DEVELOPMENT OF CRISPR-DERIVED TECHNOLOGIES FOR GENOME REGULATION AND APPLICATIONS

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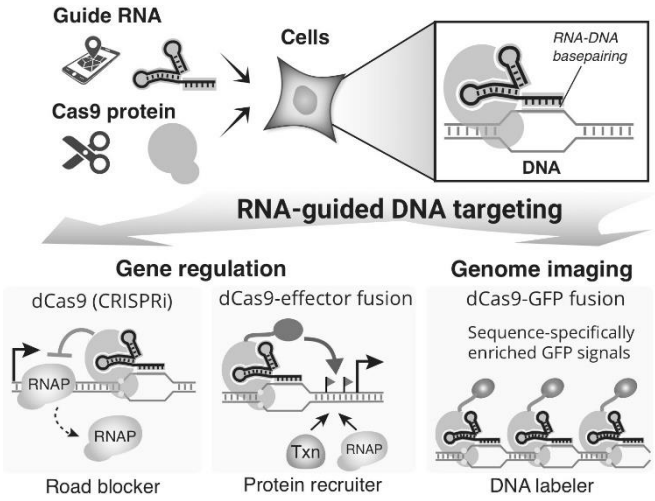

Figure 1 – A platform based on CRISPR system for sequence-specific gene regulation and applications in diverse organisms.

The ability to control the functional outcome of the genome is necessary for biological research, disease diagnosis and treatment. As cells generally use complex networks with dynamic interactions between many genes, we focus on developing novel synthetic biology technologies that enable perturbation and study of such networks. Here I will present methods (e.g., CRISPRi) repurposed from the bacterial adaptive immune CRISPR system, as a set of diverse genetic tools for multiplexed, reversible, sequence-specific gene regulation. We show these tools are universal, which can perform efficient and robust control of gene expression in diverse organisms spanning from bacteria to yeast to mammalian cells. We expand an orthogonal dCas9-based platform that enables paralleled transcriptome manipulation. We demonstrate that the CRISPRi-mediated gene regulation is suitable for genetic screens, allowing large-scale interrogation of individual or combinatorial genes with important phenotypes including cell growth, drug resistance and cellular differentiation. For applications, we further develop the non-editing based genome engineering approaches that allow one to mediate metabolic pathways, rapidly identify drug resistance gene targets, and potentially enable diagnosis and therapeutics.