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ER Intrabodies against the polysialyltransferases ST8SiaII and ST8SiaIV inhibit polysialylation of NCAM in rhabdomyosarcoma tumor cells

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Polysialic acid (polySia) is a carbohydrate modification of the neural cell adhesion molecule (NCAM), which is implicated in neural differentiation and plays an important role in tumor development and metastasis. Polysialylation of NCAM is mediated by two Golgi-resident polysialyltransferases (polyST) ST8SiaII and ST8SiaIV. Intracellular antibodies (intrabodies; IB) expressed inside the ER and retaining proteins passing the ER such as cell surface receptors or secretory proteins provide an efficient means of protein knockdown. To inhibit the function of ST8SiaII and ST8SiaIV specific ER IBs were generated starting from two corresponding hybridoma clones. Both IBs αST8SiaII-IB and αST8SiaIV-IB were constructed in the scFv format and their functions characterized *in vitro* and *in vivo*.

Stable expression of ST8SiaII-IB, ST8SiaIV-IB and luciferase in the rhabdomyosarcoma cell line TE671 reduced cell surface expression of polySia and delayed tumor growth if intrabody expressing tumor cells were xenografted into C57BL/6J RAG-2 mice.

Data obtained strongly indicate that αST8SiaII-IB and αST8SiaIV-IB are promising experimental tools to analyze the individual role of the two enzymes during brain development and during migration and proliferation of tumor cells.

Biography

Thomas Böldicke has obtained his PhD degree from Max Planck Institute of Molecular Genetics, Berlin. Since 1986, he has been working at Helmholtz Centre for Infection Research, as a Project Leader of Intracellular Antibodies.

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