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Abstract Evelien Smits

RNA-based immunotherapy using dendritic cells or natural killer cells: from the lab to the clinic

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Dendritic cells and natural killer (NK) cells as innate immune cells play an important role in efficient antitumor immune responses. These cells can be modified using RNA to increase their antitumor function.

Dendritic cells play a crucial role in initiating and regulating the immune response against cancer as professional antigen-presenting cells. Smits' research involves engineering dendritic cells to improve their ability to present cancer antigens more effectively. In this context, investigator-driven academic clinical trials are being conducted at the Antwerp University Hospital to test the in-house developed therapeutic cancer vaccine. For this, dendritic cells are used that are loaded with the tumor antigen Wilms' tumor 1 (WT1) by mRNA electroporation. The Antwerp team showed that *WT1*-mRNA dendritic cell vaccination is feasible, safe and immunogenic, with promising clinical activity in patients with acute myeloid leukemia and advanced solid tumors. In the ongoing clinical studies, the dendritic cell vaccine is further being tested as part of a combination strategy.

In addition, the team of Smits focuses on developing chimeric antigen receptor (CAR) NK cell therapy. CAR NK cells have the potential to be as efficient as CAR T cell therapy, but with significantly reduced costs and toxicity. However, for CAR cell therapy to be effective in solid tumors, still several hurdles need to be taken. Smits's research on CAR NK cells focuses on enhancing their efficacy and persistence in the tumor microenvironment. Her team showed that CD70 is an attractive target both in hematological and solid tumors. CD70-targeting CAR NK cells can eliminate both tumor cells and cancer-associated fibroblasts in colorectal cancer and pancreatic cancer. In addition to exploring other targets, the team is investigating the metabolic pathways and immune checkpoints that regulate NK cell activity, seeking ways to modulate these pathways to further boost NK cell function.