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Sommario/riassunto

The endoplasmic reticulum (ER) is an organelle crucial to many cellular functions and processes, including the mounting of T-cell immune responses. Indeed, the ER has a well-established central role in anti-tumor immunity. Perhaps best characterized is the role of the ER in the processing of antigen peptides and the subsequent peptide assembly into MHC class I and II molecules. Such MHC/tumor-derived peptide complexes are pivotal for the correct recognition of altered self or viral peptides and the subsequent clonal expansion of tumor-reactive T-cells. In line with the role of the ER in immunity, tumor-associated mutations in ER proteins, as well as ER protein content and localization can have both deleterious and advantageous effects on anti-tumor immune responses. For instance, loss of function of ER-aminopeptidases, that trim peptides to size for MHC, alter the MHC class I - peptide repertoire thereby critically and negatively affecting T-cell recognition. On the other hand, altered localization of ER proteins can have immune-promoting effects. Specifically, translocation of certain ER proteins to the cell surface has been shown to promote anti-tumor T-cell immunity by directing uptake of apoptotic tumor cells to professional antigen presenting cells, thereby facilitating anti-tumor T-cell immunity. These selected examples highlight a diverse and multifaceted role of the ER in anti-tumor immunity. Molecular biological insights from the past decade have uncovered that ER components may affect tumor immunity and have invoked a variety of follow-up questions. For instance, how and why are ER proteins over-expressed in tumors? How do nucleotide and somatic mutations in ER chaperones/processing machinery affect the MHC/peptide complex and tumor cell immunogenicity? How do ER-proteins translocate to the cell surface? What if any is the potential role of extracellular ER protein in tumor immunotherapy/vaccines, and can they be delivered to the tumor cell surface by photodynamic therapy, anthracyclines or by other means? In this special research topics issue, we welcome basic and clinical research reports covering all aspects of ER proteins in cancer recognition by the immune system, therapy and drug development. We also welcome reports describing new insights into ER stress, signalling and homeostasis in immunogenic cell death in cancer, the effect of parasitic ER proteins on tumour growth, ER protein regulation of angiogenesis. Submission of original research articles, perspective, reviews and topical comments is encouraged. We aim to provide a comprehensive series of articles that will aid our understanding in a new and exiting avenue of tumour immunology and therapeutic development, exploiting a collection of proteins within the ER that are not obvious candidates for immunity to tumors.