Cell Cycle Analysis of a Malignant Adrenocortical Cell Line: Novel Functions of Cyclin D1

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We have reported that Y1 malignant adrenocortical cells undergo senescence when stimulated by FGF2, in spite of having G0? G1? S cell cycle transition triggered (Costa et al, 2008). Y1 cells bear two main oncogenic lesions: amplification and overexpression of the ki-ras gene and a simultaneous, instead of sequential, expression of cyclins D1 and E during G0? G1? S transition. These lesions partially deregulate Y1 cell cycle causing leakiness of the G0? G1 switch under serum starvation. However, ectopic expression of cyclin D1 in Y1 cells intriguingly yielded clonal sublines (Y1D1) displaying better control of the G0? G1 switch instead of complete deregulation of the G0? G1? S transition. These Y1D1 sublines remain highly sensitive to FGF2 toxicity. To investigate the molecular mechanisms underlying this phenomenon we are analyzing cell cycle dynamics by flow cytometry and BrdU pulse labeling. Our results show that both, parental Y1 and Y1D1G subline, have their FCS-driven cell cycle progression delayed by FGF2 stimulation, showing clear arrest point in S phase. In addition, cyclin D1 expression seems not be restricted to the G1 phase of Y1 cell cycle. Taken together, these data suggest novel roles for cyclin D1 in cell survival and robustness of cell cycle control, independently of its classical function in regulation of G1 phase progression.

Key words: Cell Cycle, Cyclin D1, FGF2, Flow Cytometry

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