Histone modifications at the imprinted gene Rasgrf1

An imprinted gene is only expressed from one of the two alleles. The copy of the gene that is expressed is determined by which parent it originated from. Some imprinted genes are only expressed from the paternal copy, while others are only expressed from the maternal copy. The cell knows which copy of the gene to express based on DNA methylation and/or histone modifications on one of the alleles.

Rasgrf1 is a paternally expressed imprinted gene that is marked by DNA methylation on the paternal copy. This gene acts like an imprinted gene in mouse brain and liver, but is expressed from both alleles in mouse kidney. However, the DNA methylation pattern is the same in all tissues regardless of imprinting status. This suggests that there is a secondary marker, such as histone modification(s), that controls expression of Rasgrf1.

To determine which histone modifications play a role in regulating imprinted expression, I will be analyzing the distribution of modified histones in three regions involved in regulation of Rasgrf1. Specifically, I will be examining chromatin from five-day old mouse kidneys, which exhibits biallelic expression of Rasgrf1, and comparing the histone modification patterns for two permissive and two repressive modifications on the paternal allele versus the maternal allele using chromatin immunoprecipitation and quantitative PCR. We can tell the difference between the two alleles by using a mouse that is a hybrid of two different strains of mice that have a DNA sequence variation in the regions being investigated. I will also be comparing my findings with those obtained by another student who is carrying out the same experiments in mouse liver, which is a monoallelic tissue, to determine whether the patterns I find are unique to the biallelic tissues. This research will help advance our understanding of gene regulation.