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Evolution of NK-mediated target recognition under the pressure of physiologic or pathologic stimuli Massimo Vitale, Simona Sivori, Miguel López-Botet, Daniel Olive, 2015-03-23 Since their discovery NK cells have come out as potential tools to fight cancer and viruses This finding early urged different groups to study the mechanisms governing NK cell function The identification of the MHC I specific inhibitory receptors i e KIRs NKG2A and certain Ly49 molecules allowed defining rather rapidly how NK cells could avoid self aggression and how they could be directed towards targets that were forced by viral infection or tumor transformation to down regulate MHC I expression In a second time also the repertoire of surface activating receptors addressing NK cytotoxicity towards tumors and pathogens was mostly defined In spite of the first findings however most recent studies may suggest that NK cells and their receptors might not have been evolved to kill tumor targets and perhaps they might have been only partially influenced in their evolution by the need of recognizing viruses Indeed certain NK receptors known to activate NK cell cytotoxicity NKp30 DNAM 1 NKp80 can also participate at regulatory interactions occurring between NK and myeloid cells In addition a peculiar NK cell subset which intensively populate decidua during the first trimester of pregnancy through the engagement of specific receptors and the interaction with decidual DC produce chemokines and pro angiogenic cytokines and induce Tregs Thus in this context NK cells favor decidua vascularization and development of the semiallogeneic foetus in a tolerant environment Viruses have nevertheless played an important role in shaping the NK cell receptor repertoire Several studies have unveiled clues of the evolutionary struggle between these pathogens and NK cells Different NK receptors including NKp46 NKp30 NKp44 NKG2D NKG2C Ly49 and certain KIRs have been demonstrated to recognize virus encoded or virus induced ligands The expression of TLR specifically recognizing microbial products together with the unexpected role of KIR3DL2 in shuttling these products to TLR containing endosomes have also been documented in NK cells On the other side different viral immune evasion molecules have been shown to interfere with the expression of ligands for T or NK cell activating receptors In addition viral infections can occur in the reproductive stage of life cycle and may represent a serious threat for the species propagation Thus the control of viruses together with the maintenance of foetus during pregnancy should represent major evolutionary forces in shaping NK receptors Along this line the NK mediated control of tumors should not be under the same evolutionary pressure as tumors mostly appear later in the life cycle and the recognition of tumor encoded ligands may be less efficient as the NK cell receptors might have not been selected for such aim This may be the reason why although displaying strong antitumor activity in vitro NK cells could hardly contain tumor burden in vivo In addition the pathogen driven evolution of NK cell function may also favor the role of NK cells in the insurgence of immune mediated diseases This research topic will collect contributions that may clarify the relationships between the evolution of the NK receptors and their role in an efficient recognition of viruses and tumor cells or in immune mediated diseases *Vaccines and Therapeutics Utilizing New*

Adjuvants and Potential Inhibitors to Target Emerging Infectious Diseases Jiae Kim, Ousman Jobe, Mara Jana Broadhurst, 2025-12-01 Emerging infectious diseases such as persistent infectious diseases that have not been controlled i.e. HIV dengue fever those increasing in incidence i.e. flaviviruses food and waterborne pathogens or previously unknown diseases have impacted populations throughout the world. These diseases require either preventative vaccines or proper therapeutics to mitigate global epidemics from emerging. Recent vaccine and therapeutic candidates have emerged and are moderately successful however there is still room for improvement with either long lasting vaccine efficacy or therapeutics with maximal efficacy and minimal toxicity. New technologies are necessary for both preventative vaccines and therapeutics for emerging infectious diseases. As these diseases impact populations on a global scale preventing infection is key. However when that is not feasible treatment strategies and specific therapeutics with minimal toxicity and side effects are just as critical in fighting such epidemics. This Research Topic aims to cover current and emerging technologies being explored to prevent or treat infectious diseases including strategies currently in preclinical or clinical phase studies. We aim to bring together all aspects of research and development of these new technologies and invite vaccinologists, immunologists, pharmacologists and other multidisciplinary groups to feed knowledge into these growing fields. This research will impact the current landscape of infectious diseases and may also provide interventions against future pandemics. We welcome the submission of Review and Original Research articles focusing on preclinical and clinical vaccines or therapeutic studies and Perspective and Opinion articles highlighting the gaps in vaccines and therapeutics targeting emerging infectious diseases including viral or bacterial infections as well as multidrug resistant bacteria. Articles may focus on but are not limited to the following subtopics: Promising adjuvants in preclinical and clinical vaccine trials; Promising inhibitors that target infectious diseases in preclinical studies; Mechanism of action of novel inhibitors or adjuvants; Formulations that target different sites of action i.e. mucosal regions.

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