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Excessive insulin receptor serine phosphorylation in cultured fibroblasts and in skeletal muscle. A potential mechanism for insulin resistance in the polycystic ovary syndrome.

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First published August 1, 1995 - More info

[–] Abstract

We investigated the cellular mechanisms of the unique disorder of insulin action found in the polycystic ovary syndrome (PCOS). Approximately 50% of PCOS women (PCOS-Ser) had a significant increase in insulin-independent beta-subunit [32P]phosphate incorporation (3.7-fold, $P < 0.05$ vs other groups) in skin fibroblast insulin receptors that was present in serine residues while insulin-induced tyrosine phosphorylation was decreased (both $P < 0.05$ vs other groups). PCOS skeletal muscle insulin receptors had the same abnormal phosphorylation pattern. The remaining PCOS women (PCOS-n1) had basal and insulin-stimulated receptor autophosphorylation similar to control. Phosphorylation of the artificial substrate poly GLU4:TYR1 by the PCOS-Ser insulin receptors was significantly decreased ($P < 0.05$) compared to control and PCOS-n1 receptors. The factor responsible for excessive serine phosphorylation appeared to be extrinsic to the receptor since no insulin receptor gene mutations were identified, immunoprecipitation before autophosphorylation corrected the phosphorylation defect

and control insulin receptors mixed with lectin eluates from affected PCOS fibroblasts displayed increased serine phosphorylation. Our findings suggest that increased insulin receptor serine phosphorylation decreases its protein tyrosine kinase activity and is one mechanism for the post-binding defect in insulin action characteristic of PCOS.

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[–] Browse pages

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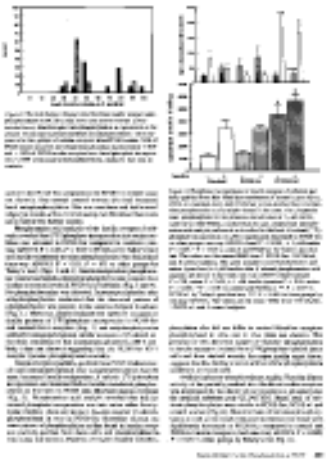
page 801

page 802

page 803

page 804



page 805

page 806

page 807

page 808

page 809

page 810

[–] Version history

- Version 1 (August 1, 1995): No description

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