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Activation of Nrf2-Antioxidant Pathway in Response to Different Concentration of Sulforaphane in granulosa cells

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Luteinizing granulosa cells (GCs) are exposed to elevated level of reactive oxygen species (ROS) during ovulation. As sulforaphane (SFN) is believed to be initiated the transcription of Phase II antioxidant genes through Nrf2 pathway activation, this study was conducted to investigate the effect high and low concentrations of SFN in activating Nrf2 pathway in granulosa cells. Results showed that expression of *NRF2* increased significantly ($p<0.05$) with fold change ranged from 2-6 in sulforaphane treated granulosa cells, whereas *KEAP1* (cytoplasmic *NRF2* inhibitor) expression was either significantly downregulated or similar as control under the same conditions. Moreover, the relative abundance of the Nrf2 downstream target antioxidant genes (*CAT, PRDX1, SOD1* and *TXN1*) were found to be higher (fold change ranged from 2-5, $p<0.05$) in sulforaphane treated granulosa cells compared to control. However, high ROS accumulation and low mitochondrial activity were found in granulosa cells treated with high concentration 20 µM of sulforaphane, whereas low concentrations (2 and 10 µM) had no such effects. These results clearly indicate that the SFN activates Nrf2 pathway in GCs at low concentrations; however, at high concentrations it generates higher level of ROS and damages cellular macromolecules and cause cellular apoptosis.

Keywords: Oxidative stress, sulforaphane, granulosa cells, gene expression, Nrf2.

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