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The influence of fibronectin modulation on tumor growth

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An emerging field in cancer research consists of the study of the role of extracellular matrix proteins. The participation of fibronectin in different stages of tumorigenesis by different mechanisms has already been confirmed in numerous studies. Therefore, the potential of use of fibronectin modulation as a therapeutic approach in cancer might be promising. In this work, the effect of peptides that target fibronectin accumulation were tested in two different cancer models.
pUR4 is a bacterial peptide which that prevents fibronectin fibril formation. Because fibronectin is required for collagen accumulation, this leads to a decrease in collagen. The recombinant version of pUR4 was tested *in vitro* and *in vivo* in human breast cancer cell line MDA and murine B16 melanoma cells. This peptide was then synthesized and modified in order to better understand its effect on the immune response against tumors and to investigate whether an improvement can be achieved by various modifications.
The fibronectin polymerization inhibitor pUR4 diminished fibronectin accumulation by MDA cancer cells in *vitro* and was able to reduce tumor growth *in vivo*. However growth proceeded nevertheless albeit at a slower rate. This was associated with an increase in a subpopulation of immune cells compatible with macrophages (CD11b-F4/80+) and a decrease in the mRNA expression of arginase in myeloid cells isolated from the treated tumors. The suppression of growth was confirmed using a second model of melanoma in immune competent mice.
Several modifications were introduced and a new peptide was synthesized, but its effect on fibronectin accumulation in vitro was not more pronounced than pUR4. In vivo, the modification diminished cancer growth further compared to pUR4 in the immune deficient MDA model, but this could not be confirmed in the immune competent melanoma B16 model suggesting it is due to the small sample size in the MDA model, or that it is not a universal effect. Interestingly, we could not detect a change in the macrophages with the modified peptide despite the decrease in cancer growth. Attempts at characterizing the best sequence within the modified peptide led to short peptides that diminish fibronectin accumulation in vitro, but none was better than pUR4.
The data indicate that pUR4 suppresses fibronectin accumulation and leads to a decrease in cancer growth. An accompanying change in the mRNA expression in the macrophages could contribute to this effect, but causality was not evaluated in this work. In summary, matrix manipulation offers new possibilities in suppressing cancer growth.