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Autor(en) des Beitrags: Mayer, A; Steimel, M; Wree, A; Kelleher, D; Vaupel, P
Titel des Beitrags: Solid tumours arising from differently pre-oxygenated cells: comparable growth rates despite dissimilar tissue oxygenation.
Abstract: PURPOSE: The hypoxia-inducible factor (HIF)-dependent transcriptional response is often very pronounced in hypoxic microregions of solid malignant tumours, leading to secretion of pro-angiogenic factors and activation of a hypoxia-tolerant, glycolytic metabolism. Here, the influence of the microenvironment of tumour-initiating cells as a factor determining intertumoural variations in the relative contributions of both processes has been examined. MATERIAL AND METHODS: The oxygenation status was assessed in rat DS-sarcomas using polarographic needle electrodes. Tumours were generated by allografting cells from either normoxic cell culture or severely hypoxic/anoxic ascites. HIF-related marker expression and intercapillary distances were analysed using immunohistochemistry. RESULTS: Cells preconditioned in hypoxic ascites form poorly vascularised, hypoxic tumours in rats, showing strong activation of HIF-1alpha and glucose transporter (GLUT)-1. Conversely, tumour-initiating DS-cells derived from normoxic cell culture form highly angiogenic, normoxic tumours with a significantly lower expression of HIF-1alpha and GLUT-1. Growth rates and the fraction of Ki-67 positive cells for both tumour groups were comparable. CONCLUSIONS: The intensity of angiogenesis in this model is primarily determined by the state of metabolic adaptation of tumour-initiating cells, rather than
being a function of HIF-activation during solid tumour growth, a finding which is highly relevant for the
design of treatment regimens targeting the tumour vasculature.