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Light-enabled drug activation

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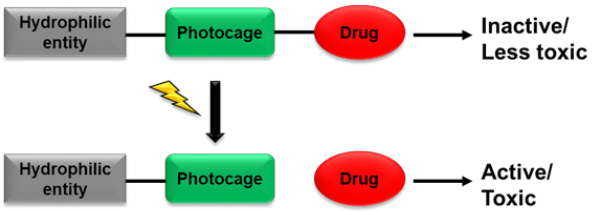

Cancer remains one of the major causes of death worldwide and its incidence continues to grow in all age groups. Decades of research has revealed that the cause of the disease is not only because of harmful habits or exposures; but also, due to inherited genetic-variations that contributes to the risk of acquiring it at some point during a person's lifetime. Chemotherapy is one of the treatment modalities that is commonly prescribed to patients with cancer. Treatment with potent drugs entail side-effects that range from hair/appetite-loss, anemia etc., to fatalities that arise due to its acute toxicity. To address this issue, we devised a simple prodrug-like approach, wherein a cytotoxic drug is coupled to a light sensitive-protecting group known as photocage. Photocaged drug is further coupled to a hydrophilic moiety, which renders the entire conjugate, cell-impermeable. When esophageal cancer cells were treated with this drug-conjugate, it localized outside the cellular membrane. But under light irradiation at an appropriate wavelength, drug was released, permeabilizing into cells and inducing cell-death, thereby increasing the specificity of drug action. We further improved upon specificity, by designing another photocage that coupled folic acid to the photocaged drug. Folic acid binds to folate receptors, which is overexpressed in certain cancers. This conjugate could be used toward targeting tumor tissues with overexpressed folate receptors. Although promising, there are limitations to these designs. Light used in these applications is UVA light, which has several limitations including low skin-penetrability. To address this issue, we used up conversion nanoparticles (UCNPs) that can convert low energy light to a high energy beam, which is sufficient to release drug. In addition, we have designed light-sensitive molecule that mimics the design of combretastatin, a cancer drug. Overall advantage of these approaches is that the small-molecules could also be used to improve efficacy of drugs with minimal to no side-effects.

Biography

Martin Michael Dcona has received his Bachelor's degree in Chemical Technology and Engineering and Master's degree in Chemical Sciences. He later moved to the USA for a PhD program in Chemistry at Virginia Commonwealth University (VCU) in Richmond, VA, USA, wherein he designed several drug-release vehicles that was used to increase specificity of anticancer drugs. Currently, he is a Postdoctoral Associate in the Department of Internal Medicine, VCU where he studies CtBP protein structure and its functions in cancer. His expertise is in multiple fields including drug delivery, drug discovery and development and cancer biology. He has authored several publications, reviews and holds a patent. He serves as Reviewer for multiple journals and serves on an Editorial Board. His current academic interest lies in light-sensitive cancer drug mimetics and novel therapeutic targets in cancer.

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