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Evaluating the effect of sonic hedgehog inhibition on differentiation of hES cells into pancreatic lineage and polycomb group protein BMI1 expression

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Differentiation of human embryonic stem cells (hES) involves interactions between various chromatin modifiers and signaling pathways. The sonic hedgehog (SHH) pathway plays an important role during development of foregut organs such as: liver, pancreas, stomach and intestines. Previous reports have shown that inhibition of SHH pathway is essential for formation of dorsal pancreas during embryonic development. Polycomb group (PcG) proteins BMI1 and EZH2 have been shown to be important for proliferation of pancreatic stem cells. Previous reports have shown that constitutive SHH signaling up regulates expression of BMI1 in medulloblastoma, pancreatic and breast cancer, leading to proliferation of cancer cells. Most research groups incorporate synthetic inhibitor of the SHH pathway during differentiation of hES cells into pancreatic lineage, but its effect on differentiation of hES cells into pancreatic lineage and expression of BMI1 has not yet been investigated. In the present study, hES cells were differentiated into pancreatic lineage in the presence and absence of SHH inhibitor. Western blot results showed that cyclopamine (SHH inhibitor) led to reduction in expression of sonic hedgehog, while the expression of PATCHED1, SMO and GLI3 by qRT-PCR indicated the inhibition of SHH pathway. BMI1 expression at both protein and transcript level, was directly affected by the sonic hedgehog pathway inhibition. However, expression of PDX1 (pancreas specific transcription factor) showed marginal reduction at protein and transcript level. The study shows the association between PcG protein BMI1 and sonic hedgehog pathway during differentiation of hES cells into pancreatic lineage in vitro.

Biography

Prasad Pethe has completed his PhD from National Institute for Research in Reproductive Health (NIRRH) affiliated with University of Mumbai on differentiation of human embryonic stem cells into pancreatic lineage. Currently, he is an Assistant Professor at SVKM's NMIMS School of Science in Mumbai and has experience of clinical and industry setup. He has published several papers in international peer reviewed journals of repute.

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