

## Wnt Signaling in Zebrafish: GSK3 $\beta$ Inhibitor Effect on Cell Proliferation

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Osteoporosis is a serious disease that impairs bone growth, especially in elderly women. In order to develop beneficial drugs for osteoporosis it is important to understand the molecular mechanisms of bone regeneration and define specific regulatory factors. Zebrafish can regenerate damaged tissues, and they prove to be a good model to study bone growth and repair. Previous research showed that GSK3 $\beta$  inhibitor compound at various concentrations and for different treatment periods effectively stimulated fin regeneration, measuring regenerative outgrowth at 4 and 7 days after amputation. In situ hybridization, experiments were performed, which showed stimulatory effects of GSK3 $\beta$  on Wnt responsive gene expression. Experiments identified temporal and spatial fluctuations on individual gene markers after GSK3 $\beta$  inhibitor treatment at various concentrations. Also, confocal microscopy and immunofluorescence labeling data indicated that the Wnt intracellular signal transducer,  $\beta$ -catenin, increases throughout GSK3 $\beta$  inhibitor treated tissue. Ongoing research shows an increase of activity of the blastema region where GSK3 $\beta$  inhibition increases cell proliferation, expanding the regenerating fin tissue. My experiment uses the Lilly Research Labs experimental compound LSN 2105786 at 3 and 5 nM to stimulate tissue regeneration to determine whether activating Wnt signaling produces cell proliferation and  $\beta$ -catenin translocation to the nucleus. I expect that GSK3 $\beta$  inhibition will stimulate proliferation and  $\beta$ -catenin nuclear localization, which improves bone growth during zebrafish regeneration. This research has potential to identify mechanism of bone growth and repair, leading to more suitable drugs for patients suffering with osteoporosis.

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