Repeated Interactions between ErbB1 Receptors and the Impact on Signal Initiation

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Short Abstract – **ErbB1 (EGRF), a transmembrane receptor tyrosine kinase, has been shown to have a strong link to cancer. Therefore, understanding the signal initiation and transduction mechanisms associated with this receptor is important. Single particle tracking experiments used to visualize ErbB1 behavior within the live cell context have shown repeated interactions between pairs of labeled receptors. We believe these repeated interactions are a critical component in the initiation of down stream signaling. To investigate this phenomenon, a model will be developed using a modified Smoluchowski approach. The results will be used to refine data collection goals by suggesting new experiments.**

I. Background

THE ErbB family of receptors is a group of four tyrosine kinases (ErbB1/2/3/4) that are activated via ligand binding and subsequent formation of homo and heterodimers. The main function of the ErbB family is to mediate important cellular processes such as homeostasis, pathology, and development [1] as well as the interactions between cells [2]. Specifically, ErbB receptors play an important part in the regulation of cell growth, proliferation, differentiation, and apoptosis [3,4]. Given these important roles in normal cell development, it is not surprising that in the early 1980's the ErbB receptor family was implicated in the progression of cancers [2] such as breast, lung, and bladder [5]. More specifically, the overexpression of ErbB1 is known to cause uncontrolled cell proliferation [5]. Due to this strong link between ErbB1 and cancer, it is important to understand signal initiation and transduction mechanisms associated with this receptor.

II. Approach

Traditionally, experimental methods are used to understand ErbB1 signaling. Single particle tracking (SPT) experiments are used to visualize ErbB1 behavior within the live cell context. Low-Nam et al (2011) reported seeing repeated interactions between ErbB1 receptors during SPT experiments. We believe the repeated interactions are critical to signal initiation and transduction in ErbB1. An important caveat of these SPT experiments is that receptors must be labeled at a sufficiently low density to permit discrimination between individual proteins [7]. Although SPT experiments have yielded useful kinetic and diffusion parameters, the contributions of the unlabeled (and therefore unseen) species remain unexplored. A model must be built in order to resolve these unlabeled species. The key to this model is ability to see when the labeled receptors interact with unlabeled receptors as well as other labeled receptors allowing us to investigate repeated interactions. While there are many models to simulate ErbB1 receptor behaviors, most lack a fundamental connection to experimental data.

III. Conclusion

In a step towards making the connection between experiments and modeling stronger, the overall goal of this work is to develop a model using parameters from live cell imaging to investigate the impact of repeated interactions seen in SPT on ErbB1 signal initiation and transduction.

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