



# Variation of DNA Methylation in Pediatric Cancer Patients

Alyssa C. Parker, Badí Quinteros, and Stephen R. Piccolo

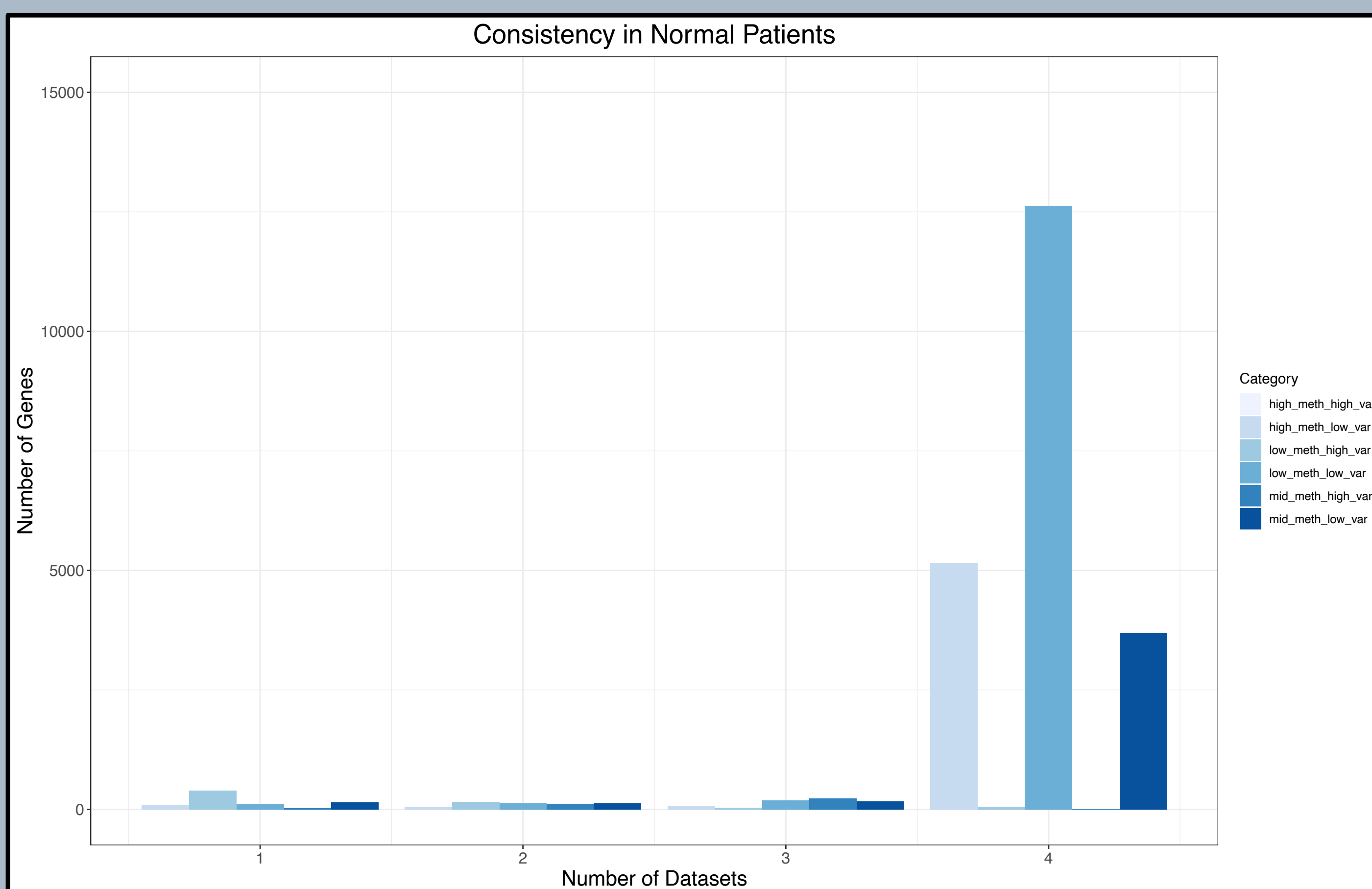
Department of Biology, Brigham Young University

## Introduction

The development of pediatric cancer is a complex process. Because fewer genetic abnormalities have been identified in pediatric cancer patients than other cancer patients, it is thought that dysregulation of the epigenome plays a role in pediatric cancer development<sup>1</sup>. DNA methylation is a mechanism of epigenetic modification in which methyl groups are attached to DNA molecules, making it more difficult for DNA to be transcribed and translated into protein. Methylation can have an impact on gene expression when methylation levels significantly increase or decrease<sup>2</sup>. **We hypothesized that methylation levels of genes are consistent in normal patients and variant in pediatric cancer patients.** We chose to focus on patients with Wilms tumor, rhabdoid tumor, clear cell sarcoma of the kidney, osteosarcoma, and neuroblastoma.

## Goal

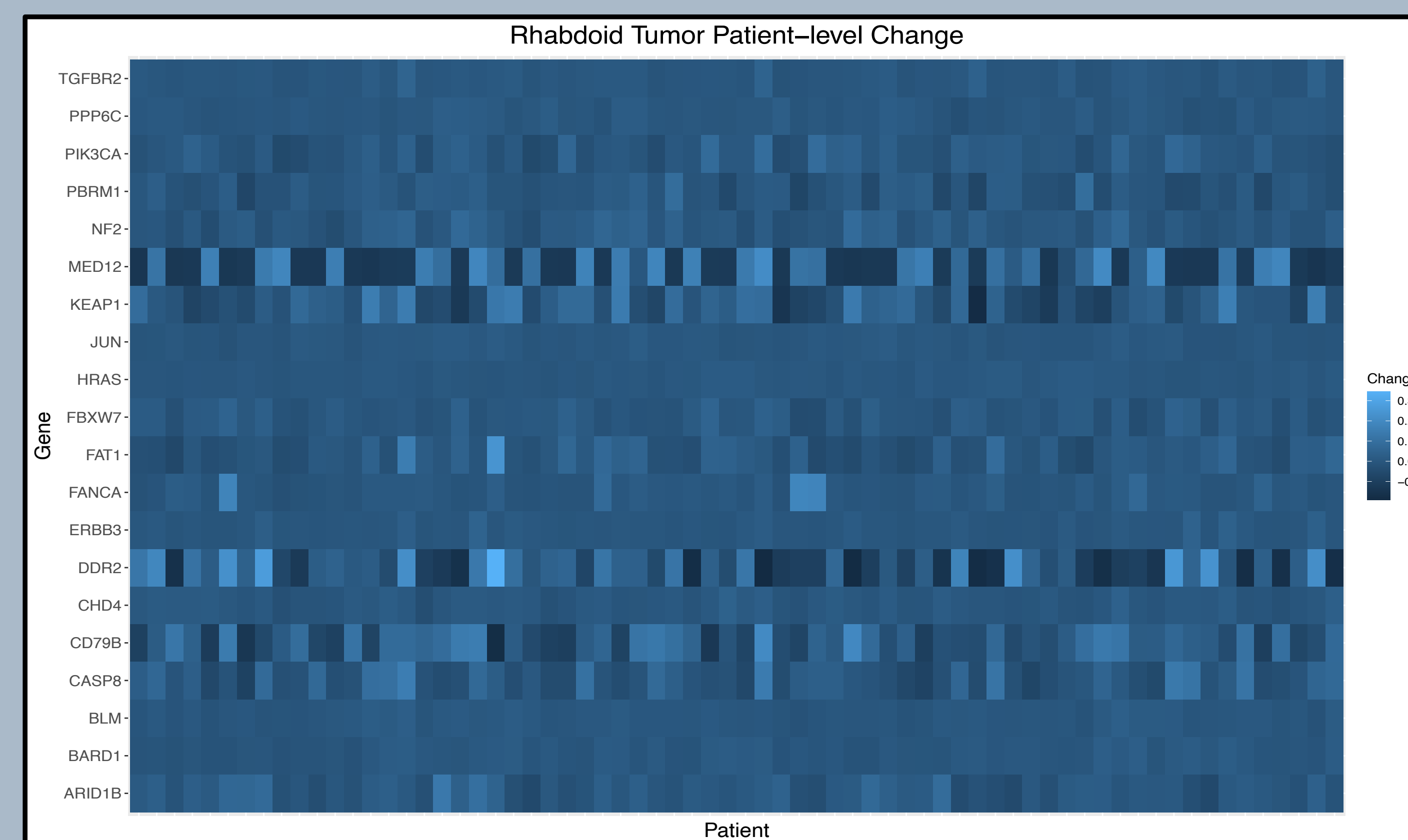
**Our goal was to understand differences in DNA methylation levels between pediatric cancer patients and normal patients.** We wanted to understand the consistency of DNA methylation in normal patients and identify patterns of change in cancer patients. Our hope is that understanding variation in DNA methylation will lead to potential therapies for pediatric cancer patients.



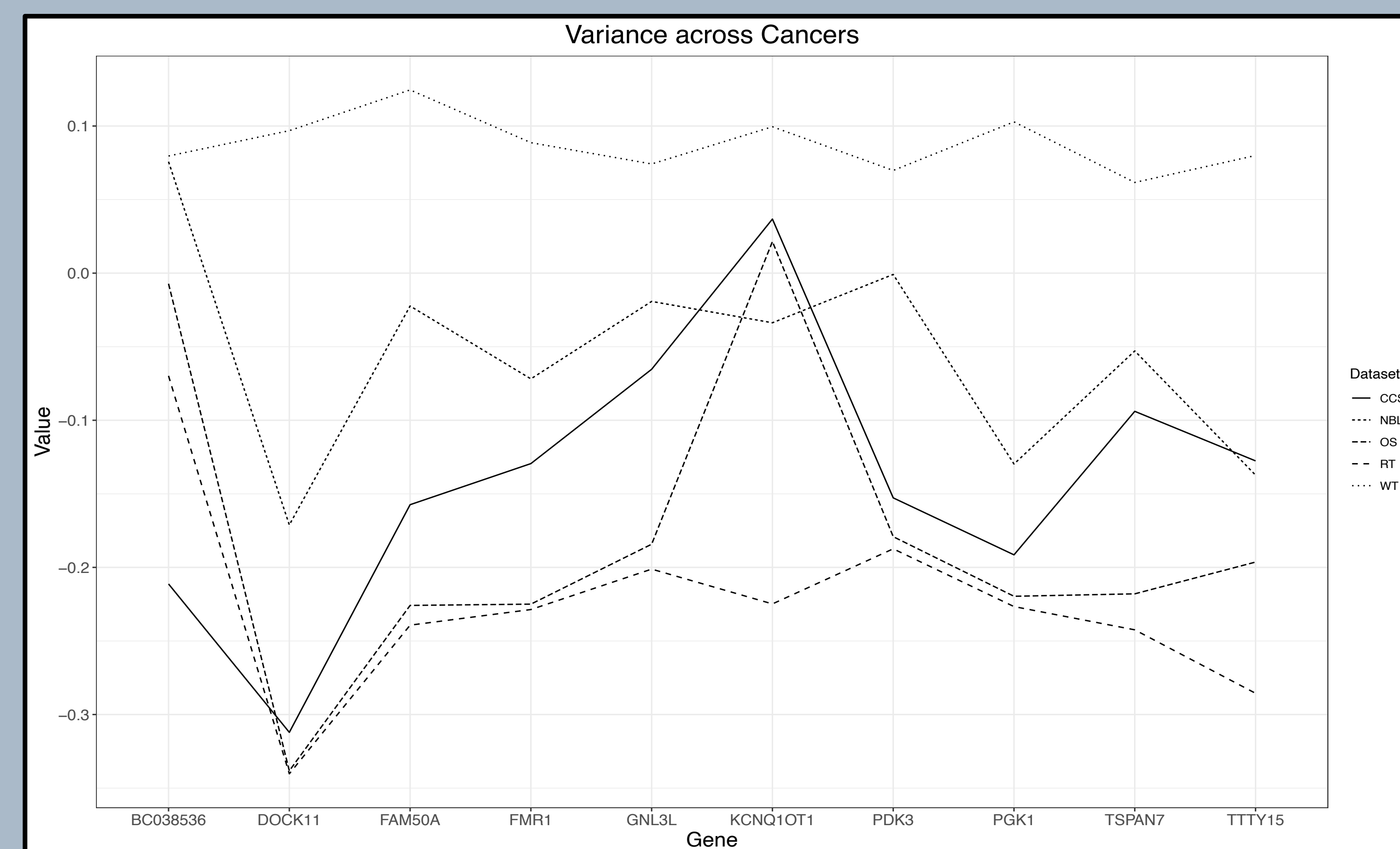
**Figure 1:** DNA methylation levels in normal datasets were highly consistent. We classified genes into categories, based on methylation level and variation. Almost every gene fell into the same category in each normal dataset.

## Data Preparation and Analysis

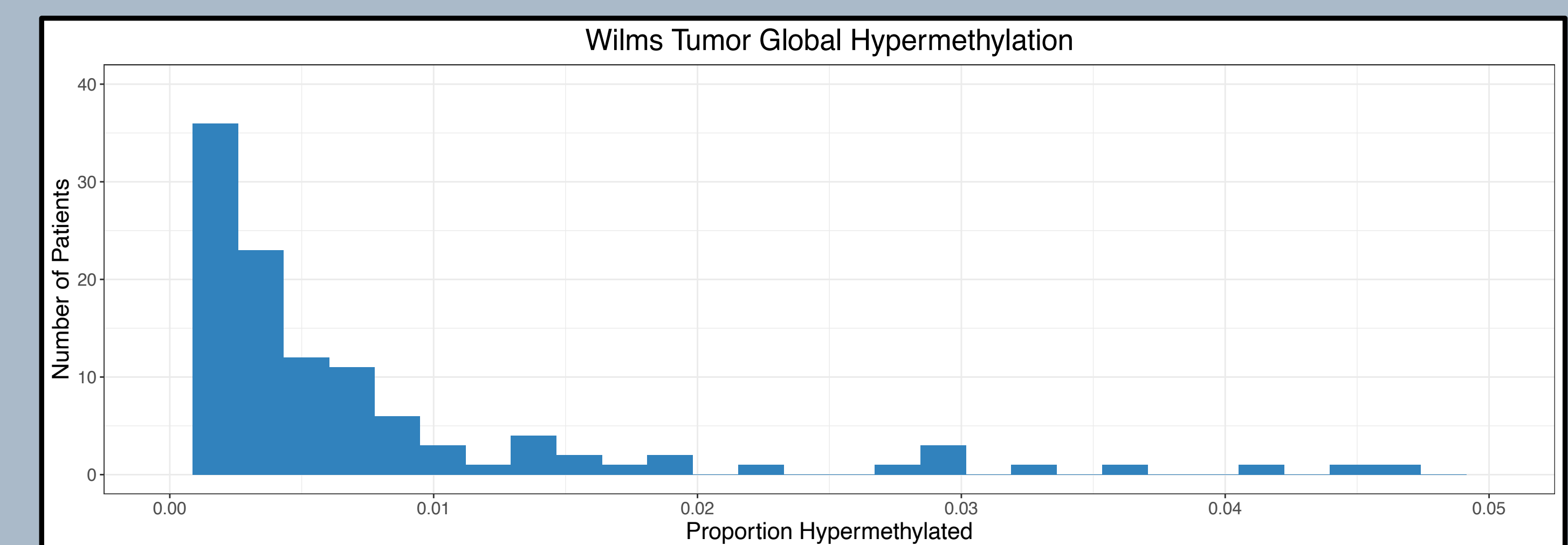
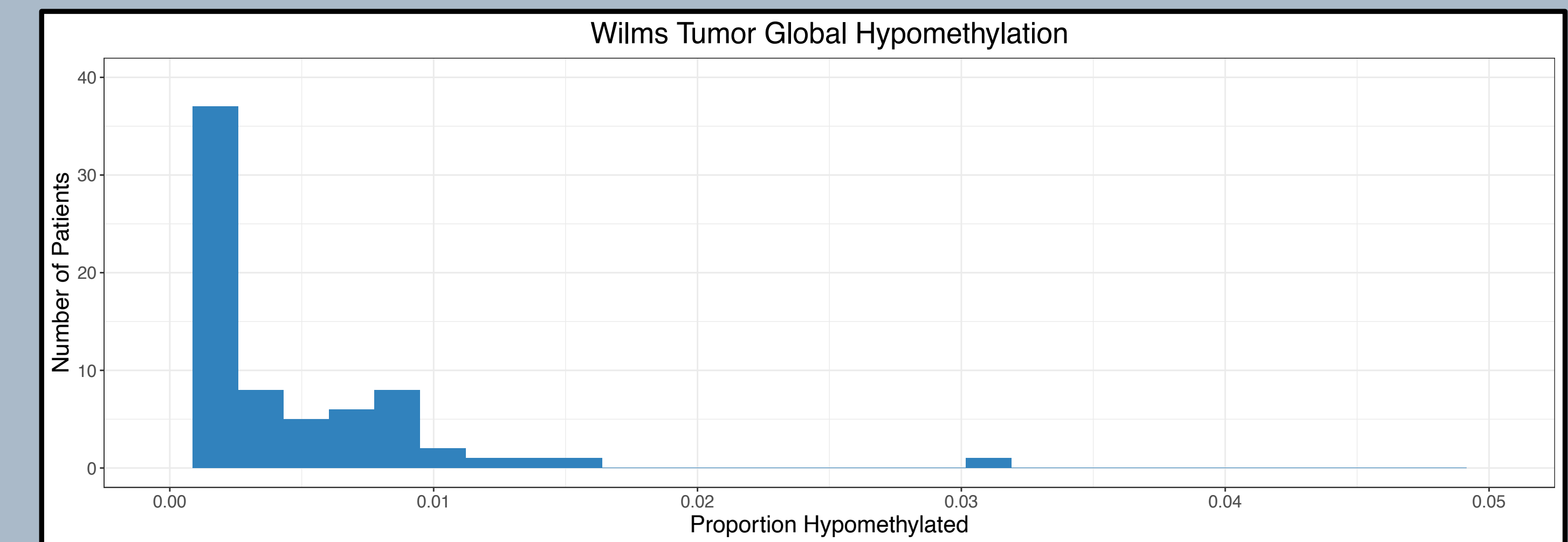
We determined baseline DNA methylation levels by combining normal patient data from four datasets. We found DNA methylation levels to be highly consistent. We then quantified changes in methylation for pediatric cancer patients and identified many genes with highly variant DNA methylation levels.



**Figure 2:** DNA methylation levels were not consistent in pediatric cancer patients. In rhabdoid tumor patients, certain genes displayed high levels of variant methylation compared to average methylation values for normal patients.



**Figure 3:** DNA methylation levels varied across cancer types. Clear cell sarcoma of the kidney patients typically had the greatest increase in methylation level and Wilms tumor patients typically had the greatest decrease in methylation level.



**Figure 4:** Wilms tumor patients had higher levels of hypermethylation than hypomethylation. While both were rare, it was much more common for a patient to have more genes that were hypermethylated than hypomethylated.

## Conclusions

We found that DNA methylation levels are highly consistent in normal patients and highly variant in pediatric cancer patients. We identified highly variant genes in each cancer type and determined that the degree of variance depends on the cancer type. We also found that hypermethylation is more common than hypomethylation in pediatric cancer patients.

## Future directions

We will continue to analyze changes in DNA methylation by studying the mutual exclusivity of DNA methylation and mutation. We will specifically focus on genes that are most consistent in normal patients. We hypothesize that if pediatric cancer patients do not have mutations in these genes, DNA methylation levels will be more highly variant.

1. Yiu and Li, "Pediatric Cancer Epigenome and the Influence of Folate."
  2. Shi et al., "Pan-Cancer Analysis of Differential DNA Methylation Patterns."
- Contact:** alyssaclaire31@byu.edu, bique2@byu.edu, stephen\_piccolo@byu.edu