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RESEARCH ABSTRACT FORM

TITLE: Splice Variants of Transcription Factor E2F7- A key to Rb dependent and independent functions of E2F7

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E2F7 and E2F8 transcription factors are conventionally classified as the fourth subgroup in the E2F family, due to their uniqueness in function and domain organization. Unlike the other E2F proteins, E2F7 and E2F8 possess two DNA binding domains, but lack dimerization and pocket protein binding/ transactivation domains leading to the belief that they function in an Rb independent manner, with ability to bind to DNA without need for DP proteins. The evidence from in-vitro experiments suggest that E2F7 acts as a transcriptional repressor that can block E2F-dependent activation of a subset of E2F target genes and negatively influence cellular proliferation, which is further supported by the fact that E2F1 is a target for E2F7 (de Bruin *et al*, 2003; Li *et al*, 2008). The mouse E2F7 gene has 13 introns and 14 exons (de Bruin *et al*, 2003). Studies using the U2OS human cell line, WI38 human fibroblasts and Rat1 cell line have shown that two splice variants of the E2F7 protein exist: E2F7a and E2F7b. The E2F7a transcript is shorter compared to E2F7b due to splice exclusion of Exon 12 and an early termination sequence in Exon 13. Protein products from these transcripts differ only in their C-terminal region, from amino acid 713 onwards. The E2F7b protein (911 residues) is, by far, the more common variant of E2F7, with cell cycle dependent expression pattern; levels being undetectable in mitosis and early G₁ but increased in S phase. This is in contrast to the expression pattern of E2F7a (728 residues), which is present in all phases of cell cycle (Stefano *et al*, 2003). Even though both E2F7a and E2F7b lack typical pocket protein binding domains, the presence of a putative Retinoblastoma protein (Rb) binding sequence in the region encoded by Exon 12 makes it likely that these variants represent two different functional aspects of E2F7, differing in their ability to interact with Rb. Moreover, our preliminary data suggests that in an in-vitro overexpression system, E2F7b has the ability to associate with Rb. Based on this preliminary data and previous studies, we hypothesize that there are two splice variants of E2F7 in mouse, with each of these variant proteins possessing independent and different functions, attributed to their differing expression patterns and Rb binding capabilities.