Background Efficacy demonstration of a unique peptide-based immunotherapy as potent approach for cancer treatment. This strategy relies on the activation of commensal-specific T cells which cross-react against peptides derived from Tumor-Associated Antigens (TAAps) found in various solid tumors, including glioblastoma, adrenocortical carcinoma and colorectal cancer. The same strategy is also used to target lineage-specific markers in hematologic cancers such as B cell malignancies.

Methods The gut microbiota has the outstanding ability of regulating the human immune system through commensal antigens. Since specific microbiota peptides exhibit significant homology with particular TAAps, the full potential of cross-reactive CD8+ T cells that recognize both commensal peptides and poorly immunogenic tumor antigens can thus be harnessed against tumor cells.

We identified a specific set of commensal derived peptides, referred to as OncoMimics™ (OMP) peptides, which elicit cross-reactive cytotoxic CD8+ T cell responses against TAAps owing to their strong sequence homology. The capacity of these OMPs to induce TAAps-specific cross-reactive CD8+ T cell responses in humans is evaluated through peptide-MHC multimer staining and flow cytometry-based cytotoxic assays.

Results Experiments conducted on human peripheral blood mononuclear cells (PBMCs) demonstrate that OMPs can be recognized by CD8 T cells in a significant proportion of healthy individuals. Upon in vitro stimulation, OMPs induce the expansion of CD8+ T cells that recognize homologous peptides derived from tumor antigen targets. Importantly, these T cells display cytotoxic capabilities against tumor cells presenting the corresponding TAAps on their surface.

Further support for this approach comes from ongoing clinical trials, since we displayed that CD8+ T cells from indolent Non-Hodgkin Lymphoma (iNHL) patients treated with EO2463 immunotherapy (SIDNEY, EONHL1–20 phase 1/2 trial) are cytotoxic against TAA protein-expressing tumor cell lines.1

Conclusions These data provide compelling evidence that OncoMimic peptides sharing a high degree of homology with TAAps can be utilized to generate an effective anti-tumor immune response.

REFERENCE