Bafilomycin A1 and its attenuating effect on tumour growth in systemic malignancies, especially gastrointestinal malignancies

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The paper by Wang et al. [1] published in Clinical Science provided for highly interesting reading. Interestingly, recent data confirms that bafilomycin A1 decreases tumour growth in a number of systemic malignancies. For instance, it decreases growth in colonic malignancies. It mediates its antineoplastic effects by attenuating lysosomal acidification within the cancerous cells. At the same time, p38 phosphorylation is markedly attenuated [2] and mitochondrial uncoupling is typically augmented. On the other hand, caspase 7 and caspase 8 cleavage is accentuated. As a result, macro-autophagy is markedly inhibited [2] and cell-cycle arrest. Bafilomycin A1 administration also has a negative impact on HIF-1α (hypoxia-inducible factor-1α) cleavage [3] and subsequent accentuation of HIF-1α levels. This results in p21 induction and consequent cell-cycle arrest. JNK (c-Jun N-terminal kinase) phosphorylation is also decreased significantly, whereas p21 is typically up-regulated. The ultimate result is augmented intratumoral apoptosis, leading to disrupted tumour progression and decreased invasiveness [4].

Similar attenuation of tumour growth is typically seen in pancreatic malignancies following exposure to bafilomycin A1. It mediates these antineoplastic effects by augmenting intratumoral apoptosis [5]. Bafilomycin A1 also decreases intracellular pH within the cancerous cells and thereby accentuates the thermosensitivity of the tumour. These effects are especially more pronounced when bafilomycin A1 is used in conjunction with EIPA [5-(N-ethyl-N-isopropyl)amiloride] therapy [6]. These effects have been seen both in vivo and in vitro.

The above examples confirm the antineoplastic effects of bafilomycin A1 and highlight the need for further studies to fully harness these effects.

REFERENCES


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Abbreviation: HIF-1α, hypoxia-inducible factor-1α.

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