Growth regulation in 3T3 cells: Role of intracellular K^+-ion content

S. Ullrich, G. Adam

Fakultät für Biologie, Universität Konstanz, Postfach 5560, D-7750 Konstanz, FRG

Evidence has accumulated in previous years showing that the intracellular K^+ concentration plays a major role in the processes of growth regulation in mammalian cell cultures in vitro (1-3).

In order to gain further insight into the sequence of events, we have made a parallel study of changes of cellular K^+ content and cellular population dynamics after stimulation or inhibition of proliferation of Swiss 3T3 cells. Cellular population dynamics were evaluated by following the proliferation behavior of about 100 individual cells reseeded from the experimental population onto a grid at a cell density of about 30 cm^{-2}. Cellular K^+ contents were determined using atomic adsorption spectrometry.

Results: 1) Between cell densities $4x10^3$ and $6x10^4 cm^{-2}$ (daily medium renewal at 5% calf serum), K^+ content drops continuously from 0.84 to 0.32 pmol/cell. Cell-density dependent growth inhibition, however, takes place only between cell densities of $3x10^4$ and $6x10^4 cm^{-2}$, where a subpopulation of long-living and long-term growth-inhibited cells emerges and rapidly takes over the culture. 2) After stimulation of these resting cells by reseeding to $10^4 cm^{-2}$ at 5% or 20% calf serum (daily medium renewal), cells do not divide for about 2 days, but cellular K^+ content rises continuously from 0.32 pmol/cell to a maximum of 0.77 pmol/cell. Thereafter, cell proliferation ensues, leading to subsequent decrease of K^+ content, which in turn is followed by growth inhibition.

The temporal sequence of changes in cellular K^+ content and proliferation in both of these experiments gives further evidence of a causal relation between these changes and is consistent with intracellular K^+ concentration acting as a second messenger in cell proliferation.

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