



Research Collaboration and Technology Licensing Opportunity: Genome editing with the Type I CRISPR/Cas3 systems

Background: CRISPR-guided immune systems have been repurposed for precise genome engineering. This technology is fueling a biotech boom that includes biomedical, agricultural, and research sectors. Early companies in this space, and their market valuations include Editas (\$900M); Intellia (\$900M) and; CRISPR Tx (\$440M). Big pharma and biotechs are also in the space with partnering agreements or internal programs. CRISPR-based technologies currently rely on Cas9 - a single enzyme that can be programmed to specified targets using a single guide RNA. However, CRISPR systems are diverse and several other systems represent an untapped resource that is largely unencumbered by the complex licensing and patent protection activity around Cas9.

Solution: Researchers in the [Wiedenheft lab](#) at Montana State University are developing CRISPR-based gene editing methods that rely on type I systems (Cascade), rather than type II (Cas9) systems for applications related to precise genome engineering. [Dr. Blake Wiedenheft](#), a former postdoctoral fellow in Jennifer Doudna's lab at UC-Berkeley, is a pioneer of the type I systems. The Wiedenheft laboratory has determined several atomic resolution structures of type I RNA-guided surveillance complexes and employed various biochemical techniques to determine the mechanism of RNA-guided DNA cleavage. MSU has filed for IP protection on the topic of bi-directional genome editing with Cascade and/or Csy as a potentially more effective strategy for gene knockouts, knock-ins (through HDR), or knock ups (increasing the amount of protein the gene makes). Market segments for this technology within human health include: gene-, cell-, and immune-therapy, genome editing for transgenic animals, drug discovery, target validation and screening.

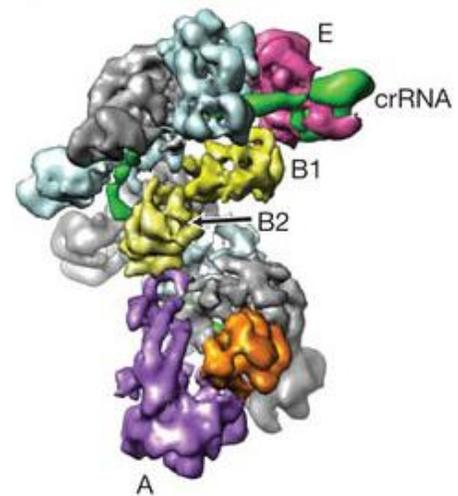


Figure 1: Cascade Complex. [High res images](#)

Benefits:

1. Alternative to the crowded Cas9 space – this is a phylogenetically, structurally, and functionally distinct CRISPR-based system for genome engineering
2. The Wiedenheft lab is using genetic and biochemical methods to streamline the multi-subunit complexes for facile delivery
3. PCT filed, further research plan defined with timeline and costs

Supporting publications:

1. [Crystal structure of CRISPR RNA-guided surveillance complex from Escherichia coli](#). *Science*
2. [Surveillance and processing of foreign DNA by the Escherichia coli CRISPR-Cas system](#). *Cell*
3. [Structural basis for promiscuous PAM recognition in type I-E Cascade from E. coli](#). *Nature*
4. [Structure reveals mechanisms of viral suppressors that intercept a CRISPR RNA-guided surveillance complex](#). *Cell*
5. [Cas1 and the Csy complex are opposing regulators of Cas2/3 nuclease activity](#). *Proceedings of the National Academy of Sciences*

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