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“Ras-mediated proteasomal degradation of ICER in melanomas.”

[This project seeks to determine whether in a melanoma animal model down-regulation of the tumor suppressor ICER is the cause for melanoma formation.]

Almost, every cell needs to multiply at some time of its life cycle to spawn a daughter cell. The process by which cells grow and replicate their genetic material (DNA) is known as the cell cycle. This process has been divided into four major stages: G1, S, G2 and M. In G1 cells grow in size in order to be prepared to duplicate its DNA at the S phase. Once they finish doubling all the DNA they go into rest at the G2 phase before entering the process of cell division, termed M. When M finished the product is two identical cells that will begin the cycle again in G1. The cell cycle is very complex and tightly regulated process.

Central to the regulation are a set of proteins that known as cyclins and cyclin-dependent kinases. Progression of cells through the cell cycle is governed by sequential expression, activation, and subsequent inactivation of such proteins. Failure to coordinates these processes can perturb the fidelity of DNA transmission and may contribute to genetics aberrations detected in cancerous cells. Proper coupling of M phase with the previous S phase is ensured by control mechanisms that prevent cells from attempting to segregate incompletely replicated DNA. These controls are achieved by restraining the cells at points during the cell cycle termed checkpoints. Two major checkpoints have been described: at the G1/S boundary and at the G2/M transition.

Recently we have shown that a protein termed ICERII γ is pivotal for the proper control of the G2/M transition. ICERII γ is a member of a family of very similar factors whose function is to bind sequences of DNA and inhibits the expression of proteins involved in cell cycle. The primary aim of this proposal is to determine if other ICER family members also regulate the cell cycle.