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Hormonal requirements for kidney cells in serum free medium reveal an admixture of growth inhibitory and stimulatory effects

Mary L. Taub
University at Buffalo, USA

Abstract

Previously, we developed a hormonally defined medium for the canine kidney epithelial cell line MDCK serum free. Growth factor requirements include insulin, transferrin, hydrocortisone, triiodothyronine and Prostaglandin E_2 (PGE_2). The PGE_2 requirement is of particular interest, given its magnitude and elevated production in the kidney. MDCK cells have Gs-coupled EP2 and EP4 receptors, as well as Gq-coupled EP1 receptors for PGE_2. Both EP2 and EP4 appear to mediate the growth stimulatory effects of PGE_2, (given the growth stimulation by EP2 agonist butaprost, and the ability of the EP4 antagonist L161, 982 to prevent PGE2 mediated growth stimulation. The Gq-coupled EP1 has a distinct role, apparently inhibiting growth. Consistent with this hypothesis, the EP1 antagonists SC51089 and ONO8711 stimulate MDCK cell growth, even in the absence of exogenous PGE_2 (presumably by counteracting effects of endogenously produced PGE_2). A number of growth regulatory factors, including PGE_2, Trans-activate the EGF receptor (EGFR). In contrast, inhibition of EP1 receptor activation by SC51089 was observed to reduce tyrosine phosphorylation of EGFR, an indicator of EGFR activation. Similarly, inhibition of EP1 receptor activation by SC51089 was associated with reduced phosphorylation of Akt in response to insulin. Further studies are in progress to evaluate the interconnections between the effects of EP1 on the EGFR and Akt. PGE_2 has an established role in the development of carcinomas. Thus, EP1 is a viable target to control such cancers.

Biography

Mary Taub completed her Ph.D at the age of 26 years from the University of California, Santa Barbara and postdoctoral studies from the University of California, San Diego. She is a professor of Biochemistry in The School of Medicine and Biomedical Sciences at the University at Buffalo. She has published more than 80 papers in reputed journals. She served as a member of Subcommittee D Study Section of NIDDK.