## **Major Research Contribution**

A fundamental question in biomedical science is why certain organs, such as the colon and lungs, exhibit higher cancer susceptibility than others, like the small intestine and heart. My early research in The Cancer Genome Atlas (TCGA) project focused on the comprehensive molecular characterization of gastrointestinal cancers by integrating multi-platform analyses to investigate tumor heterogeneity and develop molecular classifiers. We discovered that distinct regions of the colonic epithelium give rise to different colorectal cancer subtypes, highlighting the role of developmental origins and tissue-intrinsic factors in tumorigenesis. While genomic alterations have traditionally been the focus of cancer research, the developmental underpinnings of tumor initiation remain underexplored. My work integrates developmental biology with cancer genomics to uncover new insights into early tumorigenesis and potential therapeutic strategies.

- 1. Development of a new single-cell multimodal CRISPR platform that enable temporal recording, in addition to lineage and cell state information.
- 2. Identification of a novel intestinal stem cell type (pISCs) that is specified during early embryonic gut development and is indispensable for adult epithelial regeneration.
- 3. Elucidation of an evolutionary adaptation in stem cell organization across species that reveal how humans evolve to minimize cancer risk.
- 4. Discovery of clonal selection as a hallmark of the precancer-to-cancer transition and evidence of polyclonal tumorigenesis in both mice and human's colon cancer.

These achievements illuminated a distinctive niche and showcase my commitment to advancing fundamental science. With over 10 years of research experience from various scientific institutions worldwide, along with more than 20 high-impact scientific publications, I have established a solid foundation for an independent academic career.