concentration of unlabeled DNP, the dense glomerular and renal tubular bindings were completely displaced. The maximal binding densities of ^{125}I-DNP in glomerulus was higher rather than those in renal tubules. Various natriuretic peptides competed with the bindings of ^{125}I-DNP to the glomerulus and renal tubules. These results indicate that specific receptor for DNP is localized in the kidney, and DNP may be a regulator of renal functions in the freshwater turtle.

E114 Src Kinase and PKC Are Involved in CD99 Type II-Mediated Signaling Pathway Which Leads to Promotion of Cell Motility and MMP-9 Secretion in Human Breast Carcinoma Cells

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We have shown previously that expression of a splice variant of CD99 membrane protein (CD99 type II) increases cell motility and matrix metalloprotease-9 (MMP-9) secretion in MDA-MB-231 human breast carcinoma cells. When various inhibitors for signal transduction mediators were tested for their effects on motility and MMP-9 activity of CD99 type II-transfected breast carcinoma cells. PP1, a src kinase-specific inhibitor, exhibited a significant inhibition on motility of CD99 type II-expressing cells. Among src transfectants, dominant-negative src- transfected cells were 80-90% less motile than mock transfectant cells, while v-src- and c-src-transfected cells exhibited motility levels at or slightly above the mock transfectants. Meanwhile, MMP-9 activity in a culture of CD99 type II-expressing cells was completely inhibited by PKC-specific inhibitors, GF109203X and myristoylated PKC peptide, whereas PMA, a PKC activator, increased MMP-9 activity in cells devoid of CD99 type II expression to a similar level of that in CD99 type II-expressing cells. Our data strongly suggest that CD99 type II promotes motility and MMP-9 secretion of human breast carcinoma cells through the activation of src kinase and PKC, respectively.

E115 Biochemical and Biological Analyses of a Novel GTP-Binding Protein Interacting with NF2 Tumor Suppressor

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In attempt to understand the molecular mechanism allowing the neurofibromatosis-2 (NF2) gene product to function as a tumor suppressor, we have previously identified a novel GTP-binding protein, named NGB (NF2-associated GTP-binding protein) that specifically associates with NF2 protein *in vitro* and *in vivo*. GTP binding region of NGB was shown to be highly homologous to Ras and Rho small G-protein family members. In this study, we have found that NGB has a intrinsic GTPase activity as well as GTP-specific binding affinity. Although both biochemical activities of NGB protein were not affected by the NF2 binding, degradation of NF2 protein was strongly protected by NGB. Overexpression of NGB in JS-1 rat schwannoma cells *significantly inhibited cell growth in vitro* and *in vivo*, and brought about changes in cell-cell adhesion and actin cytoskeleton structure. The cell growth-inhibiting activity of NGB was shown to be partially mediated by NF2 protein. These data indicate that NGB protein in association with NF2 tumor suppressor plays an important role in controlling cell proliferation.