

Polyamine Derivatives in Growing Cells

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INTRODUCTION

Studies of the metabolism of the polyamines spermine and spermidine and the diamine putrescine have demonstrated increased polyamine concentrations in association with growth and cellular proliferative activity (3,7,8). Changes in the intracellular concentration of these amines had largely been ascribed to changes in their biosynthesis and in the activity of the enzymes catalyzing these reactions (14,18). Recent investigations in in vivo and in vitro systems have identified the prominent role of enzymes catalyzing the metabolic transformation of these compounds (5,21). These investigations have highlighted the physiological significance of conjugation (acetylation), oxidation and extracellular release of polyamines as regulators of polyamine concentration during cellular growth and division.

Recently, Rennert and associates have defined the presence of polyamine peptides in mammalian systems (6,19,20). Polyamine conjugates (17) and polyamine globulin complexes (4,13,16) have been detected in blood and urine of human subjects. Investigations in the past year in our laboratory (15) have resulted in the isolation and characterization of six polyamine conjugated proteins in human amniotic fluid. Three of these proteins contained covalently bound spermine, one covalently bound spermidine and two contained covalently bound putrescine.

To better understand the regulation and synthesis of these polyamine peptides, investigations to study the metabolic fate of radiolabelled putrescine were undertaken utilizing cultured human fibroblasts. The approach was predicated upon our previous observations indicating that polyamine peptide conjugates were found in extracellular fluid. The focus was to study the metabolic derivatives of radiolabelled putrescine by the characterization of products in the cell culture medium and within the intracellular pool. These studies document that human fibroblasts have the capacity to synthesize polyamine peptide conjugates and that these conjugates are excreted into the extracellular space.

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