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Assessing the Roles of MYC and EGR1 in Endoderm Differentiation

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The Wnt signaling pathway is evolutionarily conserved from fruit flies to humans. Strongly associated with development and embryonic morphogenesis, it is known to be required for early endoderm and later hindgut development in mammals. In adults, the Wnt signaling pathway is required for the proper maintenance of the intestinal epithelium and mutations in critical Wnt signaling pathway components are initiating events in the development of essentially all colorectal cancers. An important target gene whose expression is upregulated by Wnt signaling pathway activation is the oncogene *MYC*. This gene produces a transcription factor whose typical cellular role is to stimulate cell cycle progression and proliferation. Under specific cellular conditions, namely in the absence of functional p53, MYC has been shown to upregulate the expression of EGR1, ultimately leading to apoptosis. Interestingly, we have observed specific expression of these MYC-EGR1 pathway components during the differentiation of human induced pluripotent stem cells (hiPSCs) into definitive endoderm. These studies seek to assess the role of the MYC-EGR1 pathway in early endodermal development. Using immunofluorescence staining, we seek to assess whether MYC and EGR1 are absent from undifferentiated pluripotent stem cells by co-staining for the pluripotency marker OCT-4 and MYC or EGR1. Next, we seek to determine whether MYC, EGR1, or both are required for endoderm differentiation by specifically targeting their expression using shRNA during endoderm differentiation. These studies will contribute to our understanding of the molecular mechanisms involved in endoderm differentiation and the role of the MYC-EGR1 pathway in the process.