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Evidence for a novel role of dopamine and norepinephrine in the kidney

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Abstract

While for some time, dopamine and norepinephrine have been known to regulate motor function and behavior, more recently these catecholamines have also been found to act on peripheral tissues, including the kidney so as to modulate sodium excretion and blood pressure regulation. Initial studies have indicated that when dietary salt is elevated, renal dopamine inhibits sodium reabsorption in the renal proximal tubule (RPT), an effect reversed by norepinephrine. Previously, regulation has been attributed to affects of these catecholamines on the integration of preexisting Na,K-ATPases into the basolateral membrane of RPT cells. Our recent studies with primary cultures of RPT cells indicate that dopamine and norepinephrine act at the transcriptional level to regulate the expression of the Na,K-ATPase β subunit and thereby increase the level of Na,K-ATPase (the β subunit limits the assembly of αβ heterodimers). Two D1 antagonists, fenoldapan and SCH2390, were observed to inhibit the transcriptional effect of dopamine, while the α2 adrenergic agonist guanabenz increased β subunit expression. The inhibitory effect of dopamine on transcription was dependent upon an increase in intracellular Na^+, caused by monensin. The inhibitory effect of dopamine was prevented by cotransfection with an expression vector encoding for a mutant Salt Inducible Kinase (SIK). SIK is a member of the AMP Kinase family, which is activated by increases in intracellular Na^+. When SIK is activated, it phosphorylates cAMP activated transcriptional coactivators (CRTCs), thereby preventing their interaction with CREB on the β subunit promoter. Further studies are in progress in these regards.

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.