Larsen Syndrome (LS) is a rare heterozygous genetic disorder affecting 1 in every 100,000 births (1). Common features of LS patients are facial and skeletal malformations as well as large joint dislocations that often lead to intensive orthopedic surgeries (2). The resulting cause of LS and their large joint dislocations is because the *FLNB* protein is unable to organize the actin cytoskeleton of the cell properly leading to cartilage cells inability to compact correctly in large joints (3, 4). The *FLNB* protein is composed of two CH domains that bind to actin filaments and 24 repeating filamin domains which attach the actin filaments to the plasma membrane of a cell (5).*With this understanding of how FLNB works at the cellular level there is a lack of information as to how the role of FLNB in humans results in severe bone deformities and constant dislocation*s. To better understand how these bone deformities occur as well as affect the body through time, a knowledge of what proteins interact with *FLNB* would be helpful. *FLNB* primarily interacts with several ubiquitin proteins involved in protein degradation as well as several fibronectin receptors that are involves in cartilage cell development and migration (6). *There is a lack in knowledge though as to how these interacting proteins affect FLNBs basic role in the cell, and if they change over time leads to more developmental defects.* A clear understanding of how *FLNB* operates within the cell in different locations and with time can lead to greater hope in finding a treatment for LS.

Proper diagnosis for patients with LS is not done in a timely manner. Typically diagnosis of patients with LS is made after birth by a combination of specific phenotypic defects as well as genomic sequencing, showing a mutation in *FLNB*. With later diagnosis comes an inability to understand the disorder fully at various stages of life. Having an understanding of the wild type *FLNB* protein can lead to much advancements in understanding the abnormal *FLNB* protein and its effects. The hope is that with research, prenatal screenings can become more likely to occur as well as lead to better management for the disorder (7, 8). *When examining the roles of the wild type FLNB protein, I hypothesize that FLNBs function and interactions change over time.*

The primary goal of this study is to further understand to role of FLNB across species and time, in hopes to benefit those diagnosed with Larsen Syndrome, and other related filamin disorders, in the future. The role of *FLNB* across various homologous species can lead to a greater understanding of how *FLNB* functions in species with different characteristics, such as decreased cartilage or an absence of bones. Also examining how the role of *FLNB* is affected over time can provide much insight as to what to expect in patients as they age.

Specific Aim 1: To determine the role of *FLNB* between vertebrates and non-vertebrates.
Hypothesis: FLNB has a different function in non-vertebrates than in vertebrates.
Experimental Methods: Use Clustal Omega alignment to analyze the CH domain and filmamin domain of vertebrate and non-vertebrate species filamin B protein sequences found via BLAST. Tag filamin B protein with GFP in each non-vertebrate species to determine protein localization. Continue experiments to determine the role of filamin B in non-vertebrates to determine if a difference is seen and its role.

Specific Aim 2: To determine how *FLNB* interacting proteins change in bone development with age.
Hypothesis: Ubiquitin interacting protein's function will increase with age where as fibronectin receptor protein's function will decrease with age.
Experimental Methods: Use STRING to examine interaction protein networks of homologous species to determine a good model organism. This model organism should be very similar in terms of the human *FLNB* interaction network. Take cartilage or bone marrow tissue from model organism at embryonic, young, and adult stages. Tap tag the specific ubiquitin and/ or fibronectin receptor proteins from this tissue and sort. Run proteins through mass spectrometry to determine the levels of tap tagged proteins in this tissue as well as identify any new proteins.

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