# Exploring the role of cancer stemness and stromal interactions in therapeutic targeting of oncofetal chondroitin sulfate glycosaminoglycans in cancer

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The rising incidence of major cancer types in the ageing population calls for new therapeutic strategies. Targeting cancer stem cells is a promising approach, and the project brings together complementary expertise to address this challenge. The Pilsen group has developed reporter cell strains for direct visualization of bladder cancer stem cells, the Copenhagen group has created an innovative therapeutic strategy, and the Warsaw group provides unique expertise in Grainy-Head-Like transcription factors (GRHL), which are key mediators of urothelial differentiation.

The project builds on the Copenhagen group's discovery that oncofetal chondroitin sulfate (ofCS), a secondary modification otherwise present only in the placenta, reappears in all malignancies where it promotes rapid growth, invasion and immune escape. This finding led to the development of targeted therapies, including a monoclonal antibody binding ofCS in cancer without affecting normal tissues. The current research focuses on whether cancer stem cells express ofCS and how the cancer stroma becomes ofCS-positive, using established biological models and new systems developed through manipulation of GRHL3 to induce or inhibit urothelial differentiation.

The study will map the distribution of ofCS-modified antigens in bladder cancer stem cell models and co-cultures with stromal cells, and test therapeutic targeting of ofCS-expressing cells with antibody-drug conjugates. Improved cellular models will then undergo reanalysis to refine therapeutic strategies. The project is expected to result in a joint scientific publication or international conference presentation, while also strengthening long-term collaboration and mobility between participating groups from Charles University, the University of Copenhagen and the University of Warsaw, paving the way for future joint funding applications.