Cells and materials in immunotherapy

As the interaction of the immune system with the tumour microenvironment becomes increasingly understood, more evidence indicates how immunotherapy can be employed to better eliminate cancers.

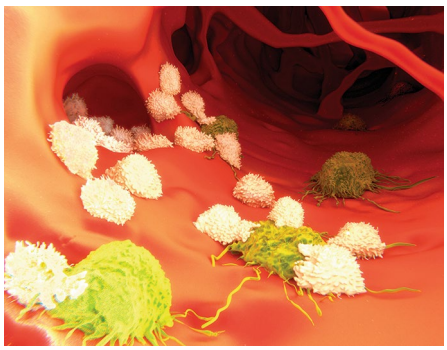
The immune system has evolved as a defence mechanism to identify and destroy any foreign material within the body. Such 'non-self' material includes transplanted grafts, bacteria and also cells within the body that become cancerous through mutations (pictured). However, the challenge for the immune system is in the discrimination of diseased from non-diseased cells in order to avoid severe inflammation of unintended tissues, as is known in autoimmune complications such as rheumatoid arthritis and psoriasis. Unfortunately, cancerous tumours have also evolved to evade immune system surveillance through a number of mechanisms that enable them to grow while limiting immune-mediated elimination. Moreover, the tumour immunogenicity varies between cancers of the same type in different individuals and between different cancer types, indicating heterogeneity in tumours[1]. Such tumour heterogeneity presents a complex problem in treating cancers and can arise because cells within a tumour express different antigens, which can lead to immunological escape when only a single antigen is targeted[2].

Immunotherapy is an ever-expanding area of cancer treatment that involves harnessing the immune system to more effectively fight the disease. Compared to the other cancer therapies such as chemotherapy and radiotherapy, immunotherapy allows more selectivity and lower toxicity in the tumour treatment while also offering long-lived immunity through immunological memory. Consequently, there has been a surge of interest in immunotherapies, and researchers have developed a number of monotherapies and combination therapies that target specific cancer types. In addition, advances in the development of artificial immune tissues as platforms to study the immune system have enabled the analysis of the efficacy of novel therapeutics and in the future may be adopted to replace defective immune tissues.

Several strategies have been developed to tackle the existing hurdles in treating cancers and a number of effective immunotherapy approaches have come to the fore. In a Feature in this issue, three teams of experts in immunotherapy and vaccine development discuss new and existing therapeutics, including the challenges and successes in their clinical use. Alexei Kirkin and colleagues highlight the need for multi-antigen targeting as a more effective approach to address the issues related to tumour heterogeneity. Equally exciting is the use of autologous dendritic cells as vaccines for tumour therapy. Carl Figdor and colleagues discuss how dendritic cells could be harvested from a patient, matured ex vivo using adjuvants and loaded with antigens before injecting them back into the patient to elicit an immune response by activating tumour-specific lymphocytes. They also mention other approaches using antibodies, nanomaterials and particles coupled with antigens to direct them towards dendritic cells[3]. The potential of materials in regulating the potency and safety of vaccines has also generated a lot of interest in immunotherapy. Darrell Irvine weighs up the advances in vaccine development and how a range of natural and synthetic materials have been used to generate safer personalized cancer vaccines for targeting patient-specific mutations.

Materials can also be employed in vaccine development to prevent the rapid clearance of peptide antigens following immunization. In a Letter by David Mooney and colleagues, mesoporous silica microrods were utilized as a platform for a personalized cancer vaccine to enhance antigen immunogenicity and drive anti-tumour immunity. Polyethyleneimine and mesoporous silica microrods were coupled to tumour viruses and neoantigens to form a vaccine that was shown to support tumour regression and increase survival following immunization. Importantly, they also demonstrated the potential of the vaccines in generating an immunological memory that prevented tumour growth after rechallenging with the same cancer cell type. Cornelis Melief highlights in a News and Views that this vaccine formulation paves the way for effective cancer immunotherapy, but that combination with additional immunomodulatory therapies would probably eradicate larger tumours.

Artificial immune tissues could be instrumental in understanding processes that govern immunity. Similar to the advent of organoid and lab-on-a-chip technologies, synthetic immune tissues could offer a tool to elucidate immunotherapeutics and immunological interactions[4]. Moreover, functional artificial immune tissues could offer the opportunity to replace or reprogramme defective organs that result in immunodeficiency. In a Review by Christopher Jewell and colleagues, they examine advances in engineering immune tissues and organs such as the bone marrow and lymph nodes, which could enable regulation of immune function and offer platforms for interrogating therapeutics. They also discuss some of the challenges in designing and translating such synthetic tissues towards clinical use.



T-lymphocytes (white) engaging and destroying cancer cells (green). Credit: Science Photo Library/Alamy

Since the late nineteenth century, when William Coley demonstrated durable remission in cancer patients after administering bacteria to create an infection and trigger an immune reaction, a growing understanding of the tumour microenvironment has presented more strategies to better engage the immune system in treating cancers safely. In this issue, we highlight further evidence of the progress in immunotherapeutics adopting cell- and material-based approaches, offering more opportunities to elucidate and tackle cancer. ❐

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