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腫瘤診治的最新進展

Latest Advances in Cancer Treatment

時　　間：114 年 6 月 28 日(星期六) 09:00~12:00
地　　點：臺北榮民總醫院 致德樓第 8、9 會議室

09:00-09:05	***Opening Remarks***	楊慕華 教授 Muh-Hwa Yang
	座長：楊慕華 教授 (Muh-Hwa Yang)	
09:05-09:30	實體腫瘤新興細胞療法：從美國 FDA 核准的產品到未來的希望 Innovations in T Cell Therapy in Solid Tumors Emerging Cell therapy in Solid Tumor: Falk from US FDA-approved Products to Future Hope	曾慧恩醫師 Huey-En Tzeng
09:30-10:05	癌症免疫治療的進展 The evolution of immune therapy	陳三奇醫師 San-Chi Chen
10:05-10:30	雙特異性 T 細胞引導劑在實體腫瘤角色：拓展精準治療的新視野 Bispecific T Cell Engagers in solid tumor: Expanding the Horizons of Precision Therapy	賴峻毅醫師 Jiun-I Lai
10:30-10:50	***Coffee Break***	
	座長：陳志丞 教授 (Chi-Cheng Chen)	
10:50-11:30	黑色素瘤與肺癌中的腫瘤浸潤淋巴細胞（TILs）：開創個人化免疫療法 Tumor-Infiltrating Lymphocytes (TILs) in Melanoma and Lung Cancer: Pioneering Personalized Immunotherapy	陳天華醫師 Tien-Hua Chen
11:30-11:55	處置細胞治療的副作用：淺談神經毒性與細胞激素釋放症候群 Managing Adverse Events in Cell therapy: Insights into neurotoxicity and Cytokine Release Syndrome	簡聖軒醫師 Sheng-Hsuan Chien
11:55-12:00	***Closing Remarks***	陳明晃醫師 Ming-Huang Chen

Innovations in T cell therapy in solid tumors emerging cell therapy in solid tumor: Falk from US FDA-approved products to future hope

實體腫瘤新興細胞療法：從美國 FDA 核准的產品到未來的希望

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In the last decade, Chimeric Antigen Receptor (CAR)-T cell therapy has emerged as a revolutionary immunotherapeutic strategy, demonstrating remarkable success in treating hematologic malignancies such as B-cell lymphoma, leukemia, and multiple myeloma. Beyond CAR-T therapy, engineered cell-based immunotherapies include T cell receptor (TCR)-T therapy and tumor-infiltrating lymphocytes (TILs), among others. Despite the transformative impact of these approaches in blood cancers, their application to solid tumors remains a formidable challenge. The hostile tumor microenvironment promotes immune suppression and CAR-T cell dysfunction, while tumor heterogeneity and physical barriers further limit effective tumor infiltration and targeting.

Recent advances have led to significant regulatory approvals, including the U.S. Food and Drug Administration (FDA) approval of lifileucel (Amtagvi), the first TIL-based therapy, for melanoma, and afamitresgene autoleucel (afami-cel) for advanced synovial sarcoma. Additionally, the FDA has approved Astellas's zolbetuximab (Vyloy) for HER2-negative, claudin-18.2-positive gastric and gastroesophageal junction adenocarcinomas. To overcome the challenges associated with CAR-T cell therapy in solid tumors, alternative approaches such as induced pluripotent stem cell (iPSC)-derived CAR-T cells, CAR-Natural Killer (CAR-NK) cells, and CAR-macrophages (CAR-M) have emerged. Notably, CAR-NK cells offer significant advantages over CAR-T cells, including HLA independence, lower toxicity, and potential large-scale production as an off-the-shelf therapy. These advances mark a pivotal shift in cell therapy, offering new avenues for improving efficacy and accessibility in treating both hematologic and solid malignancies.

The evolution of immune therapy

癌症免疫治療的進展

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The landscape of cancer immunotherapy has evolved rapidly, offering transformative treatment options across a broad range of malignancies. This lecture will trace the key milestones and emerging modalities in immune-based cancer treatment.

Immune checkpoint inhibitors (ICIs) marked a turning point by reinvigorating exhausted T cells, leading to durable responses in various cancers. However, response variability has driven efforts to optimize outcomes through rational combinations. Bi-specific antibodies and Bispecific T-cell Engagers (BiTEs) represent innovative antibody formats that redirect T cells to tumor cells with high precision, delivering potent cytotoxic effects in an off-the-shelf manner.

Cell-based therapies have also progressed significantly. CAR-T cell therapy has demonstrated remarkable efficacy in hematologic malignancies, while next-generation approaches such as CAR-NK and CAR-γδ T cells aim to enhance safety and broaden tumor targeting. TCR-T therapy offers a means to recognize intracellular tumor antigens via HLA presentation, and tumor-infiltrating lymphocyte (TIL) therapy leverages naturally primed T cells harvested directly from the tumor microenvironment.

Oncolytic viruses (OVs) provide a dual mechanism by lysing tumor cells and stimulating innate and adaptive immunity, though they are often limited to intratumoral administration. Cancer vaccines, once considered experimental, are gaining renewed interest, particularly in combination with ICIs to boost tumor-specific immunity.

Cytokine therapies such as IL-2, IL-15, and IL-12 can activate immune effectors but must be dosed carefully to mitigate toxicity. Lastly, regulatory T cell (Treg) depletion is emerging as a promising strategy to overcome immune suppression within the tumor microenvironment.

This presentation will highlight the scientific rationale, clinical evidence, and future directions for each of these immunotherapeutic strategies as we strive toward more effective and personalized cancer care.

Bispecific T cell engagers in solid tumor: Expanding the horizons of precision therapy

雙特異性 T 細胞引導劑在實體腫瘤角色：拓展精準治療的新視野

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Bispecific T-cell engagers (BiTEs) are engineered antibodies that bridge CD3 on T cells and tumor-associated antigens (TAAs) on cancer cells, enabling T-cell activation independent of MHC presentation. While transformative in hematologic malignancies, their application in solid tumors faces challenges, including immunosuppressive microenvironments, antigen heterogeneity, and on-target/off-tumor toxicity. Recent advancements in design, target selection, and combinatorial strategies are unlocking their potential for solid malignancies.

Early BiTEs like EpCAMxCD3 (catumaxomab) demonstrated efficacy in malignant ascites but highlighted toxicity risks, emphasizing the need for tumor-specific targets. Next-generation constructs targeting PSMA (prostate cancer), SSTR2 (neuroendocrine tumors), gp100 (tebentafusp for uveal melanoma), and DLL3 (tarlatamab for small-cell lung cancer) have improved safety and gained FDA approval. These successes underscore the importance of antigen selection to minimize off-tumor effects.

Overcoming the immunosuppressive tumor microenvironment (TME) remains critical. Combinations with immune checkpoint inhibitors (e.g., anti-PD-1) reverse T-cell exhaustion, while vaccines and oncolytic viruses enhance T-cell infiltration, enabling BiTE-mediated tumor clearance. Pharmacokinetic innovations, such as half-life-extended BiTEs and subcutaneous formulations, improve dosing convenience and accessibility.

The future of BiTE therapy lies in personalization and synergistic regimens. Emerging technologies, such as AI-driven antigen discovery and synthetic biology, are identifying novel targets and refining construct design. As clinical trials validate these approaches, BiTEs are poised to redefine precision oncology, offering durable responses for historically intractable solid tumors. By integrating immunology and bioengineering, this modality exemplifies the convergence of innovation and therapeutic impact in cancer care.

Tumor-infiltrating lymphocytes (TILs) in melanoma and lung cancer: Pioneering personalized immunotherapy

黑色素瘤與肺癌中的腫瘤浸潤淋巴細胞（TILs）：開創個人化免疫療法

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Tumor-infiltrating lymphocytes (TILs) have emerged as a cornerstone of personalized immunotherapy, harnessing the patient's own antitumor immune repertoire to achieve durable clinical responses. In melanoma, early-phase studies demonstrated that expanded autologous TILs, when administered following lymphodepleting chemotherapy and interleukin-2 support, induce objective response rates exceeding 50%, with complete remissions in a subset of heavily pretreated patients. These outcomes underscore the extraordinary potency of melanoma-derived TILs, whose high mutational burden and neoantigen landscape facilitate robust T-cell recognition. In contrast, non–small cell lung cancer (NSCLC) presents a more immunosuppressive microenvironment and variable neoantigen load, but recent efforts to isolate and expand tumor-reactive TIL subsets—particularly those enriched for PD-1, CD39, and CD103 expression—have yielded promising early signals of activity. Single-cell profiling has refined selection strategies by identifying clonally expanded, neoantigen-specific T-cell populations capable of mediating tumor regression. Nonetheless, challenges in lung cancer include limited TIL yield, T-cell exhaustion, and inhibitory metabolic factors within the tumor stroma. Ongoing advances in ex vivo cytokine conditioning, costimulatory molecule modulation, and combinatorial checkpoint blockade aim to overcome these barriers. Collectively, the clinical translation of TIL therapy in melanoma provides a roadmap for its extension to lung cancer and other solid tumors. By integrating high-throughput neoantigen discovery, functional T-cell assays, and next-generation manufacturing, TIL-based immunotherapy exemplifies a truly personalized approach, offering the potential for durable remissions even in refractory disease. Continued optimization and biomarker development will be critical to expand its applicability and maximize patient benefit.

Managing adverse events in cell therapy: Insights into neurotoxicity and cytokine release syndrome

處置細胞治療的副作用：淺談神經毒性與細胞激素釋放症候群

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Chimeric antigen receptor T (CAR-T) cell therapy and other adoptive cell therapies have revolutionized cancer treatment, offering promising outcomes for patients with refractory hematologic malignancies and expanding into solid tumor research. However, these therapies are associated with significant immune-related toxicities, particularly cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS), which can range from mild to life-threatening. Effective management of these adverse events is crucial for improving patient safety and treatment success.

CRS is a systemic inflammatory response triggered by excessive cytokine production following CAR-T cell activation. It commonly presents with fever, hypotension, hypoxia, and organ dysfunction. Management strategies include early recognition, supportive care, and targeted interventions such as IL-6 inhibitors (e.g., tocilizumab) and corticosteroids to mitigate severe cases.

ICANS, a neurotoxicity syndrome associated with CAR-T therapy, manifests as confusion, tremors, aphasia, seizures, or, in severe cases, cerebral edema. While the exact mechanisms remain under investigation, endothelial activation, blood-brain barrier disruption, and excessive cytokine-mediated neuroinflammation are thought to contribute. Management involves close neurological monitoring, corticosteroids, and supportive measures, with anti-IL-6 or anti-IL-1 therapies considered in severe cases.

As cell therapy continues to evolve, optimizing strategies for toxicity mitigation, such as refining CAR designs, incorporating suicide genes, and combining therapies with immune modulators, will be essential. Ongoing clinical trials and real-world experience provide valuable insights into balancing efficacy and safety. A comprehensive understanding of CRS and ICANS pathophysiology, coupled with prompt intervention, is key to maximizing the benefits of cell therapy while minimizing risks.