CALIFORNIA STATE SCIENCE FAIR
2004 PROJECT SUMMARY

Name(s)

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Project Number

S0414

Project Title

Context-Dependent Binding by the MYC Oncoprotein: The Cellular Basis for Sustainable Tumor Regression

Abstract

Objectives/Goals

Research has shown that even temporary inactivation of the oncogene c-MYC can induce osteosarcoma tumors to regress. Surprisingly, when MYC is reactivated in these differentiated cells, the oncogene lacks the ability to reinduce tumorigenesis. Once this phenomenon is better understood, oncogene inactivation will hold much promise in the clinic.

The hypothesis tested here is that the MYC oncoprotein, a transcription factor, binds to target loci differently upon reactivation, depending on cellular context (differentiated or cancerous state), which produces the behavioral change in response to MYC.

Methods/Materials

Murine cancer cell lines containing a conditionally regulated MYC transgene were compared across three conditions: #MYC-activated# (MYC on for 48 hours; cancerous); #MYC-inactivated# (MYC off 48 hours; differentiated); and #MYC-reactivated# (MYC off 48, then on 20 hours; differentiated).

Results

First, a cDNA microarray assay showed global changes in gene expression. Genes were selected for further study by a short, custom-written Perl program that searched for MYC binding loci in promoter regions, as well as confirmation of microarray results by RT-PCR. A chromatin immunoprecipitation (ChIP) assay showed up to 5-fold changes in the binding of MYC to target loci.

Conclusions/Discussion

The results suggest that MYC#s inability to reinduce tumorigenesis may stem from compromised regulation of target genes, which in turn may come from a change in MYC#s binding to target loci. Therefore, cellular context affects a cell#s vulnerability to the oncogene through binding and regulation of target genes. Future work will identify factors that affect MYC#s binding and bring oncogene inactivation therapy one step closer to the clinic.

Summary Statement

Oncogene inactivation leads to sustained tumor regression because upon reactivation the oncoprotein binds to target genes differently.

Help Received

Used lab equipment at Stanford University in lab of Dr. Dean Felsher, under the supervision of Dr. Natalie Wu; began project as a summer intern under the Center for Clinincal Immunology at Stanford Summer Internship program