The immunopeptidome puzzle

Arie Admon

Department of Biology, Technion - Israel Institute of Technology,

Abstract:

Some of the degradation products of the cellular proteins are send for presentation at the cells' surface by the Major Histocompatibility Complex class I proteins (MHC-I). The MHC is expressed by all nucleated cells in the body and is the most polymorphic human protein, with more than eleven thousand known allomorphs of MHC-I in the human population. The different MHC allomorphs binds and display tens of thousands different peptides (Immunopeptidomes) according to the properties of the peptide binding pocket, at the tip of each MHC allomorphs, and to the protein synthesis and degradation schemes of the cells. The peptides presented by the MHC are constantly screened by the immune system's T lymphocytes, which scrutinize the health-state of the cells and eliminate diseased cells, displaying abnormal peptides. The MHC bound peptides can be purified from the cancer cells by immunoaffinity chromatography of the MHC molecules carrying them and the extracted peptides can be identified on a large-scale by capillary liquid chromatography and tandem mass spectrometry. Indeed, tens of thousands of such MHC bound peptides were already identified from both normal and cancer cells, including some cancer specific ones. Thus, one of the major challenges of the immunopeptidome research field is to define the scope and consensus sequences of the peptidomes bound to each of the MHC alleles on each of the cell types in health and disease. Furthermore, while many of the identified MHC peptides fit the consensus sequence motifs of their MHC alleles, many others do not. The consensus sequence motifs of most MHCs are not yet known and the mechanism, by which such large and diverse peptide repertoires bind to each of the MHC allomorphs are open research questions that will be discussed.