PEGS EUROPE

Protein & Antibody Engineering Summit

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SPEAKER Q&A

Dr. Gonçalo J.L. Bernardes, Principal Investigator, Chemistry, University of Cambridge, recently spoke with Cambridge Healthtech Institute on his upcoming presentation, "Chemical Pharmacology of Protein Conjugates," taking place at the Engineering Next-Generation Antibody-Drug Conjugates conference on 31 October - 1 November 2016 as part of the 8th Annual PEGS Europe event in Lisbon, Portugal.

Dr. Bernardes is a Principal Investigator at the University of Cambridge where he leads a research program in Chemical Biology. He is a Royal Society University Research Fellow and the holder of an ERC grant. His presentation, taking place 31 October 2016, will address recent research in: (i) site-selective chemical modification of proteins and antibodies at cysteine and lysine, and (ii) the development of CO-releasing artificial metalloproteins that are able to deliver CO in a targeted and controlled manner to tumor tissues leading to potent CO-mediated immunomodulation.

Q: What has your research uncovered regarding site-selective chemical modification?

We are particularly excited with a new class of reagents we have developed that allow for stoichiometric and irreversible modification of cysteine residues. When applied for example to an antibody bearing engineered cysteine residues it forms a n homogenous product that is fully stable in whole blood and in the presence of biological thiols. We believe that the simplicity of the reagent combined with the selectivity and efficiency of the method (pH 8, 1 – 2 h at room temperature) will have a significant impact on antibody conjugation.

Q: How do you define "reaction engineering"? How does it fit into your research?

Reaction engineering for site-selective chemical protein modification: with this we mean engineering of reaction that may be chemoselective, i.e., only react with a particular side chain of an amino acid under biocompatible conditions (aqueous media, near neutral pH and room temperature to 37 ºC). Most of such reactions have been done exclusively on small molecules in organic solvents and thus their engineering to "aqueous" is key in order to be useful for protein and antibody conjugation.

Q: How are you able to deliver CO in a targeted and controlled manner to tumor tissues?

We have discovered that when you modify a protein with a ruthenium dicarbonyl moiety, the resulting metallotrotein is able to spontaneously release carbon monoxide (CO) in aqueous solution and live cells. When coupled to a tumour homing protein or antibody, this allows for selective delivery of CO to tumours in mice. This in turn has allowed us to unveil the roles of CO as an anti-cancer agent. On cancer cells, it directly influences inflammation and metastasis. On the other side, it can promote activation of the immune system.

Q: How does this research lead to potent CO-mediated immunomodulation?

The exact mechanism by which CO leads to immunomodulation is still not clear and we are working on it. What we showed is that there is a particular cell sub-type of the immune system that get activates through CO. When such cells are depleted from mice, the treatment looses much of its efficacy thus showing the importance of such cells to kill the cancer.

To learn more about his presentation and the PEGS Europe Summit, visit **PEGSummitEurope.com/Antibody-Drug-Conjugates**