

Background: The phytoestrogen resveratrol found in grapes and other plants has attracted considerable interest due to its proposed ability to extend lifespan, attenuate the development of metabolic syndrome in obese subjects and protect against cardiovascular disease. Self-medication with high pharmacological doses of this polyphenol with aim to improve metabolic parameters and health cannot be excluded in some sensitive health-focusing populations of humans. Prepartal voluntary exposure with resveratrol of pregnant women may negatively influence development of hormonal homeostasis and stress responsiveness in fetus.

Objective: To explore the potential of resveratrol to affect human fetal adrenal steroidogenesis at the end of the first trimester (gestational week 9-12).

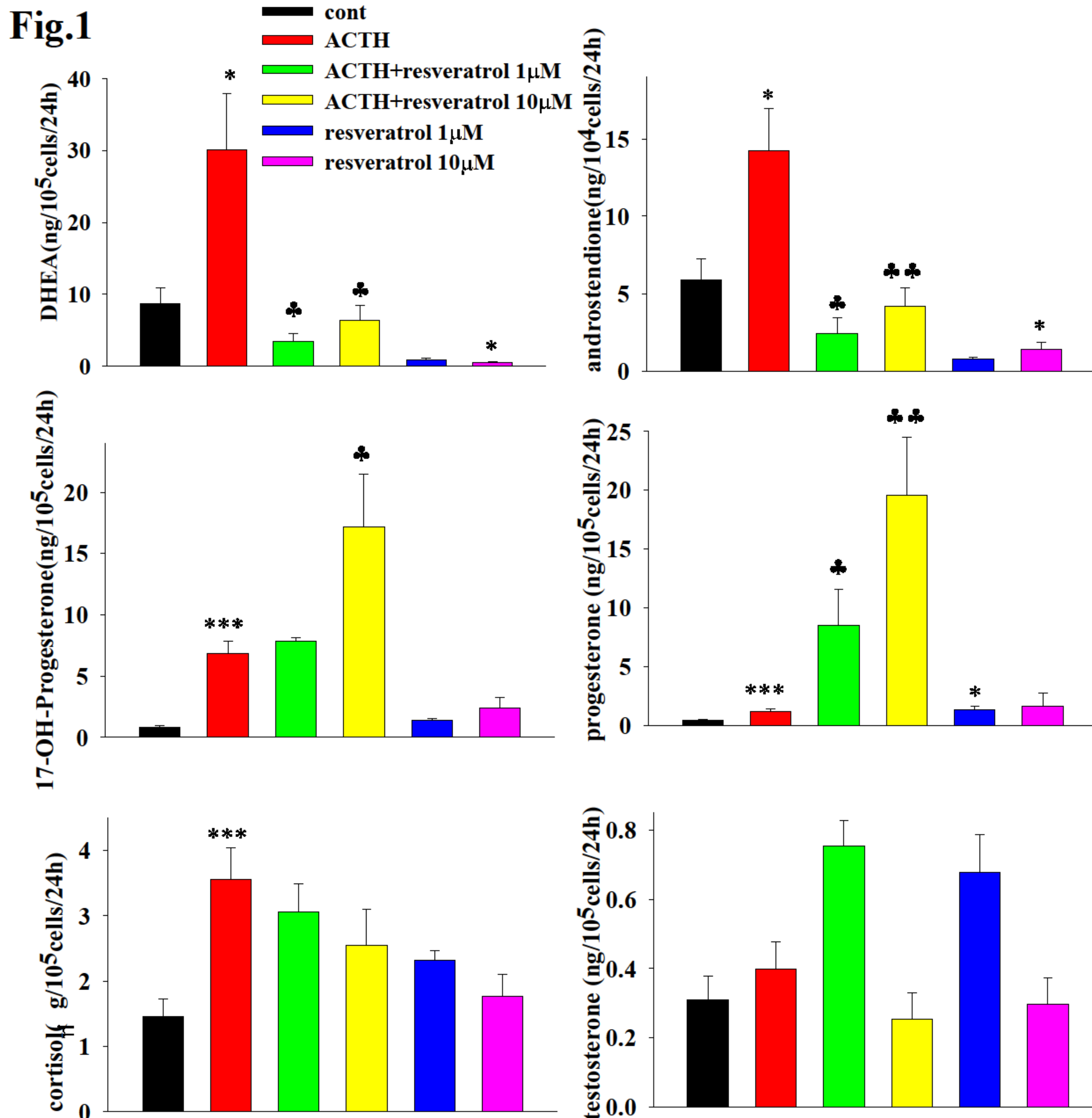


Fig.1 Effect of resveratrol on steroid production by human fetal adrenocortical cells * p<0.05, ** p<0.01, *** p<0.001 compare to control; ♣ p<0.05, ♣♣ p<0.01 compare to ACTH treatment.

Fig.2

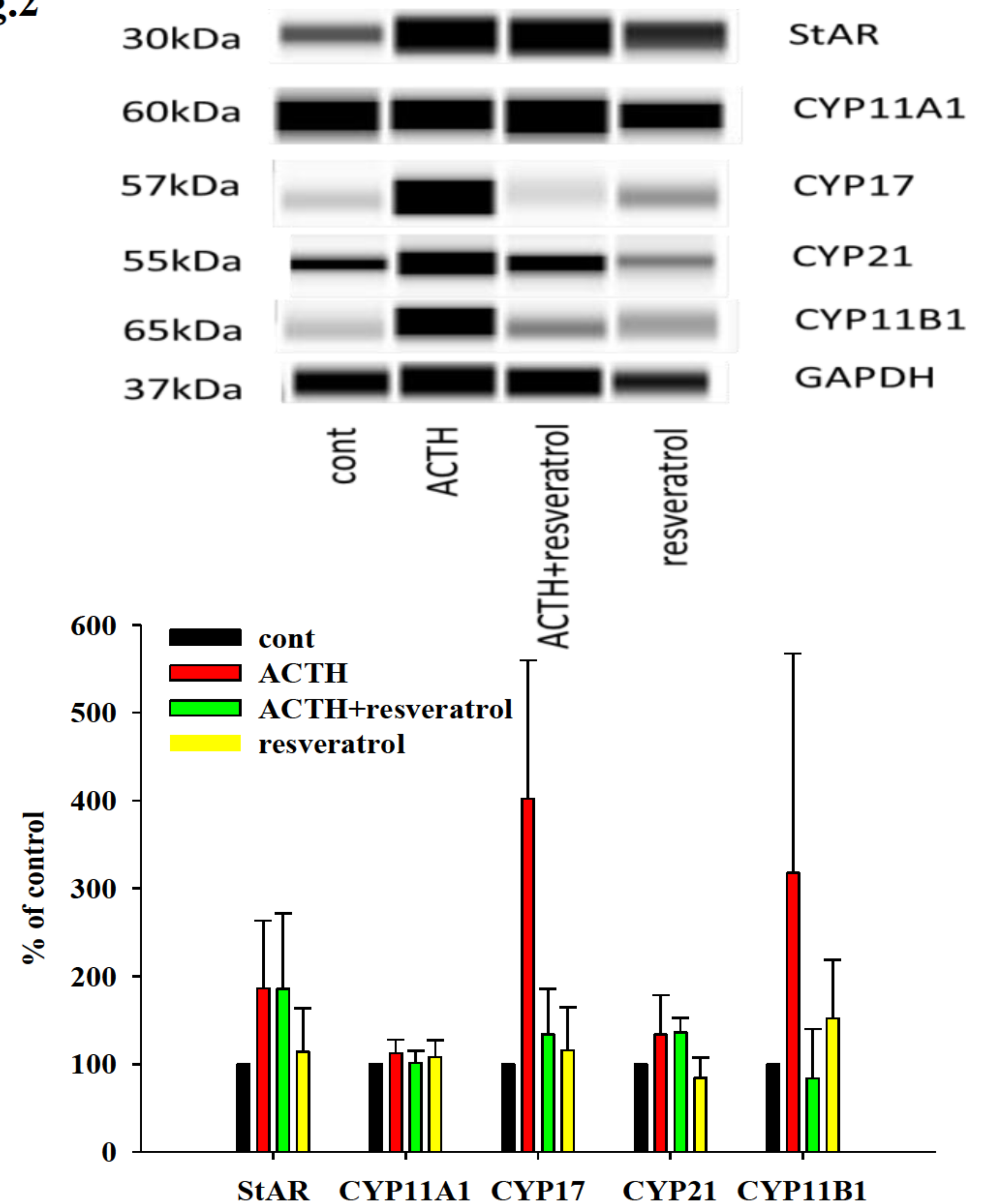


Fig.2 Effect of resveratrol on steroidogenic enzyme levels in human fetal adrenocortical cells

Material and Methods: Isolated adrenals from gestation week 9-12 were treated with collagenase and the isolated cells were cultured in vitro for 24h with concentrations of resveratrol with or without stimulation with ACTH. Levels of DHEA, androstenedione, progesterone and 17OH-progesterone, cortisol and testosterone were analysed by ELISA. Expression of steroidogenic genes was measured by Western Blotting.

Results and Discussion: We observed that resveratrol in both low (1µM) and high (10µM) concentrations significantly suppressed production of DHEA and androstenedione but elevated the release of progesterone and 17OH-progesterone by primary cultures of ACTH stimulated human fetal adrenocortical cells (Fig. 1) These alterations in steroidogenesis were associated with down-regulation of CYP17 expression at the protein level (Fig. 2), suggesting that the 17,20 lyase activity of the cytochrome CYP17 was attenuated. Resveratrol slightly decreased cortisol production by human fetal adrenocortical cells which was associated with moderate suppression of CYP21 and CYP11B1 expression. No significant effects of resveratrol on cell proliferation and mitochondrial function were found (data not shown).

Summary and conclusions:

- Resveratrol inhibited CYP17 expression and the 17,20 lyase activity in primary culture of human fetal adrenocortical cells.
- Resveratrol has a potential to disrupt steroidogenesis in human fetal adrenals at the end of the first trimester.
- Pregnant women should avoid exposure to high concentrations of resveratrol.

References:

1. Oskarsson, A., Spatafora, C., Tringali, C., and Andersson, A. O. (2014). *Prostate* 74(8), 839-51
2. Goto, M., Piper Hanley, K., Marcos, J., Wood, P. J., Wright, S., Postle, A. D., Cameron, I. T., Mason, J. I., Wilson, D. I., and Hanley, N. A. (2006). *J Clin Invest* 116(4), 953-60