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Mystery story about erythropoietin (Epo) and erythropoietin receptor (EpoR) are disguised?

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In this review- lecture we would like to focus our attention upon very controversial reports on Erythropoietin (Epo) and Erythropoietin Receptor (EpoR) expression in cancer patients. The effects of Epo on cancerous tissues are poorly understood. Hypoxia results in an increase in the level of the production of both Epo and EpoR via activation of the hypoxia-inducible factor 1 (HIF-1) pathway. HIF-1α, promotes the expression of vascular endothelial growth factor (VEGF). The signaling through VEGF in both a paracrine and an autocrine manner is required for the homeostasis of adult vessels. Macrophages stimulate vessel sprouting via a soluble factor other than VEGF, rather than through direct contact with endothelial cells. The intriguing questions are set about many researches to link Epo/EpoR expression and function in order to establish one of the mechanisms of tumor growth, disease progression of cancer patient. However, it is uncertain role in tumour angiogenesis as promoter and stimulator of tumour growth which should need to be furtherly validated.

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Lipogenic metabolism in ovarian cancer cells and its non-malignant precursors

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Ovarian cancer (OC) is caused by genetic aberrations in networks that control growth and survival. Importantly, aberrant cancer metabolism interacts with oncogenic signaling providing additional drug targets. Tumors over express the lipogenic enzyme fatty acid synthase (FASN) and are inhibited by FASN-blockers, whereas normal cells are FASN-negative and FASN-inhibitor-resistant. Here we demonstrate that this holds true when ovarian/oviductal cells reside in their autochthonous tissues, whereas in culture they express FASN and are FASN-inhibitor-sensitive. Upon subculture, non-malignant cells cease growth, express senescence-associated-β-galactosidase, lose FASN and become FASN-inhibitor-resistant. Immortalized ovarian/oviductal epithelial cell lines – although resisting senescence – reveal distinct growth activities, which correlate with FASN-levels and FASN-drug-sensitivities. Accordingly, ectopic FASN stimulates growth in these cells. Moreover, FASN-levels and lipogenic activities affect cellular lipid composition as demonstrated by thin-layer chromatography. Correlation between proliferation and FASN-levels was finally evaluated in cancer cells such as HOC-7, which contain sub-clones with variable differentiation/senescence and corresponding FASN-expression/FASN-drug-sensitivity. Interestingly, senescent phenotypes can be induced in parental HOC-7 by differentiating agents. In OC cells, FASN-drugs induce cell cycle-blockade in S and/or G2/M and stimulate apoptosis, whereas in normal cells they only cause cell cycle-deceleration without apoptosis. Thus normal cells, although growth-inhibited, may survive and recover from FASN-blockade, whereas malignant cells get extinguished. FASN-expression and FASN-drug-sensitivity are directly linked to cell growth and correlate with transformation/ differentiation/senescence only indirectly. FASN is therefore a metabolic marker of cell proliferation rather than a marker of malignancy and is a useful target for future drug development.

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