

B15 Can cellular uptake of polyamines be exploited in drug delivery?

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The ability to actively transport polyamines appears to be a ubiquitous property of mammalian cells. Exploitation of polyamine transport pathways to effect intracellular delivery of chemotherapeutic agents, particularly to cells expressing high levels of the polyamine transport system, represents a potentially novel approach to drug targeting. A range of fluorescently-labelled polyamine derivatives with varying degrees of N-alkylation have been synthesised and used to probe both the specificity of polyamine transport in A549 human lung carcinoma cells and their sub-cellular distribution. In keeping with our earlier conclusions concerning the broad specificity of the polyamine transport protein, N-alkylated polyamines appear to be efficiently translocated. Confocal laser scanning microscopy has been used to determine the intracellular location of these alkylated polyamines. In contrast to our earlier studies, significant amounts of these N-alkylated polyamines are found in the nucleus. The distribution between the cytoplasm and the nucleus appears to be influenced by the degree of alkylation. The implications of these studies in terms of the using the polyamine transporter system for drug delivery will be discussed.