福昕PDF编辑器

• 永久 • 轻巧 • 自由

点击升级会员

点击批量购买

永久使用
无限制使用次数

极速轻巧
超低资源占用，告别卡顿慢

自由编辑
享受Word一样的编辑自由

扫一扫，关注公众号

The critical role of p66shc oxidative stress pathway in hyperandrogen-induced ovarian fibrosis

Daojuan Wang and Yong Wang, State Key Laboratory of Analytacal Chemistry for Life Science & Jiangsu Key, Laboratory of Molecular Medicine, Medical school, Nanjing University,, Nanjing 210093, China

Abstract

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 demonstrate 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 a-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 a-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.

Image

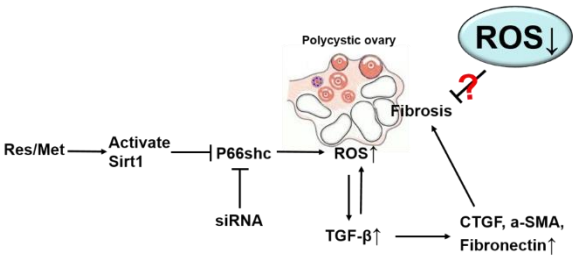


Fig.1 Interaction of oxidative stress and fibrosis in polycystic ovary

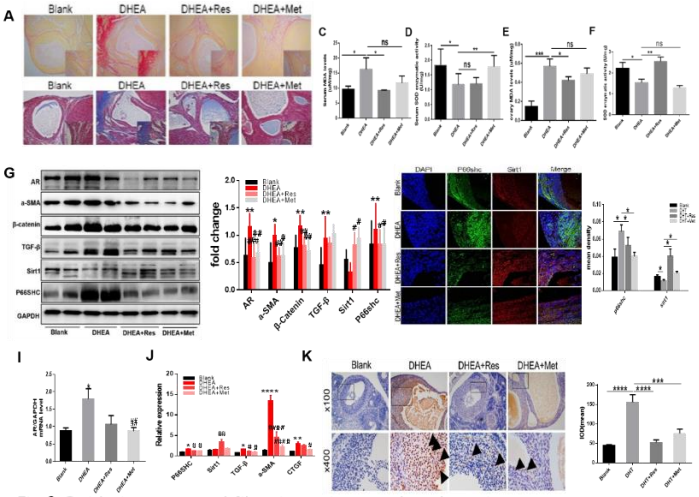


Fig.2 Oxidative stress and fibrosis are improved as shown in rat serum responses and ovarian tissue histology following treatment with Res and Met.

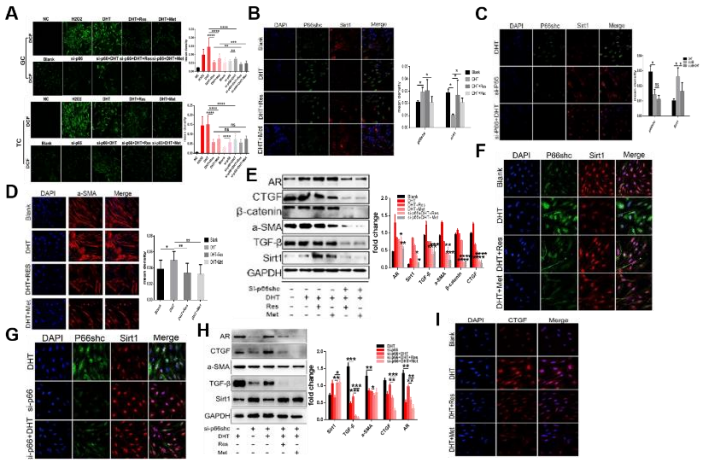


Fig.3 Inhibition of p66shc down-regulate levels of oxidative stress and fibrotic factors in ovarian granulosa cells (GC) and theca cells (TC).

Recent Publications

1. Daojuan Wang, Yong Wang (2018) DHEA-induced ovarian hyperfibrosis is mediated by TGF-β signaling pathway. J OVARIAN RES 11（1）:6.

2. Xinlin Zhang, Yong Wang (2013) Dehydroepiandrosterone induces ovarian and uterine hyperfibrosis in female rats. Human Reproduction 11:3074-3085.


Daojuan Wang;  Yong Wang

Daojuan Wang, graduate student at Medical School, Nanjing University. Yong Wang, professor at Medical School, Nanjing University whose research interest focuses on polycystic ovary syndrome, and who is dedicated to the teaching of histology and embryology.

Email: yongwang@nju.edu.cn

Notes/Comments: