中文題目：酪氨酸去磷酸酶在瘦體素所誘發表皮生長因子接受器轉活化及內皮素表現於初生鼠心臟細胞上所扮演的角色

英文題目：**Role of Src Homology 2-containing Tyrosine Phosphatase in Leptin-induced Epidermal Growth Factor Receptor Transactivation and Endothelin-1 Expression in neonatal rat cardiomyocytes**

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前言：Evidence indicates that leptin, the obese gene product, is linked with cardiac hypertrophy in obese humans and directly induces cardiomyocyte hypertrophy in vitro. However, the signaling mechanisms remain to be extensively examined.

材料及方法：Cultured neonatal rat cardiomyocytes were stimulated with leptin, protein synthesis and the endothelin-1 (ET-1) expression was examined. Antioxidants pretreatment on leptin-induced effects were performed to elucidate the redox-sensitive pathway in cardiomyocyte hypertrophy and ET-1 expression.

結果：Leptin increased protein synthesis which was inhibited with ET_A receptor antagonist (BQ485). Leptin increased ET-1 expression, phosphorylation of epidermal growth factor receptor (EGFR) and reactive oxygen species (ROS) generation in cardiomyocytes. Antioxidants and $p47^{phox}$ small interfering RNA knockdown all inhibited the EGFR transactivation induced by leptin. We examined the effect of ROS on Src homology 2-containing tyrosine phosphatase (SHP-2) in cardiomyocytes using a modified malachite green phosphatase assay. SHP-2 was oxidized during leptin treatment, and this oxidization could be repressed by antioxidants treatment. In SHP-2 knockdown cells, leptine-induced EGFR phosphorylation was dramatically elevated and is not influenced by antioxidants. In addition, leptin activated the transcription factor activator protein-1 (AP-1), as well as the phosphorylation of extracellular signal-regulated kinase (ERK). Mutational analysis of the ET-1 gene promoter showed that AP-1 binding site was an important cis-element in leptine-induced ET-1 gene expression.

結論：These findings indicate that ROS-EGFR-ERK pathway may be involved in ET-1 induction and thereafter cardiomyocyte hypertrophy induced by leptin.