Immunopeptidomics — MS-Based Neoepitope Discovery — Hands-on

Build an intuitive view of immunopeptidomics and HLA ligandomics for neoepitope discovery. This module focuses on conceptual MS workflows, peptide identification, linking HLA ligands to variants and summarising neoepitope evidence for vaccine, immunotherapy and translational oncology teams.

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Session Index

Session 1

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Foundations of Immunopeptidomics & HLA Ligandomics

T cell epitopes, antigen processing and the surface peptide repertoire (conceptual recap)

MHC class I and II presentation overview **endogenous versus exogenous processing picture** **relationship between predicted epitopes and presented ligands**

What immunopeptidomics measures in practice (orientation)

peptides actually bound to HLA molecules | ligandome versus proteome concept | value for vaccine, immunotherapy and tolerance studies

Sample types and experimental outline (high level only)

cell lines, tumours and primary tissues | concept of HLA enrichment and peptide elution | overview of LC MS based acquisition in simple terms

Session 2

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MS Workflow & Peptide Identification Concepts

Mass spectrometry readouts in an immunopeptidomics setting

precursor and fragment spectra in plain language | peptide features such as charge and length enrichment | differences from conventional proteomics at a glance

Conceptual view of database search and scoring for peptides

matching spectra to candidate peptides narrative | false discovery rate and confidence levels (no equations) | separate handling of class I and class II like length ranges

Basic quality filters and ligandome sanity checks (conceptual)

discarding low confidence identifications | checking length and motif patterns against HLA types | simple plots for ligandome composition overview

Session 3

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Neoepitope Discovery from Tumour & Pathogen Data

Linking HLA ligands to genomic and transcriptomic context (conceptual)

mapping peptides back to source proteins **overlaying variant calls for tumour or pathogen samples** **idea of proteogenomic search space at a high level**

What makes a peptide a neoepitope candidate in this context

presence of a sequence change relative to normal reference **support from both MS and sequence level evidence** **alignment with HLA type and binding motifs**

Prioritising candidate neoepitopes using simple conceptual criteria

confidence of peptide identification and variant call expression and clonality context (orientation) **link to T cell and vaccine design modules in this category**

Session 4

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Reporting HLA Ligand & Neoepitope Evidence

Designing clear tables and summaries for HLA ligands (conceptual)

peptide sequence, length and source annotation **HLA restriction and confidence indicators** **basic quantitative columns such as counts or intensities**

Neoepitope specific evidence blocks for translational teams

link to underlying variant and transcript context **summary of supporting MS and sequence features** **simple flags for prioritisation and follow up**

Packaging findings for vaccine, immunotherapy and biomarker discussions

figures that show ligand landscape at a glance **short narratives on opportunities and caveats** **handoff to neoantigen, onco immunology and trial modules**