Optochemical Tools to Control Gene Expression

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Life is highly dynamic relaying on a myriad of carefully orchestrated processes with strict spatial and temporal control. To decipher cellular functions and, in turn, address complex biological questions is necessary to have precise control. In my group, we pursue such the dream of *achieving a molecularly precise understanding of biology to address the problems arising from misregulation*. For this purpose, we focus on the design of innovative chemical biology tools. In particular, optochemical tools based on the synthesis of photosensitive molecules such as fluorophores, photosensitizers and photoswitches enabled us the desired conditional modulation in disease-related processes. In this talk I will make a brief summary about our projects where fluorophores have demonstrated the possibility of efficiently labelled multidrug resistant bacteria[1] as well as the development of bioorthogonally activatable photosensitizers for photodynamic therapy.[2-3] However, the main part of this presentation will deal with the use of photoswitches for light-controllable gene expression.

All cells in an organism contain the same DNA sequence but vary greatly in gene expression. Epigenetics deals with these phenotype changes that retains the same DNA sequence. Importantly, misregulation of these epigenetic processes is implicated in the pathophysiology of numerous human diseases,[4] including: cancer, autoimmune disorders and neurodegenerative disease. Therefore, epigenetic regulation is at the core of both natural and pathological states. The current available methods do not have sufficient spatiotemporal resolution to deal with the challenges of targeting the dynamic epigenome. We and others [5] envision that light could offer new possibilities and achieve molecular functionality. Reversible photoswitches, which have demonstrated their potential in diverse areas such as material science, have hardly implemented as genome regulators. Modulating the epigenome to tune transcription profiles, and cellular phenotypes in a programmable manner is of wide interest, and may ultimately lead to novel epigenetics-based therapeutics. Here, I will present our journey to achieve *in vivo* manipulation. [6-9]

References

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