Fatty Acid Synthase: A Novel Target for Antineoplastic Therapy? (Acta Biomedica Lovaniensis)

This is a Ph.D. dissertation. Fatty acid synthase (FAS) is a key lipogenic enzyme catalyzing the terminal steps in the synthesis of fatty acids. In the majority of normal tissues, FAS expression is low. In many human cancers, however, including cancer of the prostate, FAS expression and FAS activity are very high. As shown in the laboratory, overexpression of FAS in tumor cells is part of a more general and coordinate upregulation of multiple lipogenic genes caused, at least in part, by activation of sterol regulatory element binding proteins (SREBPs), transcription factors that play a key role in cellular lipid homeostasis. The mechanisms underlying the activation of the SREBP pathway and the increase in lipogenesis in tumor cells as well as the ultimate biological significance of this phenomenon remain poorly understood. Nonetheless there is evidence that overexpression of lipogenic genes occurs early in tumor development and that the degree of overexpression correlates with increasing tumor grade. Moreover, a number of studies suggest that inhibition of FAS selectively reduces proliferation of tumor cells and causes apoptosis, implying that FAS and other lipogenic enzymes may constitute interesting targets for antineoplastic therapy.

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