Nanomedicines mimicking cancer immunity against colorectal cancer

Period: 6 months from January/February to June/July 2025

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Internship locations: Utrecht University & University Medical Center Utrecht, Utrecht, The Netherlands

The work will take place in different Research HUBs at Utrecht University (see descriptions below).

Summary

This internship will focus on cancer immunotherapy – a form of treatment that reinforces our immune system to eliminate cancer, as a potential way to tackle colorectal cancer. Cancer immunotherapy has gained interest and improved significantly over the last decades with therapies for numerous types of tumors entering the clinic. Nevertheless, chemotherapy is still among the conventional treatments strategies for solid tumors, which is often accompanied by severe adverse events during treatment and can result in chronic side effects. Moreover, chemotherapy resistance, particularly after cancer recurrence, poses a significant clinical challenge. Hence, there is a pressing need for new targeted therapies with immunotherapy emerging as a promising alternative for cancer treatment.

The immune system employs various cells to combat tumor cells, with cytotoxic CD8+ T cells playing a crucial role in current anticancer immunotherapy (Fig 1A). Tumor cells typically exhibit a specific protein complex called MHC-I, which is recognized by the T cell receptor (TCR) on CD8+ T cells. This recognition prompts the release of specific granules containing proteins like perforin and granzymes, which initiate apoptosis. However, tumors often evade immune detection by downregulating MHC-I molecules or expressing immune checkpoints (Fig 1B).

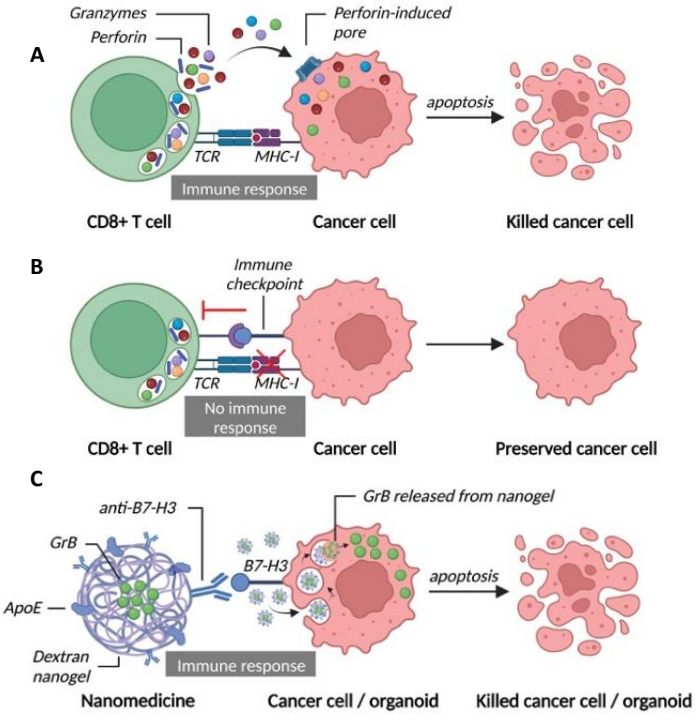

Figure 1. Project overview (example).

Nanoparticles, for example nanogels, represent an attractive carrier system for delivering various therapeutics, including granzymes (Fig 1C). These 3D structures safeguard encapsulated therapeutics from degradation in the body and allow for precise targeting of cancer cells while minimizing impact on healthy tissue, thereby reducing side effects compared to traditional treatments like radiotherapy and chemotherapy. By modifying the surface properties of nanoparticles, drug uptake by cells can be enhanced, while also enabling delivery to difficult-to-reach areas within the body.

Aim

In this project, we aim for a novel class of nanomedicines, loaded with immune cell-derived toxins and decorated on the outside with target-specific ligands, to tackle colorectal cancer.

Student work

During this internship, students will work in the continuum of Translational Medicine, i.e., bridging a gap between bench (Nanomedicine Engineering Student Research HUB and Biotechnology Student Research HUB, Faculty of Science) and bedside (Biomedicine Student Research HUB, Faculty of Medicine). At their disposal, students will have human colorectal cell lines, colorectal patient-derived tissue samples, as well as immune cells (both human natural killer cell lines and access to healthy donor peripheral blood), and means to develop and test advanced 3D tumor *in vitro* models (e.g., organoids), nanobodies and nanomedicines. Students will devise a strategy on how to best target colorectal cancer, by determining the specific targeting ligand, suitable immune system cargo and nanoparticles to efficiently deliver the cargo to the tumor site, and subsequently synthesizing and testing the nanomedicines. Students will collaborate closely within participating Research HUBs at Utrecht University but also with partners at University of Montpellier.

Requirements:

1. Scientific English (spoken and written)
2. Knowledge of cancer biology and biochemistry is appreciated
3. Autonomy, scientific curiosity, rigor
4. Good interpersonal skills and willingness to work in an interdisciplinary team

Research HUBs

Biomedicine Student Research HUB: The Biomedicine Student Research HUB is centrally-located laboratory in the University Medical Centre Utrecht, embedded within the Faculty of Medicine with short lines to medical specialists, research groups, and other stakeholders including patients and patient organizations. It offers the possibility for the students to perform innovative fundamental and applied research to find interdisciplinary solutions for complex societal challenges in the field of life sciences. Techniques available in the HUB include but are not limited to, for example, advanced 3D *in vitro* models, cell culture, confocal microscopy, immunohistochemistry, killing assays, qPCR, flow cytometry, western blot, xCELLigence, transfection, molecular biology, and CRISPR/Cas9 gene-editing technology. Principal investigator in this Research HUB is prof. dr. Niels Bovenschen.

Nanomedicine Engineering Student Research HUB: The Nanomedicine Engineering Student Research HUB at the Department of Pharmaceutical Sciences (Faculty Betasciences) at Utrecht University has a long-standing interest in targeted delivery of drugs, nucleic acids and proteins using nanoparticles/nanogels based on biodegradable polymers. They have access to fully equipped labs for polymer synthesis and for characterization of polymers, hydrogels and nanoparticles, with facilities for *in vitro* studies. Principal investigator in this Research HUB is dr. Rene van Nostrum.

Biotechnology Student Research HUB: The Biotechnology Student Research HUB is the (wet) laboratory space where students from the Departments of Biology, Chemistry, and Pharmacy from the Utrecht University Faculty of Science perform innovative and applied research to find interdisciplinary solutions for complex societal challenges in the field of life sciences. They have access to fully equipped labs for producing nanobodies for purposes of, for example, imaging and therapy, including the nanobody-targeted photodynamic therapy as well as conjugating nanobodies to nanocarriers for a more specific target-cell uptake. Principal investigator in this Research HUB is dr. Sabrina Oliveira.