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THE CRITICAL ROLE OF P66SHC OXIDATIVE STRESS PATHWAY IN HYPERANDROGEN-INDUCED OVARIAN FIBROSIS

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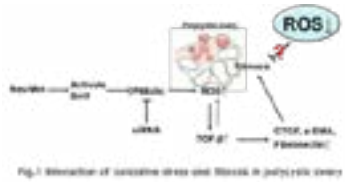
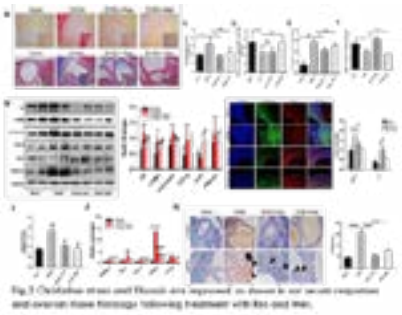
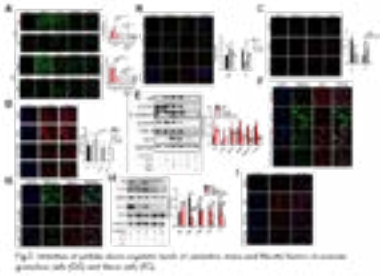
Androgen excess is generally considered as one of the major characteristics of polycystic ovarian syndrome (PCOS). Evidence from clinical research has revealed increased levels of oxidative stress (OS) in PCOS patients. Recent research showed that androgen induced PCOS rat existed over fibrosis, which may have influence on ovary function. Our study aimed to investigate the possible inhibition of hyperandrogenic ovarian fibrosis by preventing p66shc-induced oxidative stress. Our data demonstrated that inhibiting the expression of p66shc could suppress ovarian oxidative stress, thereby restraining further fibrosis. In ovarian tissues, reduced fibrosis together with lowered expression of p66shc and ROS was observed in resveratrol- and metformin-treated rats. Down-regulation of fibrogenic factors including collagens, TGF-β, CTGF, β-catenin and α-SMA as a result of the inhibition of p66shc was confirmed by western blot, Q-PCR, immunofluorescence and immunohistochemistry. We also observed that p66shc was mainly expressed in the nuclei of granulosa cells (GC) and theca cells (TC). Knockdown of p66shc resulted in dramatic down-regulation of ROS and fibrogenic factors such as TGF-β, CTGF, β-catenin and α-SMA in ovarian granulosa cells and theca cells. Furthermore, inhibition of fibrosis was accompanied with markedly improved ovarian morphology, increased luteal cell number and lowered levels of androgen. These findings suggest that p66shc may be a direct target of SIRT1 for inducing ROS and thus promoting fibrosis. We believe that further exploration of the mechanisms of p66shc in both fibrosis and oxidative stress may provide therapeutic strategies in improving PCOS symptoms and reproductive function.







Biography

Yong Wang is a Professor at Medical School, Nanjing University, China whose research interest focuses on Polycystic Ovary Syndrome. He is dedicated to the teaching of Histology and Embryology.

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