Executive Summary

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Project "Intelligent synthetic nanosize organelles for cancer therapy"

This project aimed at the development of smart nanomaterials for cancer, with the larger vision to attain in an academic research project materials and results that then can be translated to clinical reality and to the benefit of patients, a goal that requires translation to the manufacturing industry at a given time point. Because of this vision, a particular emphasis of the project was also to identify and to circumvent risks that could put in danger a later clinical translation, in particular questions of quality, reproducibility, toxicity, and scalability.

Smart cancer therapies will be targeted to the cancer and will thus spare healthy tissues; smart functionality allows to switch on the anticancer effect only at the cancer site (and not in the other organs), further reducing damage; smart materials also circumvent a too early elimination of the drug from the body before they act, and they avoid side effects that can be caused by an undesired immune system response.

The methods to achieve such new cancer therapies include chemical synthesis, physicochemical characterization methods, biochemical in vitro tests, cell cultures and various advanced cancer models, but also including computer modelling and simulation.

A number of novel polymer-based hybrid nanomaterials was designed, synthesized, assembled and tested. We found structure-function relationships for our new materials and derived design criteria for optimal targeting and minimized side effects. We successfully produced multifunctional nanomaterials that combine cancer tissue targeting, cell receptor targeting, stealth properties, and documented that the desired triggered function of such materials, like cancer cell killing upon near-infrared light stimuli, takes place at the desired target.

One class of materials thus allowed receptor-specific detection of a specific cancer cell type in a mix with other non-cancerous cells, followed binding to and uptake into these cells, thereby delivering a photo-sensitizer selectively to these cells, resulting in highly efficient cancer cell killing upon a light trigger to a degree that exceeded all other tested treatment variants.

Novel polymer-based hybrid materials were also achieved that are able to switch off gene expression through RNA interference of a strongly expressed protein in target cells; these materials are compatible with in vivo application, in contrast to most current material which are mainly used in vitro, and therefore call for industrial translation.

We studied cell binding, biodistribution, cancer targeting, of such materials in vivo in cancer models and found excellent cancer targeting capabilities combined with absence of observable remote toxicity. New synthesis and assembly protocols were produced by iterative optimization with the goal to have industry-ready processes suit-able for industrial scale-up. Specifically for this project, novel approaches based on time-of-flight secondary ion mass spectroscopy were developed by the EMPA partners, thereby allowing detection of very small concentrations of otherwise invisible nanomaterials in biologic tissue.

A regular interaction with the key international regulatory agencies to streamline future production and assessment of such materials for clinical use was established.

The results of this project have led to patent submissions, were disseminated in major academic congresses across the continents, are progressively being published in scientific journals, and have contributed to two Swiss start-up companies originating from our research team.

In parallel with the research project and with SNF support, with contributions of the NFP62 collaborators, the CLINAM nanomedicine summits were built up which now form a platform of excellence and interaction for the global nanomedicine community and have rendered Switzerland highly visible in this field.

A challenge and a strength of this project is the strong interdisciplinarity that was required to achieve the goals. Another challenge in such projects is to balance between scientific publication and securing intellectual proper-ties to assure future success in real life/industrial translation.

A limitation to such interdisciplinary, application oriented research that bridges academia and industrial application is the paucity of financing opportunities for such bridging projects.