THE SUMMARY OF Ph.D.DISSERTATION

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Title

Effect of cellular responses
induced by cell cycle regulatory molecules

Abstract

Overexpression of cyclin D1 due to gene rearrangement, gene amplification or simply increased transcription frequently occurs in several types of human cancers. However, overexpression of cyclin D1 in cell culture system is insufficient, by itself, to cause malignant transformation. In this study, the author found that when rodent fibroblasts that overexpress cyclin D1, but not normal fibroblasts, were treated with basic FGF (bFGF), there was enhanced cell cycle progression, Erk2 activation, induction of anchorage independent growth and enhanced invasion of a matrigel barrier. These enhanced responses to bFGF appear to be due to increased expression of FGF receptor-1 (FGFR-1), at both the mRNA and protein levels, in the cyclin D1 overexpressing cells. The author obtained evidences that this increase in FGFR-1 expression is mediated through cyclin D1 activation of the pRB-E2F pathway. Taken together, these results suggest that *in vivo* cyclin D1 overexpression can enhance tumor progression, at least in part, by potentiatory the stimulatory efforts of bFGF, which is often produced by stromal cells, and the growth of adjacent tumor cells.