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uPAR Immuno-PET: Advancing Pancreatic Cancer Imaging and Therapy

Pancreatic cancer remains one of the deadliest cancers, characterised by poor survival rates and high resistance to chemotherapy. A significant component of this resistance stems from cellular senescence, a process where cells cease to divide but remain metabolically active, contributing to therapy resistance. Advances in molecular imaging, particularly immuno-PET, have opened new avenues for non-invasive tumour monitoring. One such advancement is the use of urokinase plasminogen activator receptor (uPAR) as a target for immuno-PET, which shows promise for detecting senescence and treatment resistance. A recent review published in the Journal of Nuclear Medicine explores the role of uPAR in pancreatic cancer, chemotherapy-induced senescence, and how immuno-PET can enhance treatment strategies.

Role of uPAR in Pancreatic Cancer and Senescence

Pancreatic cancer is notorious for its aggressive nature and poor prognosis, with five-year survival rates barely exceeding 10%. Chemotherapy remains the primary treatment, but many patients develop resistance. uPAR, a membrane-bound glycoprotein, plays a crucial role in cancer progression, particularly in pancreatic cancer. Its expression correlates with poor clinical outcomes and increased metastasis.

In addition to its role in cancer progression, uPAR has been identified as a marker of cellular senescence. Chemotherapy can induce senescence in cancer cells, especially through agents like trametinib and palbociclib (TP). While halting cell division, this state enables the cells to adopt a secretory profile that promotes tumour growth and spread. Thus, detecting uPAR expression through immuno-PET provides valuable insight into tumour progression and chemotherapy-induced senescence. By tracking uPAR levels in vivo, clinicians can better understand the dynamics of pancreatic cancer and adjust treatment strategies accordingly.

Immuno-PET Imaging with uPAR Antibodies

Immuno-PET imaging combines the specificity of antibody-based targeting with the sensitivity of positron emission tomography (PET). Labelling antibodies with a radioisotope makes it possible to visualise the distribution of specific proteins, like uPAR, within the body. In this context, two antibodies targeting murine and human forms of uPAR have been developed, both of which have demonstrated efficacy in tracking uPAR expression in pancreatic cancer models.

In preclinical studies, uPAR-targeting immuno-PET showed higher selectivity and sensitivity than traditional imaging agents like [18F]FDG, commonly used in PET scans. For pancreatic cancer models, uPAR imaging revealed increased uptake in tumours following TP-induced senescence. This suggests that uPAR immuno-PET could be used to identify tumours undergoing senescence, providing a non-invasive means of assessing chemotherapy efficacy and tumour response.

Furthermore, studies have shown that uPAR expression can vary with age and treatment. In aged mice, uPAR uptake in tumours remained significant, even without chemotherapy. This indicates that uPAR immuno-PET can also help study the effects of ageing on cancer progression and treatment response. The ability to track senescence through uPAR expression provides a more comprehensive understanding of tumour biology, which could lead to more personalised treatment approaches.

Clinical Implications of uPAR Immuno-PET in Pancreatic Cancer

The clinical implications of uPAR immuno-PET in pancreatic cancer are significant. First, it offers a new avenue for early detection of chemotherapy resistance. As senescent cells contribute to resistance, the ability to visualise uPAR expression in real time can help clinicians adjust treatment plans before resistance becomes clinically apparent. This could improve patient outcomes by allowing earlier intervention with alternative therapies or combinations targeting resistant cell populations.

Moreover, uPAR immuno-PET can be a valuable tool in developing new therapies. By identifying tumours with high uPAR expression, researchers can better target these tumours with uPAR-specific treatments, including uPAR-targeted radioisotopes or immunotherapies. This theranostic approach, where diagnosis and therapy are combined, holds promise for improving the specificity and efficacy of pancreatic cancer treatment.

Additionally, uPAR immuno-PET could be used to monitor the effects of ageing on cancer progression and treatment response. As ageing is associated with increased levels of soluble uPAR, which can influence treatment outcomes, imaging uPAR expression in older patients could provide insights into how age-related changes affect cancer biology. This could lead to more tailored treatments for older patients, who often respond differently to therapy than younger individuals.

The development of uPAR-targeting immuno-PET agents represents a significant advancement in pancreatic cancer imaging and treatment. UPAR immuno-PET offers clinicians a new tool to monitor treatment efficacy and adjust therapies as needed by providing a noninvasive means of tracking tumour progression and chemotherapy-induced senescence. Furthermore, the ability to detect uPAR expression across different age groups and treatment conditions provides valuable insights into the complex biology of pancreatic cancer and therapy resistance.

uPAR immuno-PET could play a central role in developing personalised treatment strategies and improving outcomes for patients with pancreatic cancer. By enabling earlier detection of treatment resistance and providing a platform for the development of uPAR-targeted therapies, this technology has the potential to significantly impact the future of cancer care.

Source: Journal of Nuclear Medicine

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