REGULATORY EFFECTS OF NITRIC OXIDE ON SRC KINASE, P130CAS AND PTPα, MAJOR COMPONENTS OF FOCAL ADHESION COMPLEXES

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Nitric Oxide (NO) is a free radical able to diffuse across membranes and travel long distances implicated as a signaling molecule in a number of physiologic processes. We showed previously that treatment of fibroblasts with NO donors activates Src Kinase through autophosphorylation at Y416 (FRBM 28: 174; 2000). Src Kinase is constitutively phosphorylated at Y527, and dephosphorylation of Y527 by PTPα is the most well characterized mechanism of kinase activation. Then, we hypothesized that activation of Src by NO was a result of the cooperation between cysteine S-nitrosation and tyrosine phosphorylation. Presently, we describe S-nitrosation and phosphorylation of Y416 of Src Kinase in fibroblasts "knock-out" for PTPα exposed to 500 μM SNAP (NO donor). P130 Cas a Src Kinase substrate was phosphorylated on tyrosine after exposure of these cells to SNAP. On the other hand, in PTPα-expressing cells, SNAP stimulated S-nitrosation of Src kinase in a lesser extent. SNAP promoted tyrosine dephosphorylation of p130 Cas in these cells. Furthermore, we found high expression levels of thioredoxin in PTPα-expressing cells. In conclusion, the expression of PTPα may determine the extent of S-nitrosation on Src Kinase and the regulation of signal transduction through Src by S-nitrosation.
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