NEK2 Plays an Essential Role in Mitotic Division and DNA Damage Response by the Wnt/β-Catenin Signaling Pathway in Porcine Embryonic Development

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NIMA-related kinase 2 (NEK2) is a serine/threonine protein kinase involved in cell cycle regulation, differentiation, and the DNA damage response system during a variety of cellular events. Inhibition of NEK2 is known to cause abnormal nuclear morphology in a variety of cell types and disrupt cell cycle progression, including the G2/M phase. However, the role of NEK2 in porcine embryonic development is unknown. In this study, we investigated the role of NEK2 in embryonic development and its underlying regulatory mechanisms using the NEK2-specific inhibitor, JH295. Inhibition of NEK2 after parthenogenetic activation significantly reduced cleavage and blastocyst formation rates, trophectoderm and total cell numbers, and cell survival compared to control. NEK2 inhibition delayed cell cycle progression at all stages from interphase to cytokinesis during the first mitosis. Additionally, NEK2 inhibition caused abnormal nuclear morphology in 2-cell and 4-cell stage embryos. Moreover, NEK2 inhibition significantly increased DNA damage and apoptosis, and it altered the expression levels of DNA damage repair- and apoptosis-related genes. Intriguingly, NEK2 inhibition downregulated the expression of β-catenin and Wnt signaling-related genes. To determine the relationship between Wnt/β-catenin signaling pathway and NEK2 in porcine embryonic development, we cultured porcine embryos in JH295-treated medium with or without Wnt activator CHIR99021. CHIR99021 treatment strongly restored developmental parameters reduced by JH295 treatment to control levels. In conclusion, these results demonstrate that NEK2 plays an essential role during porcine embryonic development by regulating mitosis and DNA damage repair systems by the Wnt/β-catenin signaling pathway.

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