Innovative Catalytic Strategies to Combat Cancer

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Project description Within this PhD project, it is proposed to target metal-containing cofactors (**M_{cof}**) to the surface of cancer cells, and to use their catalytic properties to uncage drugs. With this ambitious goal in mind, the **M_{cof}** will be equipped with a high-affinity antagonist that binds tighly to proteins which are overexpressed on the surface of cancer cells.

To evaluate the therapeutic potential of this strategy, we have selected somatostatin, a G-coupled protein receptor that is highly present on the surface of various forms of cancer. Cyclic disulfide-bridged peptides (**Cyc-pept^{S-S}**), developed in the group of Prof. Fani, display exquisite affinity and selectivity for somatostatin receptors. Upon covalent linking of the peptide with the metal cofactor to afford **Cyc-pept^{S-S}–M_{cof}**, we anticipate that the catalytically active cofactor will accumulate in the proximity of cancer tissues that display multiple copies of the somatostatin receptor. Upon addition of a caged drug, the catalytic activity of the cofactor **Cyc-pept^{S-S}–M_{cof}** will lead to the site-specific uncaging of the drug where its action is required, Figure 1.

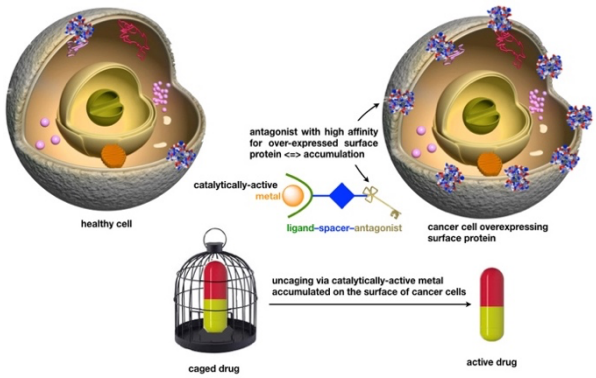

Figure 1. Catalytic uncaging of high potency drugs by a metal cofactor accumulated on the surface of cancer cells leads to targetted drug delivery

In the past years, the Ward group has pioneered several catalytic strategies that lead to the uncaging of various fluorescent probes and drugs in the presence of cells. Reactions include: olefin metathesis, transfer-hydrogenation, allylic substitution, hydroamination reactions, etc. In the course of his/her PhD, the researcher will work in a highly stimulating environment at the interface between chemistry, biology and medicine. The work will be carried out in close collaboration between the Ward and Fani groups.

We expect candidates for the position to have a relevant experimental background in organic synthesis as well as in any of the following: mammalian cell-culture, molecular biology, flow cytometry and FACS, high-througput experimentation. The selected PhD candidate will become a junior member of the SNI and benefit from personal support, a strongly interdisciplinary social environment, training in soft skills offered by the PhD program and many internal SNI events.

Applications should be made online at: phd.nanoscience.ch

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