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Summary

Coding the future: mRNA vaccines against gastrointestinal cancers

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Endoscopy | Mechanisms & Personalised Medicine | Digestive Oncology

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mRNA vaccines complexed with lipid nanoparticles can systemically target dendritic cells in lymphoid organs to generate tumor-specific T cell responses, with preclinical and early clinical data showing anti-tumor efficacy in multiple cancer types including melanoma, colorectal, pancreatic, and breast cancers.

KEY POINTS

- The speaker reported that negatively charged mRNA-lipid complexes delivered intravenously target dendritic cells in spleen, lymph nodes, and bone marrow, activating both antigen-specific T cells and innate immune responses via interferon alpha secretion.
- In mouse models, the speaker stated that mRNA vaccines encoding tumor antigens achieved complete tumor protection in metastatic colon carcinoma (CT26) and 90 to 100 percent survival in head and neck cancer (TC-1), with surviving mice showing long-term protection against tumor rechallenge.
- The speaker reported that combining mRNA vaccines with PD-L1 antibody, radiation, or chemotherapy was more effective than single therapies in preclinical models.
- In a human melanoma dose-escalation study, the speaker stated that mRNA vaccination induced new T cell responses not present before treatment, and isolated T cells could kill autologous tumor cells ex vivo more than 100 days after vaccination.
- The speaker reported that individualized neoantigen mRNA vaccines (encoding up to 20 patient-specific mutations) induced durable T cell responses detectable 4.5 years after vaccination start in melanoma patients, who experienced fewer disease relapses post-vaccination.

– In early-phase pancreatic cancer and triple-negative breast cancer adjuvant studies, the speaker stated that vaccine responders had significantly higher progression-free survival and that up to 10 percent of circulating T cells became antigen-specific in some patients.

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