Myostatin-Related Muscle Hypertrophy is a single gene disorder characterized by an increase in muscle mass and strength. Patients with Myostatin-Related Muscle Hypertrophy are able to live a normal life with no other functional or cognitive effects. Mutations in the MSTN gene, lead to failure to produce the protein, myostatin, a member of the TBFB superfamily which are important for tissue development throughout the body. Myostatin plays a role in keeping muscle growth in check by inhibiting myoblast differentiation. Myostatin is in initially in the form of two inactive subunits and is only activated when cleaved by protease. The active COOH-terminal dimer then binds to the activine type ll receptor, which recruits Alk-3 or Alk-4. These are co-receptors that activate a cell signaling cascade that that induces the activation of transcription factors, thus inducing myostatin related gene regulation. When these are applied to myoblasts, myostatin genes inhibit their differentiation into mature muscle fibroblasts. While the process is well characterized, the effects on other body systems, besides muscular, are not well defined. Alk-4, otherwise known as ACVR1B, also plays roles in cell growth, differentiation and death. Because Alk-4 is not recruited when the myostatin gene is mutated, it’s control over other cell systems is compromised. This could be especially important for control of tumor causing cells.

**Long term goal:** Discover if people with Myostatin-Related Muscle Hypotrophy have a higher risk of developing cancer.

**Hypothesis:** A mutation in the myostatin gene effects the function of Alk-4 and will decrease control of differentiation and apoptosis in cells, which would lead to higher cancer prevalence.

**Specific AIMS 1:** Identify other cells in the body that are regulated by Alk-4

**Approach:** Tag the DNA sequence that codes for the protein ALK-4 with fluoresces.

**Hypothesis:** The Alk-4 protein will be present in the musculature, but also in other parts of the body

**Rational:** Because Alk-4 is present in other parts of the body, that means it regulates other body systems and it’s decreased recruitment by the activated myostatin subunit will effect more than just muscle differentiation.

References

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