Immunicum

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Leveraging allogeneic dendritic cells to boost immunity against cancer

Immunicum is exploiting the power of allogeneic dendritic cells to evoke immune responses that reduce tumor burden and recurrence.

Immuno-oncology is a promising treatment approach that stimulates the immune system to detect and attack cancer cells. "We've seen an initial wave of checkpoint inhibitors and systemic agents that can help the immune system elicit an anti-tumor response," explained Sijme Zeilemaker, Chief Operating Officer at Immunicum, a Sweden-based company advancing novel cell-based therapies for cancer. "However, most of these agents require a properly activated immune response or inflamed tumor tissue to be effective".

A growing appreciation of the mechanisms through which different immune cell types can be directed to attack cancer cells is helping overcome shortcomings of current immunotherapies, including tumor-induced immunosuppression. "We are just scratching the surface of what cell therapies beyond T cells can do," Zeilemaker said.

Immunicum is developing a novel class of immunotherapies based on dendritic cells. These cells are orchestrators of the immune response due to their key role in bridging the gap between innate immunity, the first line of defence against invading pathogens in a non-specific manner, and adaptive immunity, mediated by T and B cells to protect the host from a specific pathogen or toxin.

Dendritic cell subtypes work in concert to activate each other and trigger different immunological responses[1]. "The end goal of immunotherapy is to activate antitumor T cells and we are exploring various ways to achieve this using allogeneic dendritic cells," Zeilemaker added.

Following a merger with DCPrime in December 2020, Immunicum is developing two complementary approaches using allogeneic dendritic cells derived from monocytes from a healthy donor or from a human myeloid leukemia cell line.

Allogeneic dendritic cells provide both 'stranger' and 'danger' signals to the immune system that are crucial for it to sense a cell-associated threat such as cancer. These signals activate the patient's alloreactive T cells, NK cells and bystander dendritic cells, kickstarting an adaptive response against the tumor.

One of Immunicum's approaches involves injecting highly inflammatory dendritic cells into solid tumors to trigger innate immunity at the tumor site. This leads to activation of a potent tumor-specific T cell response against the injected tissue. The other approach involves injecting dendritic cells expressing tumor-associated antigens subcutaneously, to prevent cancer relapse through a vaccination approach (Fig. 1). "The principle behind our approaches is the same, to prime an immune response against tumor antigens using allogeneic dendritic cells," said Zeilemaker.

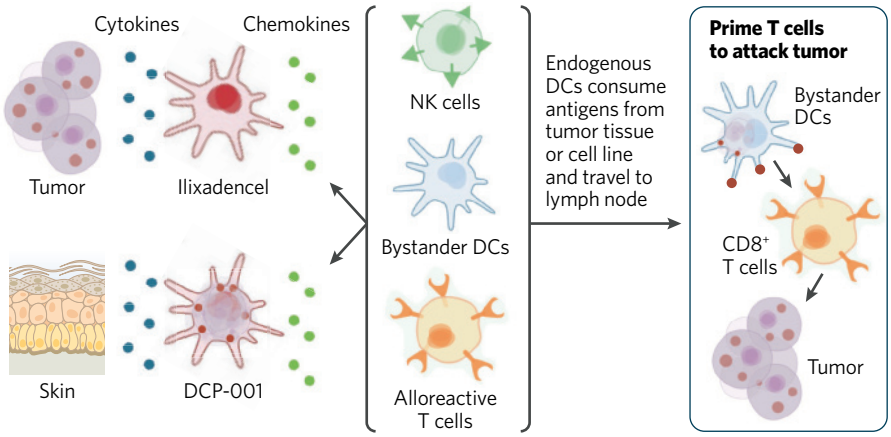

Fig. 1 | Immunicum's programs. A combination of both programs (in different tissues) with the same outcome of endogenous bystander DCs cross-presenting such tumor antigens to the ultimate activated T cell. DC, dendritic cell; NK, natural killer.

Making immunologically 'cold' tumors 'hot'

Immunicum's lead product ilixadencel, has completed phase 2 clinical evaluation in kidney cancer and is in phase 1 trials in multiple indications. Ilixadencel consists of dendritic cells that have been activated with cytokines and toll-like-receptor ligands so they 'act' as if they have been infected by a virus. The cells are injected directly into tumors to create localized inflammation and change the tumor microenvironment. "Ilixadencel labels tumors as 'sterile' infection sites and directs the immune response against cancer cells which become a direct neoantigen source," Zeilemaker explained.

Immunicum is also advancing the development of DCP-001 as a cell-based relapse vaccine. Because DCP-001 cells are derived from a cancer cell type they express multiple tumor-associated antigens, but with a mature dendritic cell phenotype. These antigens have been shown to overlap many cancer types and induce epitope spreading, boosting a more complete and tumor-specific immune response. Upon intradermal injection, DCP-001 induces a strong inflammatory response and attracts host immune cells, kickstarting the patient's innate immunity against cancer and, ultimately, priming T cells to attack cells expressing these antigens either in circulation or solid tumors.

DCP-001 is showing promising effects in controlling residual disease in an ongoing phase 2 trial in patients with acute myeloid leukemia (AML) in remission. "DCP-001 could improve long-term survival in AML patients who are not able to receive stem cell transplantation," said Zeilemaker. The potential of DCP-001 to prevent relapse is also being explored in a phase 1 clinical study in ovarian cancer patients in which antigen overlap with DCP-001 has also been established.

Finding synergies

Many immunotherapies target the mechanisms mediating tumor immunosuppression, but they may not be able to clear all cancer cells on their own. "We believe that both activation of the immune system and treatment with a systemic agent to reduce tumor immunosuppression are required to dramatically improve survival," said Zeilemaker.

Immunicum is leading the way in using allogeneic dendritic cells and is furthering research into novel concepts, including the combination with CAR-T cell therapies. Dendritic cell therapies could not just increase the efficacy of existing therapies, but lead to long-lasting responses and remission. "The biology of dendritic cells is very exciting, we are only beginning to see the potential of these cell therapies," Zeilemaker concluded.

1. Fu, C., Jiang, A. *Front Immunol.* **2018**, 9:3059 (2018).

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