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“Mechanisms of RI-alpha and RIAZ in Cell Growth Regulation”

[To investigate how the interaction of RI-alpha with a novel BTB-POZ domain zinc finger protein, RIAZ, regulates cell growth.]

This grant application seeks to investigate the functions of a novel gene that we have identified in our laboratory recently and to determine whether it is involved in controlling cancer cell growth. We found this gene, that we named RIAZ (RI-alpha interacting zinc finger), to be overexpressed in breast cancer cell lines. RIAZ belongs to a family of BTB/POZ domain containing zinc finger proteins, which function as transcription factor and in cell growth regulation. We reason that RIAZ may also function as a transcription factor and play critical role in cell growth regulation. Our preliminary results showed that RIAZ can activate c-Myc gene promoter activity, thus suggesting that it may be a transcription factor. We propose in this grant application to first characterize the transcriptional property of RIAZ by examining its DNA binding site and the domains in the protein require for transcription activation. We will also attempt using DNA microarray or gene chip technology to identify the genes that may be activated by RIAZ. We also propose to study whether RIAZ is involved in cell growth control by gene transfer methods in cell culture. We will test the effects of RIAZ on cell growth by various standard growth assays after introducing the gene into tissue culture cells. We will also abolish RIAZ expression by RNA suppression in breast cancer cells that overexpressed RIAZ and determine whether it has effects on the growth of these cells. We believe that the proposed studies will increase our understanding of the function of RIAZ. Since RIAZ is overexpressed in breast cancer cells and also targeted for genetic mutation in Ewing sarcoma, it may be a target for drug intervention, which may be a subject for future pursuance.