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Diatoms, Cobalamin & Rhenium Complexes: New Approaches to Address Targeted Drug Delivery in Colorectal Cancer

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Cancer is a term encompassing several pathologies affecting self-cells with common characteristics including cell degeneration and excessive proliferation. The development of new treatments targeting cancer cells through their specific abnormalities while not affecting normal cells is a major challenge in modern chemotherapy. Diatoms offer a wide panel of choice for specific applications in medicine and a great potential in drug delivery systems when coupled with vitamin B_{12} as tumor targeting agent.
Diatoms functionalized with vitamin B_{12} showed increased adherence properties toward cancer cells that have been proven correlated with Transcobalamin II receptors expression. Moreover, the newly reported construct was demonstrated able to convey poorly water-soluble anticancer drug models with selective release in lipophilic environments.
In a second step, a small library of rhenium(I) tricarbonyl complexes presenting interesting anti-metastatic and anti-angiogenic activities were synthetized and characterized. The evaluation of their anticancer potential was assessed *in vitro* and *in vivo*. Even at high doses, the two most interesting candidates did not induce *in vivo* damaging side effects such teratogenic malformations, cardiac dysfunctions, myelotoxic response or liver failure, and appeared safer and more effective than sunitinib malate, doxorubicin or cisplatin. Studies implied that they act at the cytoplasmic level by altering cellular processes perhaps *via* alkylation of different key proteins.
Finally, we designed two different constructs able to deliver an anticancer to a targeted tumor before being photo-activated in order to enhance the treatment by releasing additional cytotoxic species in the cancer surroundings. The two drug delivery systems based on diatom microalgae as container and vitamin B_{12} as targeting agent incorporate a photo-activatable component as tetracarboxyphenyl porphyrin PS in case I or tricarbonyl bipyridyl Mn(I) photo-CORM in case II. MTT assays under dark/light conditions on HCT-116 colorectal cancer cell line demonstrated the potentiation effect of the drug by the different light-activatable components at the surface of diatoms. These results paved the way of new multi-faceted strategies to fight cancer diseases with improved efficiency and reduced side effects.

Jury:
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