Sixth International Joint Meeting on THORACIC SURGERY
Barcelona - 20th, 21st and 22nd November 2024
Auditorio Foment del Treball Nacional. Barcelona (Spain)

11th International Meeting on General Thoracic Surgery
Clínic Barcelona | Universitat de Barcelona | Hospital Universitari Sagrat Cor

5th Meeting of the Thoracic Oncology, Thoracic Surgery, Techniques & Transplant, Respiratory Nursing and Respiratory Physiotherapy Areas of the Spanish Society of Pneumology and Thoracic Surgery (SEPAR)
Sociedad Española de Neumología y Cirugía Torácica (SEPAR)

10th International Workshop on Surgical Exploration of the Mediastinum and Systematic Nodal Dissection
Hospital Universitari Mútua Terrassa | Universitat de Barcelona

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3rd Joint Meeting of the Spanish Society of Thoracic Surgery (SECT)
SECT Sociedad Española de Cirugía Torácica

30th Congress of the "Asociación Iberoamericana de Cirugía Torácica" AIACT

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HOW DOES IMMUNOTHERAPY WORK?

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Cancer occurs as a failure of immune surveillance and tolerance. Cellular genomic changes occur at an increasing level with age and such genetically altered cells that are viable are killed by immune surveillance, a critical biological process. This mechanism primarily involves the recognition of tumour-associated antigens by T cells, which play a pivotal role in antitumor immunity. Central to this process is the formation of the T cell immune synapse, a specialized structure that facilitates communication between T cells and antigen-presenting cells (APCs). Upon recognition of antigens presented by major histocompatibility complex (MHC) molecules on APCs, T cells undergo activation, leading to proliferation and differentiation into CD8+ effector cells capable of targeting and destroying malignant cells and resulting immunological memory, which can be lifelong. The T cell immune synapse is characterized by a dynamic assembly of signalling molecules, including T cell receptors (TCRs), co-stimulatory receptors (e.g., CD28), and various adhesion molecules, which collectively enhance T cell activation and effector functions and are known as immune checkpoints. However, cancer cells often exploit immune checkpoint pathways to evade immune detection. The programmed cell death protein 1 (PD-1) and cytotoxic T-lymphocyte-associated protein 4 (CTLA-4) are key inhibitory receptors that, when engaged, dampen T cell responses and regulate autoimmunity. PD-1, upon binding to its ligand PD-L1, inhibits T cell activation and promotes an exhausted phenotype. Similarly, CTLA-4 competes with CD28 for binding to CD80/CD86 on APCs, leading to decreased T cell co-stimulation. Cancers evade immune surveillance through a number of different mechanisms including over-expressing PD-L1. Immune checkpoint inhibitors targeting PD-1/PD-L1 and CTLA-4 have revolutionized cancer therapy by reinvigorating T cell responses against tumours. By blocking these inhibitory pathways, these therapies enhance the formation and stability of the T cell immune synapse, thereby promoting effective immune responses and improving patient outcomes in various malignancies. Adverse effects of immune checkpoint inhibitor therapy are due to autoimmunity and generally commence weeks or months after therapy, requiring immunosuppression initially with steroids for management. In non-small cell lung cancer (NSCLC), the magnitude of effect of PD-1 and PD-L1 inhibitors is proportionate to the PD-L1 tumour proportion score (TPS: the PD-L1 expression amount).