Novel ERK1c substrates regulate mitotic Golgi fragmentation

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Introduction

I completed my coop experience in Prof. Rony Seger’s laboratory at the Weizmann Institute of Science. Prof. Seger’s lab is interested in understanding the mechanisms of various intracellular signaling cascades including the ERK signaling cascade. The ERK cascade is involved in various cellular processes such as proliferation, differentiation, and apoptosis. When there are alterations in the normal signaling of the cascade, it results in diseases of deregulation such as cancer and diabetes.

Activity

Under the direction of Inbal Wortzel, a PhD student in Prof. Seger’s lab, I conducted research on how the ERK cascade regulates mitotic Golgi fragmentation. My research focused on ERK1c, a spliced isoform of ERK1 that acts downstream of MEK1b to regulate Golgi fragmentation. It has been shown that ERK1c localizes to the Golgi during mitosis.

How can a linear cascade regulate all of these distinct and even opposing cellular processes?

Since the molecular mechanism was not understood I conducted a series of knockdown experiments combined with the over-expression of ERK1c to find potential substrates of ERK1c. The screen revealed 4 proteins of interest. The localization of these proteins and their expression during mitosis was further studied.

Outcomes

Fig 1. Significant differences in the % Golgi fragmentation in ERK1c over-expressed cells indicates PAK4, CCDC86, HOOK3, and GRASP55 are potential substrates of ERK1c.

Fig 2. Differences in Golgi fragmentation in over-expressed ERK1c and over-expressed ERK1 cells under different siRNA treatments. siRNA of CCDC86 decreases the % Golgi fragmentation, while siRNA of HOOK3 increases the % Golgi fragmentation compared to the scramble control.

Fig 3. The over-expression of ERK1 and ERK1c does not effect the knockdown and the knockdown does not effect the over expression. I achieved a knockdown for PAK4, HOOK3, and GRASP55. CCDC86 needs to be repeated with a better antibody.

Fig 4. HeLa cells were synchronized by a Double Thymidine block and separated into distinct cell cycle populations by Imagestream.

Fig 5. HOOK3 correlation to the Golgi decreases throughout the cell cycle.

Fig 6. PAK4 correlation to the Golgi increases throughout the cell cycle.

Fig 7. GRASP55 is correlated to the Golgi throughout the cell cycle.

Fig 8. CCDC86 is not correlated to the Golgi during the cell cycle.

Fig 9. HOOK3 correlation to the Golgi increases throughout the cell cycle.

Reflection

I was exposed to many new scientific methods and lectures while completing my coop in Prof. Rony Seger’s lab. I learned how rewarding it can be to work as hard as you can at a goal. Although I worked 40+ hours a week, I was also able to travel throughout Israel with friends I had met at the Weizmann. My experience at Weizmann has shaped my career goals in that I am applying to the graduate school at the Weizmann Institute of Science for the coming Fall.

Literature Cited


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