The onset of differential methylation at the imprinted gene Dlk1

Every mammal inherits two copies of each gene, known as alleles; one from the mother, the other from the father. Generally, both of these alleles contribute equally to the expression of a gene, resulting in biallelic expression. There are some cases of monoallelic expression, however, when the alleles do not contribute equally, and only one allele determines the gene's function. This preferential expression of one parental allele while the other is silenced is known as imprinting.

During transcription, the cellular machinery carrying out the process must be able to identify which allele of an imprinted gene needs to be expressed. Differential DNA methylation is one of the primary epigenetic modifications that indicate which allele is to be expressed. DNA methylation occurs when a methyl group is covalently bonded to the nucleotide cytosine. The addition of a methyl group changes the structure of the nucleotide, allowing the cellular machinery to differentiate between the differentially methylated parental alleles and determine which is expressed and which silenced. Differential methylation at imprinted genes can be complex because imprinted genes often appear in clusters close to or adjacent to other imprinted genes and may be expressed differently in different tissues.

One such cluster is the Dlk1-Gtl2 imprinting cluster, which is studied in our lab. This cluster contains several imprinted genes and three differentially methylated regions (DMRs): Dlk1-DMR, IG-DMR, and Gtl2-DMR. My research focuses on understanding the Dlk1-DMR. Dlk1 is involved in cell differentiation and may be a tumor suppressor. I seek to identify when during the course of development differential methylation occurs at the Dlk1-DMR as well as which tissues exhibit differential methylation at the Dlk1 locus in mouse. I am studying liver tissue from newborns to determine patterns of differential methylation, to be compared to methylation in lung tissue being studied by a fellow student. In addition, I will compare my findings on the onset of differential methylation in the Dlk1-DMR with data from the IG-DMR and Gtl2-DMR. Because of the closeness of the three DMRs, we expect to see similar patterns of tissue specific differential methylation, which would suggest that the Dlk1-Gtl2 cluster experiences some coordinate control.