

**P016** Monolayer investigations into the cell penetrating peptide Tat

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The protein transduction domain of the HIV-1 transactivator of transcription, Tat (Tat<sup>(48-60)</sup>), has been shown to transport P10, a cytotoxic peptide mimic of the cyclin dependent kinase inhibitor, p21WAF1/CIP1 into the nucleus of cancerous cells and induce apoptosis. Here monolayer studies are used to investigate the membrane interactions of Tat<sup>(48-60)</sup>, P10 and the construct Tat<sup>(48-60)</sup>-P10. It was found that Tat<sup>(48-60)</sup> showed no significant surface activity but that both P10 and Tat<sup>(48-60)</sup>-P10, were highly surface active, inducing surface pressures of 9.74 and 8.9 mN m<sup>-1</sup> respectively. With monolayers formed from phosphatidylserine (PS) at an initial surface pressure of 30 mN m<sup>-1</sup>, mimetic of naturally occurring membranes, Tat<sup>(48-60)</sup> induced surface pressure changes of 2 mN m<sup>-1</sup>. These data suggest that the strongly cationic peptide was bound to the surface of the anionic monolayer, consistent with the targeting function. In contrast, P10 induced surface pressure changes of 9 mN m<sup>-1</sup> in PS monolayers and 6 mN m<sup>-1</sup> in monolayers formed from phosphatidylcholine, showing the peptide to be highly membrane interactive. The construct Tat<sup>(48-60)</sup>-P10 was found to induce surface pressure changes in lipid monolayers of *circa* 8 mN m<sup>-1</sup> comparable to P10 alone, and taken together these data are consistent with Tat<sup>(48-60)</sup> mediating transport of the P10 peptide across membranes.