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Single-cell gene expression analyses reveal principles of allelic transcription in mammalian cells

Assessing gene expression in individual cells holds promise to reveal the extent, function and origins of cell-to-cell variability. To this end, my lab has been developing single-cell RNA-sequencing methods that we applied to analyze patterns of genome-wide gene expression across thousands of individual cells. These analyses revealed that a substantial fraction of the genes only expressed one of the parental alleles, chosen randomly, at any given point in time. The expression of alleles in a cell was dynamic and varied over time. Interestingly, we found little evidence for allele-level regulation of gene expression of autosomal genes so that the single-cell gene expression landscape is to a much larger extent affect by dynamic cell-to-cell variability in allelic expression. The revealed pattern of allelic transcription increases the heterogeneity among cells, and likely contributes to the phenotypic variance among individuals of identical genotype. It will also be important to determine to what extent this variability in allelic expression can result in phenotypic variability observed in human disease, such as incomplete penetrance and variable expressivity.