T cells capable of targeting neoepitopes (neoE) from tumor-specific mutations hold the potential to recognize and kill tumor cells. However, most cancer patients fail to mount a sufficient intrinsic T cell immune response to translate into clinical benefit. PACT Pharma has developed an ultra-sensitive and high-throughput sequencing approach (imPACT™) for identifying and capturing of neoE-specific T cells from blood. Whole exome sequencing of tumors and computational prediction identify patient-specific neoepitopes from tumor mutations. We then interrogate patient blood for neoE-specific T cells using human leukocyte antigen (HLA) protein-based reagents comprising a spectrum of HLAs, thus enabling the evaluation of ~99% of cancer patients. We have identified and isolated neoE-specific T cells from the peripheral blood of ~80% treatment-naive patients with five different solid tumors. Primary human T cells engineered with T cell receptor sequences (neoTCRs) identified by imPACT gain the ability to kill cognate neoE-presenting tumor cells, confirming the specificity of the isolated neoTCR to its neo target. This approach is also amenable to the longitudinal analysis of patients undergoing treatment for their cancers, to characterize the neoE-specific T cell populations likely to confer clinical benefit. In summary, the imPACT technology efficiently discovers meaningful intrinsic neoTCRs from patients, enabling the development of personalized neoTCR-T cell therapies for the eradication of solid tumors.

**Abstract**

- **ImPACT Technology** is efficient for capturing neoE-specific T cells directly from blood of patients with solid tumors
  - Useful for all ethnicities - PACT HLA catalog enables imPACT analysis of >99% of all individuals
  - imPACT process is ultra-sensitive - capturing neoE-specific T cells at a frequency as low as 1 per 5M PBMC
  - imPACT process has been qualified to be robust and reproducible - neoTCRs have been captured from blood of ~80% treatment-naive patient with different solid tumors, to date.
- imPACT technology is a highly effective platform for immune monitoring of studies from clinical trials & authenticating tumor-exclusive mutation targets for manufacturing personalized neoTCR-T cell therapies

**Methods**

- **imPACT™ Isolation Technology – Capturing Neo-E-Specific T Cells from Patient Blood**
- **Needle-to-Needle**
- **PACT Personalized NeoTCR T cell Product**

**Conclusions**

- imPACT technology is efficient for capturing neoE-specific T cells directly from blood of patients with solid tumors
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