Colorectal cancer is the third leading cause of cancer death in the United States, with a risk of development in 1 out of 20 people. It is expected to take 49,700 lives by 2015 [1]. There is no cure for colorectal cancer, and current treatments involve radiation and chemotherapy. The 14-3-3σ-tumor suppressor gene is associated with colorectal cancer. 14-3-3σ is a p53-dependent, negative regulator of the cell cycle and plays a specific role during translation, as mutations in 14-3-3σ lead to cytokinesis failures [2]. 14-3-3σ is a member of the 14-3-3 superfamily which all regulate cellular signaling by interacting with serine/threonine phosphorylated residues on a variety of proteins [3]. A hyper-methylation in the promoter region renders 14-3-3σ unable to produce a viable protein [3]. *Though much is known about the role of 14-3-3 σ in translation, its role in cell division as it relates to colorectal cancer is unclear.*

The **primary goal** is to determine the role that 14-3-3σ plays in cell division. To observe its role in cytokinesis, I will use the *C. elegans* 14-3-3σ homolog, PAR-5*,* to understanding this function because cell division is easily assayed and imaged in C. elegans embryos [4]. The **long-term goal** is to determine how 14-3-3σ functions in cell division events.

Hypothesis: 14-3-3σ/PAR-5 and its binding partners regulate the activity proteins necessary for cytokinesis by binding to serine/threonine sites.

Aim 1: Identify and characterize the function of 14-3-3/PAR-5 interacting partners and determine if they play a role in cell division.
Approach: Use STRING to identify binding partners of PAR-5 in C. elegans. Then using Gene Ontology, I will sort proteins based on biological function to determine if these interactions play a role in cell division. Then I will determine if they share similar domains using SMART known to be regulated during cell division.
Rationale: By doing this, I will determine if PAR-5 interacting proteins function in cell division.

Aim 2: To identify conserved serine/threonine phosphorylation sites on PAR-5 binding partners that function during cell division.
Approach: Using NetPhos 2.0, I will locate the serine/threonine phosphorylation sites on candidate PAR-5 interacting proteins and then use Clustal Omega to determine which of these sites are the most conserved.
Rationale: I will be able to determine where the well-conserved phosphorylation sites are on proteins that function in cell division

Aim 3: Determine which PAR-5 interacting proteins functions in cell division.
Approach: Using *C. elegans* and CRISPR-Cas9 technology, I will mutate conserved phosphorylation sites in several of the PAR-5 interacting proteins, create transgenic lines and determine which sites are important for cytokinesis via video microscopy. Once this is determined, I will then tag these proteins with GFP via CRISPR and determine if they localize to cell division structures, such as the spindle or actin ring.
Rationale: By performing this assay, I can identify phosphorylation sites on PAR-5 interacting proteins that are important for cytokinesis and then determine if these proteins localize to structures involved during cell division events.

Outcomes: With this knowledge, I will be able to apply the fundamental aspects of this research to well conserved binding partners of 14-3-3σ to discovery interaction pathway targets in cell division that are necessary for tumor growth. This would allow for treatments/drugs to be created at these sites.

References:

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