Understanding the cellular impact of low dose rapamycin treatment

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Abstract

The need for improved influenza vaccines is highlighted every year through the infection of vaccinated patients and the emergence of new pandemic strains. Recent work from our lab showed that a low dose of rapamycin given during influenza vaccination significantly improved protection against subsequent infection with multiple strains. These data indicate that dampening aspects of the immune response paradoxically enhances immunity to multiple subtypes of influenza virus, which is the goal of a “universal” influenza vaccine. However, it is still unclear how the low dose of rapamycin enhances immunity to different influenza subtypes and what particular cellular population is important for this increased protection. In order to better understand how to generate the optimal immune response against multiple influenza subtypes, we are investigating how this low dose of rapamycin impacts B cell signaling. Interestingly, we found that a low dose of rapamycin blocks B cell class switching without having an impact on proliferation. Thus, we are investigating which components of the mTOR pathway are required for class switching, but not proliferation. Early work indicates that this dose of rapapmycin alters the speed and activation potential of several mTOR signaling components. Using this system, we hope to identify the signaling components and kinetics that generate the optimal immune response to multiple subtypes of influenza, which is important for generating a universal influenza vaccine.

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