly sought after. In this context, we will also present our recent development emissive upconversion nanoparticles systems using the TTA-UC strategy[4] (for Red or NIR to blue light upconversion). And we will present how we have been able to further functionalize those nanoparticles with blue light-sensitive photocleavable linkers in order to trigger drugs releases using Red to NIR light in *vivo*.

References

*[1] R. Weinstain, et al. Chem Rev, **2020**, 120 (24), 13135-13272; C. Morville et al., J Incl Phenom Macrocycl Chem, **2021,** 101, 291-304, A. Gautier, et al. Nat Chem Biol, **2014**, 10, 533-541; M. M. Lerch, et al. Angew Chem Int Ed, **2016,** 55, 10978-10999; P. Paoletti et al., Nat Rev Neurosci, **2019**, 20, 514-532.*

*[2] J. Chaud et al., Org Lett, **2021,** 23, 19, 7580–7585.*

*[3] B. Goegan, et al. ChemBioChem, **2018,** 19, 1341-1348, Z. Kiy et al. Angew Chem Int Ed, **2024,** 63, e202317675; E. Brandhorst, et al. JACS Au **2024**, 4(8), 2818-2825*

*[4] A. Brion et al. Adv Healthcare Mater **2023**, 12, 2201474; A. Brion et al. Bioconjugate Chem, **2023,** 34(7), 1304-1315 (2023); M. Klimezak et al. Adv Healthcare Mater **2024**, 13, 2400354.*

Biography

Alexandre Specht got a PhD in chemical biology from Strasbourg University under the supervision of Prof. M. Goeldner, focusing on caged compounds for time-resolved crystallography. Following post-doctoral research at the Howard Hughes Medical Institute at UCLA with Prof. H.R. Kaback on the molecular mechanisms of membrane transport, he joined the Centre National de la Recherche Scientifique (CNRS) in Strasbourg in 2004 as a researcher (CR CNRS). He was promoted to research director (DR CNRS) in 2015. Since 2011, he is group leader at the Faculty of Pharmacy in Strasbourg (UMR 7199, University of Strasbourg / CNRS). His team develops photochemical tools for regulating various biological activities and nanoparticles for light-induced drug release.