Towards light induced drug release using photoremovable protecting groups

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The use of photolabile protecting groups (PPGs) has been a growing focus for decades, enabling cutting-edge advancements across numerous fields, from organic synthesis to biology.[1] PPGs are chemical entities that can be conjugated to biological effectors to temporarily mask their activity, forming stable so called "caged compounds." These conjugates can be cleaved by light, thereby restoring the functionality of the biological effector while producing a PPG by-product.

Over the past two decades, a major challenge has been addressing the reliance on high-energy light (e.g., UV light, which damages biological tissues) to induce photochemical reactions. One strategy to reduce phototoxicity in one-photon excitation processes involves designing caging groups with extended π-conjugation and incorporating heteroatoms and functional groups into their ring systems. This approach has led to the development of blue light-sensitive photoremovable groups.[2] This strategy opens up new biomedical applications, particularly for treating retinopathy. In this context, we will discuss the development of blue light-sensitive caged small gene inducers.[3]

For broader biomedical applications, the development of red to near-infrared (NIR) sensitive systems is highly desirable. In this regard, we will present our recent advancements in emissive upconversion nanoparticle systems employing the triplet–triplet annihilation upconversion (TTA-UC) strategy[4] for red or NIR-to-blue light upconversion. Additionally, we will demonstrate how these nanoparticles can be functionalized with blue light-sensitive photocleavable linkers to enable in vivo anticancer drug release triggered by red to NIR light.

References

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