1421 TH1-SPECIFIC EPITOPE SELECTION FOR AN OFF-THE-SHELF TYPE KRAS CANCER VACCINE: EPITOPES OF NON-MUTATED LESION

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Background KRAS plays a role in cellular growth, differentiation, and signaling processes. Mutations in the KRAS gene (i.e., codon 12 or 13) are frequently associated with the development and progression of cancer, particularly lung cancer, colorectal cancer, and pancreatic cancer. Recently, it has been captured that KRAS targeting cancer vaccine research and clinical trial have been conducted in certain tumor types and vaccine approaches are encouraged to move forward.[1] It has been well known that tumor-eradicating efficacy of cancer vaccines arises from Th1 epitope-selection.[2] Though tumor growth after immunization with non-selected epitopes (including full-length) vaccine could be persistent, immunization with a highly selected Th1-specific epitope vaccine would demonstrate a tumor regression via the mechanism of inhibiting an activation of immune inhibitory cells. Th-Vac® discovery platform is aimed to generate a CD4+ T cell-driven vaccine. Through multiple in-silico, in-vitro, and in-vivo studies incorporated in a platform, Th1-specific epitopes are precisely identified. Cancer vaccine harnessing Th1-specific epitopes strives to elicit a potent and sustainable T cell immunity against tumor antigens and overcome either the absence of a precise T cell immune response or a preexisting tolerant response which tends to be immune-suppressing TME. This study was aimed to explore Th1-specific epitopes for KRAS vaccine to be potentially effective in numerous KRAS mutation-driven cancers.

Methods Peptide sequence candidates that have highly potential of MHC class II binding affinity were comprehensively predicted via a module 1 (ASEP program). All of peptides selected in ASEP were synthesized as 9 to 17 mers peptides followed by running a FACS and an ELISpot analysis using human PBMCs (Module 2a). These kinds of in-vitro immunogenicity evaluation were conducted using type 1 and/or type 2 cytokine(s) produced by CD4+ T cell.

Results In ASEP prediction, seven peptides were selected as potential candidates demonstrating a high affinity to MHC class II, which were in different lesions of common mutation of KRAS. In module 2a using ELISpot and FACS analysis, four epitopes (non-mutated sequences) were finally selected as Th1-specific epitopes based on the type 1 T cell response.

Conclusions Unlike previous vaccines using mutant lesions, in this study, four non-mutated Th1-specific epitopes are under the in-vivo immunity and efficacy studies as mono and combining regimen(s) in certain tumor types. Additionally, the Th-Vac® platform were fully validated in terms of the performance and its application would be expanded beyond a cancer vaccine.

REFERENCES

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http://dx.doi.org/10.1136/jitc-2023-SITC2023.1421