



**myTomorrows**

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*Keynote speaker afternoon programme*

A library of Neo Open Reading Frame peptides (NOPs) as a sustainable resource of common neoantigens in up to 50% of cancer patients

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Somatic mutations in cancer can result in neoantigens against which patients can be vaccinated. The quest for tumor specific neoantigens has yielded no targets that are common to all tumors, yet foreign to healthy cells. Single base pair substitutions (SNVs) at best can alter 1 amino acid which can result in a neoantigen; with the exception of rare site-specific oncogenic driver mutations (such as RAS) such mutations are private. Here, we describe a source of common neoantigens induced by frame shift mutations, based on analysis of 10,186 TCGA tumor samples. We find that these frame shift mutations can produce long neoantigens. These are completely new to the body, and indeed recent evidence suggests that frame shifts can be highly immunogenic. We report that many different frame shift mutations converge to the same small set of 3' neo open reading frame peptides (NOPs), all encoded by the Neo-ORFeome. We find that a fixed set of only 1,244 neo-peptides in as much as 30% of all TCGA cancer patients. For some tumor classes this is higher; e.g. for colon and cervical cancer, peptides derived from only ten genes (saturated at 90 peptides) can be applied to 39% of all patients. 50% of all TCGA patients can be achieved at saturation (using all those peptides in the library found more than once). A prefab library of vaccines (peptide, RNA or DNA) based on this set can provide off the shelf, quality certified, 'personalized' vaccines within hours, saving months of vaccine preparation. This is crucial for critically ill cancer patients with short average survival expectancy after diagnosis.

