Phosphatidylserine Exposed by Cancer Cells as New Target for Peptide Drugs

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A novel strategy is used for the design of new antitumor drugs, taking advantage of the fact that unlike healthy human cells cancer cells expose negatively charged phosphatidylserine (PS) on the outside of the plasma membrane. Positively charged host defence derived peptides are optimized in their specific interaction with PS to enable them to kill cancer cells rapidly and specifically by lysis of the membrane.

Several peptide-derivatives (8-11 amino acids) of Lactoferricin, a human host defence peptide, and N-acylated derivatives thereof were selected regarding their activity against a HeLa cell line (cancer cell line) and negatively charged model membranes.

In a preliminary screening study these peptides were tested for selectivity towards cancer model membranes and the outcome revealed that some of the peptides have strong and specific impact on the lipid membrane of cancer cells. First experiments with cancer cell lines to check for exposed PS were performed successfully by specific binding of fluorescently labeled AnnexinV to PS on the outside of cells. Thereby it could be shown that melanoma cells, prostate - and kidney cancer cells expose their PS to high amounts, whereas healthy cells do not expose any PS.

One of the strategies for optimization of the specific interaction with PS is to vary amino acid residues for optimal interaction with phosphatidylserine. From the outcome of the first screening with model membranes most active peptides were chosen for *in vitro* studies with cancer and non cancer cells, showing already promising cytotoxicity on cancer cells.

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