

## **TITLE: TIP150 Potential Interaction with Glycogen Synthase Kinase (GSK)-3-Beta to Facilitate Cell Migration**

**AUTHOR: Maryam Chaudhry**

**Introduction:** Cell migration regulation is a highly complex process that is often compromised as cancer cells become metastatic. The cytoskeleton, both microtubule and actin, are necessary modalities for cell migration. It is now known that GSK-3 $\beta$  functions in diverse cellular processing. However, it is not fully elucidated how microtubule plus-end binding proteins (+TIPs) mediate cell migration through association with GSK-3 $\beta$ .

**Purpose:** The purpose of this study was to determine if TIP150, a +TIP, interacts with GSK-3 $\beta$  to impact cell migration and the mechanism by which this occurs. To this end, this study will help further the understanding of breast cancer metastasis.

**Method:** The metastatic breast cancer cell line, MDA-MB-231, was utilized to study the function of TIP150 and the regulation of cell migration based on the interaction of TIP150 and GSK-3 $\beta$ . In addition to this, HeLa cells were also utilized in order to illustrate the localization of TIP150 to the plus-ends of microtubules. Both cell lines were transfected with the necessary plasmids. The HeLa cells were then fixed in methanol in order to perform immunofluorescence and obtain live cell images. A migration assay was also performed using the MDA-MB-231 cell line in order to track cell movement.

**Results:** Localization of TIP150 to the plus-ends of microtubules was demonstrated in the HeLa cell line. TIP150 was shown to bind to End Binding protein (EB)-1 in order to polymerize the plus-ends of microtubules. An interaction between TIP150 and GSK-3 $\beta$  was demonstrated. Suppression of TIP150 in MDA-MB-231 cells resulted in the inhibition of cell migration.

**Conclusion:** The ability of TIP150 to bind to EB-1 in order to polymerize the ends of microtubules illustrates the role this particular +TIP plays in the mechanisms of microtubules, particularly in regards to migration. Additionally, the phosphorylation of TIP150 by GSK-3 $\beta$  allows for GSK-3 $\beta$  to interact with TIP150 and therefore result in directional cell migration. The ability of this interaction to govern the dynamics of the microtubule network suggests that cancer metastasis may also be regulated by the activation state of these cellular components.