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## Effect of Membrane-active Microbial Autoregulators on the Growth of Cultured ras-Transformed Fibroblasts

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### Abstract

Differential effects on proliferation of individual vs. combined administration of high- and low-molecular-weight microbial autoregulators (extracellular RNase from *Bacillus subtilis* and anabiosis-inducing factor d1) are reported for the first time for cultured cells of higher eukaryotes. Proliferation of ras-transformed mouse fibroblasts was affected by both autoregulators dose-dependently. The cytotoxic activity of individual regulators was directly related to their concentration. Unlike RNase, factor d1 (which functions as a chemical chaperone) exerted reversible effects. Studies of the effects of combined administration of the autoregulators demonstrated that pretreatment of the cells with low-dose d1 decreased the toxicity of RNase. Higher doses of d1 were required to attenuate the effects of toxic agents with more pronounced membrane tropism. The results obtained suggest that a universal system regulating the physiological activity of cells is operative in taxonomically remote organisms. The operation of the system is based on sequential changes in the structural organization and function of subcellular structures, induced by low- and high-molecular-weight autoregulators.

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