Taiwanese American Association of Pharmaceutical Sciences

台美藥劑學會

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Speaker Introduction

Bio

Sharon Lin, Ph.D, currently working at MustangBio as a Senior Scientist. She focuses on optimizing process development of autologous CAR-T program(s) to support the readiness of Phase I trial and IND filing. She is leading in-process assay design and trouble-shooting cell processes within a GMP facility. Prior to MustangBio, she has 3-year postdoc experience at University of Pennsylvania (UPENN). She utilized CRISPR/Cas9 to knockout PD1, an immunosuppressive receptor so that CAR-T cells are more resilient to exhaustion. In addition, her project involved in gene editing endogenous TCR using CRISPR/Cas9 to generate allogeneic T cell therapy. She got her PhD degree in Biochemistry and Molecular Biology at New York Medical College where she designed and purified recombinant proteins, characterized their catalytic functions and assisted in their crystallography. Sharon Lin grew up in Taipei, Taiwan and got her bachelor's degree in Biological Science Technology at China Medical University, Taichung, Taiwan.

Abstract

On August 30 th 2017, FDA has green lighted the first gene therapy, chimeric antigen receptor T cell (CAR-T) therapy targeting CD19 (an antigen expressed on B cells) in acute lymphoblastic lymphoma. Two years later on November 7 th 2019, the headline on PENN today's news stated "Positive results in first-in-U.S. trial of CRISPR-edited immune cells". These exciting news on personalized T cell therapy opens a new era for cancer immunotherapy but there are limitations to overcome. CAR-T is efficacious in treating hematologic malignancies but faces great challenge in treating solid tumor due to tumor microenvironment. Half million dollars is the price tag for each CART infusion which reflects a strong urgency for universal/allogenic CAR-T cells. With CRISPR knocking out endogenous T cell receptor, β2-microglobulin (a component of HLA class I) and/or PD1 (an immunosuppressive receptor), there had been reduced alloreactivity with increased tumor cytotoxicity observed in mouse Xenograft model. The combination of CAR-T and CRISPR technology is the future direction for cancer immunotherapy; however, there are problems that are discreetly, urgently and competitively studied by small/large biotech companies. Manufacturing large-scale gene-edited primary T cells requires extensive process development designs; in addition, cGMP facility with experienced Quality Control and Quality Assurance are also the key to bring the therapy to the clinic.