Epigenetic Causes of Monoallelic Expression of the *Rasgrf1* Gene in Mouse Tissue

Abstract: Genomic imprinting is the process by which genes are expressed in a parent of origin specific manner. The Rasgrf1 gene is paternally expressed in brain and liver tissue but biallelically expressed in other mouse tissues such as kidney and lung. DNA methylation often occurs near the promoter of a gene where it silences gene transcription by blocking the binding site of transcription factors. Because the genomic imprinting is tissue specific, DNA methylation at the promoter of the silent allele in tissues with imprinting expression could explain why Rasgrf1 is silenced on the maternal chromosome; however, prior research indicates that there is no difference in methylation patterns near the promoter of Rasgrf1 in maternally derived vs. paternally derived DNA. Thus the differences in Rasgrf1 imprinting are likely caused by methylation in a different region of the genome, which regulates Rasgrf1 expression, or by histone modifications. This summer I am using DNA sequence polymorphisms in the differentially methylated region (DMR) and promoter of the Rasgrf1 gene in two strains of mice to differentiate maternally and paternally derived DNA. Using chromatin immunoprecipitation (ChIP) and quantitative PCR I will isolate and amplify DNA fragments which are bound to specific modified histones to determine whether differential distribution on maternal vs. paternal DNA correlates with these Rasgrf1 regulatory regions. We expect that any regulatory regions, which inhibit Rasgrf1, will be bound more to repressive histones in brain and liver as compared to tissues with biallelic expression.

This summer's research is also devoted to another project using castaneus and black 6 strands of mice. Past research has indicated that the published mouse genome sequences do not contain all single nucleotide polymorphisms (SNPs) for mice as our lab identified several SNPs, which are not published. One of our goals this summer is to resequence the mouse genome of castaneus and black 6 mice in the regions where we believe unpublished SNPs exist. This project will identify additional sites of DNA sequence variation to be used in our primary experiments, described above.