Establishing the mechanism by which cell-penetrating peptides such as oligoarginine, and HIV-TAT gain access to the interior of cells is fundamental to their utilisation as drug-delivery vectors. Current research provides evidence supporting a role for both endocytosis and direct plasma membrane translocation. Here we have compared the uptake and distribution of a fluorescent-octaarginine peptide when incubated at different temperatures and concentrations with three leukaemia cell lines, KG1, KG1a and K562. At 4°C the peptide diffusely labels throughout the cytosol, the extent of which is highly cell-type dependent. At 37°C the pattern of labelling changes to vesicular; but in all cells studied, cytosolic labelling is enhanced at concentrations exceeding 5μM. Our previous studies showed depletion of plasma membrane cholesterol caused an influx of octaarginine into the cytoplasm of cells incubated with the peptide at 37°C [1], and we now extend this further to studies in a number of different adherent and non-adherent cell lines.