We are interested in understanding the mechanism of chromosome fragility in eukaryotic cells. Chromosome fragile sites are non-random locations in the genome that are more susceptible to DNA strand breaks, either spontaneously or under mild DNA replication stress. Increasing evidence suggests that chromosome fragile site formation is the underlying cause of genome instability, which can lead to a multitude of human disorders ranging from neurological diseases to cancer. My laboratory uses a powerful genomic tool called Break-seq to identify these breakage hot spots in the human genome. We then utilize the awesome power of yeast genetics to test our hypotheses based on the observations we make in the human genome. This combinatorial approach has enabled us to make exciting discovery of a novel function of the Fragile X Mental Retardation protein, whose deficiency leads to the Fragile X Syndrome, in genome maintenance. With these discoveries we hope to further understand the etiology of the Fragile X Syndrome and rationalize disease intervention.