The secretion of urokinase?like plasminogen activator is inhibited by microtubule?interacting drugs

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The secretion of proteinases into the extracellular matrix is one of the main features of tumour cells, as related to their invasive behaviour. Considering the role of the microtubule cytoskeleton, and particularly the action of microtubule?associated protein (MAPs) in mediating protein secretion, the effects of the anti?microtubule drugs estramustine and taxol, on the secretion of urokinase?type plasminogen activator (u?PA) and the 72 kDa gelatinase were investigated. Treatment of 5637 bladder carcinoma cells with estramustine and taxol inhibited u?PA secretion into the conditioned medium in a drug concentration?dependent fashion. This inhibition was confirmed by determinations of u?PA enzymatic activities and by measurements of the levels of immunoreactive activator. Studies using gelatin zymograms also showed an inhibition of another tumoural proteinase namely the 72 kDa gelatinase. Time?course uptake experiments showed that estramustine was incorporated into the cells, a process wh