Chemical induction of splice-neoantigens enhances anti-tumor immunity and immunotherapy response

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Abstract

Neoantigen production is a determinant of cancer immunotherapy. However, the expansion of neoantigen abundance for cancer therapeutics is technically challenging. Recently, we reported that our synthetic compound RECTAS can induce the production of splice-neoantigens that could be used to boost antitumor immune responses (Matsushima et al. Sci Trans Res 2022). Because aberrant RNA splicing regulations are widely observed in cancer cells, creation of novel coding sequences by small chemicals may provide peptide sequences that potentially function as neoantigens. Therefore, we chemically developed new chemicals from RECTAS and found that one of them could efficiently induce neoantigen candidates in human cancer cells through splicing alteration. Validation by ELISpot assay confirmed antigenicity of some splice-neoantigens. As the chemical modulation of RNA splicing offers a source of common neoantigens in various types of cancer cells, combination of splicing modulators and immune-checkpoint inhibitors would dramatically improve the efficiency of current cancer immunotherapy.

Biography

Professor and Chairman, Graduate School of Medicine, Kyoto University
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He was born in Mie prefecture, Japan and entered into Mie University School of Medicine in 1978. When he returned from the Salk Institute in 1993, he started his laboratory in the Nagoya University School of Medicine as an Assistant Professor. He moved to Tokyo in 1997 as a Professor of the Medical Research Institute of Tokyo Medical and Dental University and decided to try deciphering the splicing code to cure some genetic diseases caused by aberrant splicing. He moved to Kyoto University in 2010 as Professor of the Department of Anatomy and Developmental Biology in the Graduate School of Medicine. He is now Professor and Chairman of Department of Drug Discovery Medicine and Director of Medical Research Support Center.