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# Modulation of Human Oct-4 Function

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The *Oct-4*gene encodes a transcription factor that is expressed in embryonic stem cells and germ cells. Oct-4 is known to function as a transcriptional activator of genes involved in maintaining an undifferentiated totipotent state and possibly in preventing expression of genes activated during differentiation. In addition, it is an putative proto-oncogene and a critical player in the genesis of human testicular germ cell tumors. Although much effort has gone towards characterizing the Oct-4, there is still little known about the molecular mechanisms and the proteins that regulate Oct-4 function. To identify cofactors that control Oct-4 function *in vivo*, we used a recently developed bacterial two-hybrid screening system and isolated a novel ES cell-derived cDNA encoding Ewing's sarcoma protein (EWS). EWS is a proto-oncogene and putative RNA binding protein involved in human cancers. By using GST pull-down assays, we were able to confirm the interaction between Oct-4 and EWS *in vitro*, and moreover, coimmunoprecipitation and colocalization studies have shown that these proteins also associate *in vivo*. We have mapped the EWS interacting region to the POU domain of Oct-4. In addition, three independent sites on EWS are involved in binding to Oct-4. In this paper, we report that Oct-4 and EWS are co-expressed in the pluripotent mouse and human embryonic stem cells. Consistent with its ability to bind to and colocalize with Oct-4, ectopic expression of EWS enhances the transactivation ability of Oct-4. Moreover, a chimeric protein generated by fusion of EWS (1-295) to the GAL4 DNA-binding domain significantlyincreases promoter activity of a reporter containing GAL4 DNA-binding sites, suggesting the presence of a strong activation domain within EWS. Taken together, our results suggest that Oct-4-mediated transactivation is stimulated by EWS.