# Targeting Siglec10-CD24 in feline mammary carcinoma – a glimpse of a new immunotherapy approach

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Immunotherapies have revolutionized the fight against cancer yet response rates are still low, dictating the need for new therapeutic targets. The interaction of tumoral sialosides with immune cell sialic-acid-binding Ig-like lectins (Siglecs) has emerged as a key immune response modulator. Recently, the Siglec10-CD24 axis was proposed as a major immune-checkpoint in human breast cancer [1]. Given the similarities between this cancer and feline mammary carcinoma (FMC) we sought to describe this axis in FMC and develop a new immunotherapy based on the targeted desialylation of Siglec-10 ligands.

CD24 and Siglec10 expression was studied by IHC on tumoral samples from FMC patients, revealing marked Siglec10 and CD24 staining on TAMs and poorly differentiated neoplastic cells, respectively. A panel of putative novel sialidases was designed, expressed in *E. coli* and purified. Enzyme activity was tested using a fluorogenic substrate. Desialylation of mammary carcinoma cell lines with selected sialidases was analyzed by flow cytometry. A total of 74 proteins were identified and characterized, 10 of them with high expression yield and sialolytic activity. The enzymes' ability to remove MALII and SNA ligands were tested in cell lines, revealing their potential to degrade α2-3 and α2-6 linked sialic acids.

The present results suggest the presence of a Siglec10-CD24 axis in FMC and identified a set of sialidases with ability to degrade sialosides. In the future, these enzymes will be tested as part of an antibody-sialidase conjugate to assess their potential anti-tumoral effect.

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