



**CALIFORNIA STATE SCIENCE FAIR  
2014 PROJECT SUMMARY**

<b>Name(s)</b> <b>Prem M. Talwai</b>	<b>Project Number</b>  34367
<b>Project Title</b> <b>An Investigation of the p53 Ubiquitin-Proteasome System Using a Novel Non-Steady-State Enzyme Kinetic Model</b>	
<b>Abstract</b> <b>Objectives/Goals</b> Existing steady-state models have failed to accurately describe the cancerous mechanism known as overzealous p53 ubiquitination because they rely on the quasi-steady state assumption, which is invalid in the p53 ubiquitin-proteasome system (UPS). My project aims to develop a novel non-steady-state mathematical model of reversible sequential bi-substrate enzyme kinetics, which can be used to analyze the nonlinear dynamics of the p53 ubiquitination reaction for various initial concentrations of targeted p53, MDM2, and E2D3-Ub. <b>Methods/Materials</b> By exploiting the recurrence of certain rate terms in the conventional nine-dimensional mass action model of reversible sequential bi-substrate enzyme kinetics, a novel set of mathematical expressions were derived for the concentrations of each of the four intermediate complexes, which enabled the elimination of four superfluous variables from the existing model without the use of inaccurate steady-state or rapid equilibrium assumptions. The resulting five-dimensional mass action system was then linearized using conventional perturbation methods and subsequently solved using standard linear algebraic techniques. The model was then simulated in Mathematica to analyze the effects of E2D3-Ub and MDM2 concentrations on the rates of p53 ubiquitination at different temperatures. <b>Results</b> At each temperature, it was observed that the ubiquitin-ligase MDM2 accelerates the carcinogenic ubiquitination process, while ubiquitin-conjugated E2D3 inhibits it. It was also discovered that E2D3-Ub is a more effective inhibitor of overzealous p53 ubiquitination when present at higher concentrations. However, it was observed that high concentrations of p53 hinder the ability of E2D3-Ub to decelerate the reaction. The mathematical model successfully reproduced the experimentally observed p53-MDM2 interaction. <b>Conclusions/Discussion</b> The derived model therefore suggests MDM2 as a prospective target for cancer therapy. In addition, the findings of this project propose recombinant E2D3-Ub as a new promising protein-based anticancer drug for targeting overzealous p53 ubiquitination. The derived model can suggest new therapeutic strategies for targeting various neurodegenerative diseases characterized by an overzealous UPS. Finally, computational simulation of this novel model provides a safe, fast, and cost-effective preliminary alternative to expensive in vitro experimentation.	
<b>Summary Statement</b> My project derives a novel non-steady-state mathematical model of reversible sequential bi-substrate enzyme kinetics, which suggests E2D3-Ub as a new promising protein-based anticancer drug for targeting overzealous p53 ubiquitination.	
<b>Help Received</b> No help was received.	