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Experimental RNA therapy reduces lung cancer tumours in preclinical model

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Gem-miR-129 combines a tumour-suppressing microRNA with gemcitabine to target multiple pathways associated with non-small cell lung cancer and treatment resistance.



Researchers at Stony Brook Cancer Center have developed an experimental RNA-based therapy that reduced non-small cell lung cancer tumours by more than 95% in a preclinical model.

The therapy, known as Gem-miR-129, combines the tumour-suppressing microRNA miR-129 with gemcitabine, a chemotherapy agent used in cancer treatment.

MicroRNAs are non-coding RNA molecules that regulate gene expression. MiR-129 has demonstrated tumour-suppressing activity, but its development as a treatment has been limited by challenges involving stability, delivery and uptake by cancer cells.

The Stony Brook team modified miR-129 using gemcitabine to produce a dual-action molecule capable of entering cancer cells without a separate delivery vehicle.

Gem-miR-129 is designed to suppress multiple oncogenic pathways associated with cancer growth and treatment resistance. These include the HMGB1, YAP1 and PBX3 proteins.

The researchers evaluated the candidate in a mouse model of non-small cell lung cancer. The treatment reduced tumour growth by more than 95%, while treated animals survived several weeks longer than untreated animals.

The research was led by Jingfang Ju, professor in the Department of Pathology at Stony Brook University's Renaissance School of Medicine.

The candidate is being developed partly to address resistance to tyrosine kinase inhibitors among patients with epidermal growth factor receptor mutations.

These targeted therapies can produce strong initial responses, but many tumours eventually develop resistance and begin progressing again.

By acting as both a microRNA mimic and a gemcitabine-modified therapeutic, Gem-miR-129 is intended to target cancer cells through several pathways rather than relying on a single molecular mechanism.

The gemcitabine component may also reduce tumour-infiltrating regulatory T cells, which can suppress the activity of CD4 and CD8 T cells within the tumour microenvironment.

Reducing these regulatory cells could help restore immune activity against the tumour while the miR-129 component suppresses pathways involved in cancer progression and drug resistance.

The findings were published in Molecular Therapy. The researchers plan to conduct Investigational New Drug-enabling studies to further assess safety before seeking approval to begin clinical trials.