Bioinformatics strategies for the comprehensive characterization of antigen processing and presentation

International Centre for Cancer Vaccine Science

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Introduction:

(a)

The bioinformatics group at the International Center for Cancer Vaccine Science (ICCVS) is engaged in a few key activities related to neoantigen discovery, the biology of antigen processing, and the development of new immunotherapies.

Pipelines for immunopeptidome characterization

immunoaffinity purification of MHC class I

Applied clinical proteogenomics



Nuclear hotspots of antigen-presentation







(b) **DDA:** MS¹ followed by targeted MS²



Figure 3: Clinical application. (a) Proof of concept in 25 melanoma tumours of the existance of hotspots of antigen presentation within chromosomes and between chromosomes. **(b)** RNA-to-protein abundances in a single oesophageal cancer patient, highlighted points are proteins with identified mutations at the protein level. The RHS figure shows the fragment ion evidence for a single mutation.

genomically informed proteomics search databases

immunopeptidome peptide spectrum matches

Figure 1: Immunopeptidomics pipeline. We have developed computational pipelines for the proteogenomic interrogation of immunopeptidomics datasets. (a) immunopeptidomes are typically characterized by immunoaffinity purification followed by tandem mass-spectrometry. (b) patient specific genomics and transcriptomics data along with publicly available mutation data can be used to identify variants within immuno-peptidomics datasets.

Translating emerging proteomics technologies



Figure 2: The need for new Understanding technologies. sequence coverage in global proteomics. (a) Average sequence coverage of proteins identified in HeLa cell lysate acquired from a single injection into different mass spectrometers. (b) Focus on the highlighted sample in (a). More abundant proteins tend be to covered by more peptides. (C) Distribution of proteins in (b) (d) The single best run from 47 publications present in proteomicsDB.

Structure-based drug design for immunotherapy



Figure 4: A platform for structure-based drug design. ICCVS is searching for novel within pathways drugs implicated in immune-evasion. We have a pipeline for the high-throughput screening of putative drug candidates. Once drug candidate has been а selected, its structure IS perturbed to maximize binding affinity. The compound depicted red fits well into the in RNA-binding pocket of ADAR1, recently which has been implicated in immune-evasion.

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