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Matrix Gla protein (MGP) was first isolated from the matrix fraction of bone. This highly conserved vitamin K-dependent protein of 14 kDa has been identified in numerous tissues and cells, and its mRNA was recently found to be abundant in rat lung. Relatively low MGP protein levels in many soft tissues where its mRNA is high suggests an important secretory function for this protein. We have found a high specific activity of vitamin K-dependent carboxylase in microsomes of rat pulmonary type II cells and the presence of numerous endogenous substrates, including one of 13-15 kDa. To investigate the possibility that MGP and its mRNA could be localized in type II cells, rat MGP and actin cDNA probes were hybridized to total RNA obtained from freshly isolated type II cells and from cells cultured for up to 6 days. MGP mRNA increased 5- to 6-fold relative to beta-actin mRNA from days 3 to 6 in primary culture and MGP secretion increased nearly 60-fold during that interval. MGP mRNA and MGP secretion decreased 25-75% if cultures were supplemented with vitamin K quinone. Vitamin K deficiency, caused by carbon stripping the serum or treatment of cell cultures with warfarin, resulted in an induction of carboxylase activity and elevated MGP mRNA. In parallel experiments, carboxylase specific activity also increased during culture in the presence or absence of vitamin K. Retinoic acid further increased steady-state mRNA levels and MGP secretion at later culture intervals, an effect which was serum dependent.