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Novel RNA-Based Cancer Vaccine For AML Immunotherapy

Acute Myeloid Leukaemia is a rapidly progressing malignancy relying primarily on chemotherapy as the frontline treatment option. We hypothesize that mRNA cancer vaccine can be a viable treatment strategy for AML patients. A fundamental component in cancer vaccine strategy is the identification of neoepitope candidates that can be delivered as vaccine to bring about therapeutic outcome. As AML cell possess low mutational burden, this may suggest that it may not harbour a large number of immunogenic neoepitopes. However, other study suggests that there may exist other types of immunogenic neoeiptopes on top of those derived through somatic mutations. In our study, using mouse AML cell line, we have utilized three different neoepitope prediction pipelines. We have found candidate neoepitopes within intron polyadenlyation sites (iPAS), retained-intron (RI) sites and somatic mutation sites. Contrary to what was initially predicted, our validation experiment using end-point PCR showed that the iPAS and RI derived neoepitopes were leukaemia associated antigens and not leukaemia specific antigens. We have also identified a total of 285 somatic epitopes and selected the top 38 highly expressed genes for further validation. Using Sanger sequencing, we confirmed 37 out of the 38 mutations. The unverified mutation is likely attributed to its location within genomic region of low complexity. With these candidates, we did a preliminary screen for immunogenic epitopes using a total of 71 synthetic peptides (Including controls) in an ELISpot assay. Conventional ELISpot assay initially narrowed our potential candidates down to six. The result was however non-reproducible, thereby propelling us to change to another assay - Culture ELISpot. Throughout the screening process, we have accidentally found that peptides, when coupled with AML cell lysate, can enable us to create a better screening outcome. The mechanism is however unclear. In bringing forward mRNA cancer vaccine as a therapeutic strategy for AML, ongoing works aim to validate these candidates further. We are in the midst of synthesizing the mRNA vaccine and will be evaluating the cancer vaccine treatment efficacy in AML mouse model in months to come. Combination therapy with checkpoint inhibitors will also be explored in the next few phases of our experiments.

Research in Progress

Wednesday, 24th February 2021 | 4-4.40PM | Zoom in via computer or phone
Zoom Meeting ID: 419 293 1311 | Meeting password: 579786