



Origins of neoantigens for the major histocompatibility complex class I pathway

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Abstract

Neoantigens are antigens generated by somatic mutations that can be recognized by the host immune system. Firstly, described as differentiating, or tumor antigens, back in 80s and 90s in research related to mice melanoma and breast cancers carried out by Houghton's and Cheever's teams, respectively. Now, during the era of potent immunotherapies, cancer vaccines and immune checkpoint inhibitors (CTLA-4, PD-1), neoantigens again attract much attention. With the use of cutting edge technologies like next generation sequencing, mass spectrometry, predictive algorithms more is known about antigen presentation and the links between occurrence of somatic mutations in cancer cells and antigen recognition by CD8+T cells. Interestingly, discoveries of alternative sources of antigenic peptides (e.g. DRIPs and PTPs) challenged the notion about full-length proteins being the main supplier of material for MHC class I pathway and shifted focus of search for new sources to ribosomal scanning during pioneer round of translation. Despite the fact that pathways involved in processing and presentation of peptides has been thoroughly studied, there is still more to be learnt about the sources of peptide material for the endogenous and exogenous MHC class I pathways. Based on works related to Epstein-Bar virus it has been shown that MHC class I immune surveillance is directly correlated with the mechanism that regulate mRNA translation. Together with other results it highlights the importance of pre-mRNA and mRNA processing in providing antigenic peptides for MHC class I surveillance.

Here we revise some significant data related to the production of alternative antigenic peptides, their importance in cancer research, immunosurveillance and generation of tolerance. The lack of animal models to study the origin of alternative antigenic peptides hinders research in the field of neoantigens. I will describe results of the presentation of intron derived antigenic peptides in mice model developed by our team.

