


Human leukocyte antigen II immunopeptidomics in dendritic cells in response to immune-complexes of TNF with anti-TNF biotherapeutics

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The administration of biotherapeutics such as monoclonal antibodies may lead to unwanted immunogenicity in the clinic, i.e. the generation of anti-drug antibodies that potentially inactivate therapeutic effects. The characterization of Human Leukocyte Antigen (HLAII)-presented peptides derived from biotherapeutics identifies sequence liabilities responsible for the immunogenicity response. However, the regulatory principles for DC uptake of the biotherapeutic, proteolytic processing and peptide presentation remain incompletely understood. This work evaluates the effect of *in vitro*-formed complexes of TNF and its antagonists adalimumab, infliximab and certolizumab on the HLAII-immunopeptidome in human DCs. HLAII-associated peptides were identified by LC-MS/MS analysis using trapped ion mobility time-of-flight mass spectrometry (timsTOF-MS), consisting in a range of 18,000-30,000 peptides. These peptides derived form an heterogenous protein set, including self-presented components, cell culture media-presented proteins and therapeutic antibodies, shedding light into the effects of immune-complexes at the level of HLA-II presentation and its potential role in immunogenic responses.