

Anti-PEG antibodies: Detection, targeting and impact on PEGylated proteins and stealth nanomedicines

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Lecture 4:00-5:00 p.m. | NANOENGINEERING 181

Abstract

Attachment of polyethylene glycol (PEG) to drugs, peptides, proteins, liposomes, and nanoparticles can improve their pharmacokinetic properties and in vivo biological efficacy. Since the first PEGylated product was approved by the Food and Drug Administration in 1990, increasing numbers of PEGylated compounds have entered clinical use. Successful development of PEGylated pharmaceuticals requires accurate methods for the qualitative and quantitative analysis of intact PEG conjugates in biological fluids. We describe our experiences in developing anti-PEG monoclonal antibodies that are widely used for the detection and measurement of PEGylated pharmaceuticals in complex biological samples. We also describe a general targeting approach to deliver PEGylated nanomedicines to cancer cells based on bispecific molecules that bind to both polyethylene glycol on nanomedicines and surface receptors that are overexpressed on cancer cells. The development of new stable PEGylated liposomes for cancer drug delivery is described. Finally, we introduce the concept of pre-existing anti-PEG antibodies and their potential impact on the safety and efficacy of PEGylated medicines.

Bio

Steve is a Distinguished Research Fellow and Coordinator of the Cancer Division in the Institute of Biomedical Sciences at Academia Sinica in Taipei, Taiwan. He received his B.S. degree in Chemical



Engineering from the University of Washington in 1981 and then went on to the University of California, Berkeley to complete a PhD in Chemical Engineering in 1986. He studied Chinese in Taiwan at the Stanford Center in Taipei in 1986 and stayed in Taiwan to carry out post-doctoral research in the laboratory of Ming-Yang Yeh in the National Defense Medical Center. Steve became an Assistant Research Fellow in the Institute of Biomedical Sciences at Academia Sinica in 1991, Associate Fellow in 1998 and a Full Research Fellow in 2004. His research interests include antibody engineering, anti-polyethylene glycol antibodies, directed

evolution of human enzymes for the treatment of cancer and rare diseases, targeted nanomedicines and enzyme-targeted prodrug therapy. His lab developed the first monoclonal antibodies with specificity for polyethylene glycol, which have been used worldwide to accelerate the clinical translation of PEGylated medicines such as PEGasys and Mircera. His lab is currently investigating the influence of naturally occurring anti-PEG antibodies on the safety and efficacy of PEGylated medicines, developing stable and targetable nanoliposomes for cancer therapy, and creating humanized enzymes for selective cancer treatment. He has mentored more than 30 graduate and post-graduate students, published more than 140 papers in peer-reviewed journals, is a co-inventor of more than twenty patents and is responsible for over 800 commercial licenses and material transfers. Steve won the AIChE Outstanding Senior Chemical Engineering Student Award while he was an undergraduate student at the University of Washington. He recently received the Taiwan Ministry of Science and Technology Outstanding Research Award in 2017, the 14th Tien Te Lee Outstanding Award and the 25th TECO Technology Foundation's Outstanding Achievement Award in Biomedical Technology in 2018 and the Taiwan Ministry of Economic Affairs 6th National Industrial Innovation Award in 2019.