Waardenburg syndrome type 2A (WS2A) is a rare autosomal dominant syndrome that affects the auditory system and causes pigmentation abnormalities in the skin, hair, and eyes. This is attributed to the loss of the MITF gene. MITF mutations can include full or partial hearing loss, a patch of white hair in the front hairline, and brilliant blue coloring of eyes [1]. In some cases of WS2A, only one eye is phenotypically affected by the mutation. Waardenburg syndrome patients fail to activate tyrosinase, a melanocyte-specific enzyme [1], *however little is known about MITF’s role in melanocyte differentiation in the eyes*.

My **primary goal** is to understand the incomplete penetrance of MITF mutations in the role of melanocyte differentiation in the eyes.

**Aim 1:** Determine the strength of mutant MITF binding domains (HLH) to the tyrosinase promoter. **Approach:** Using domain analysis, we will create different mutations in the HLH domain to test if the mutants change the strength of binding affinity to the tyrosinase promoter. **Hypothesis:** Some mutations will weaken binding affinity more than others, with the result of some full phenotypic mutants and some partial phenotypic mutants. **Rationale:** This information is important for understanding if protein-protein interactions play a role in the severity of the penetrance of MITF mutations.

References

1. Shi Y, Li X, Ju D, Li Y, Zhang X, Zhang Y. A novel mutation of the MITF gene in a family with Waardenburg syndrome type 2: A case report. Experimental and Therapeutic Medicine. 2016;11(4):1516-1518. doi:10.3892/etm.2016.3042