Title:
How precise is precise? Pursuing specific editing outcomes with CRISPR nucleases

Abstract:
The last decade has produced a massive expansion in the genome editing toolset, paving the way for new therapies, diagnostics and technologies. Cas9, Cas12a, and related CRISPR nucleases form the foundation, offering precise genome editing at target sites that complement their RNA guide (gRNA). Yet, two major phenomena limit their utility: 1) Occasional "off-target" cutting activity at sites with just partial gRNA complementarity, and 2) heterogeneous editing outcomes at the intended target site. My team develops high-throughput strategies that benchmark and quantify the off-target propensity of leading CRISPR nucleases, uncovering their precise rates and sites of cutting with nucleotide resolution. Armed with this data, we pursue re-engineering gRNAs to make editing outcomes less variable and more predictable. Our efforts help provide CRISPR users with greater genome editing success without increasing cost or complexity.