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In this issue

Regulating U-PAR in tumour metastases

In this issue of EJC, Heike Allgayer writes a summary of her European Association for Cancer Research Award Lecture, presented at ECCO13 in Paris, 2005. The article reviews the most important transcriptional mechanisms regulating the *u-PAR* gene encoding urokinase receptor, and focuses on the differential binding of transcription factors to *u-PAR* promoter elements, elucidated from studies using resected colorectal and gastric tumours. Invasion and metastasis of malignant cells require the degradation of extracellular matrix components, allowing tumour cells to enter systemic circulation. These events involve "tumour-associated proteases" that have been classified into serine, aspartic, cysteine, threonine and metalloproteinases. One of the proteases implicated in the invasive phenotype of tumour cells is the urokinase-type plasminogen activator (u-PA), which, via activation of plasminogen to active plasmin, is able to cleave several components of the extracellular matrix. Urokinase, secreted from fibroblasts, leukocytes, urogenital and tumour cells, is proteolytically activated either extracellularly or by binding to the urokinase receptor (u-PAR). Mechanisms regulating u-PAR has important implications for the development of therapies against invasion and metastases in cancer.

Palliative chemotherapy: To prolong life or for better QoL?

The goal of palliative chemotherapy (PCT) is to increase quality of life (QoL) and, if possible, to prolong life while preserving QoL. However, many oncologists disagree on the emphasis of PCT to improve QoL; and it is widely held that the main objective of PCT is to prolong life. Supposedly, patients attach great importance to survival gain, even as minimal as few weeks or months, and if QoL improvement is the central goal, then the use of difficult PCT regimens in asymptomatic patients cannot be easily justified. To address the lack of clarity about the intention and effectiveness of PCT, de Kort and colleagues have reviewed selected randomized controlled clinical trials of PCT in advanced colorectal cancer, to assess if PCT is used to prolong life or QoL. The study found that contrary to the original aim of PCT, QoL was not the main outcome of PCT.

p53 and p21 polymorphisms in cervical and ovarian cancer

Cervical cancer (CC) and ovarian cancer (OC) are the most frequent gynaecologic malignancies among women worldwide. Persistent infection with high risk human papillomavirus (HPV) is necessary, but not sufficient, for CC development. Genetic alterations or decreases in p53 protein levels result in progression through cell cycle, and the p53 target gene *P21* is responsible for blocking cell cycle progression. Attenuation of either p53 or p21 leads to increased tumour development. A common polymorphism on the p53 gene (*TP53*) is the presence of either arginine or proline on codon 72. The arginine p53 form is more susceptible to HPV mediated degradation and increases chances of CC, while a significantly higher frequency of the p53 Pro allele has been found in patients with OC. Polymorphisms in the untranslated regions (UTR) of *P21* have also been shown to be important in tumour suppression. In this issue of EJC, Santos and colleagues report on the first study evaluating the combined effect of *TP53* codon 72 and *P21* 3'UTR single nucleotide polymorphisms in CC and OC.

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