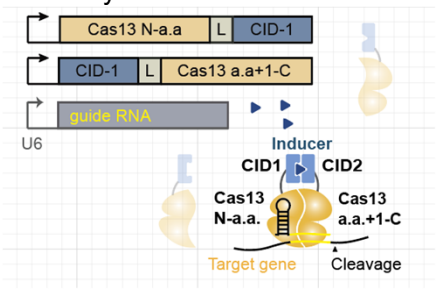
Orthogonal inducible Cas13 platform for programmable RNA regulation

Boston University | Boston, Massachusetts

Overview

Since its recent discovery, Cas13, a class of RNA-guided ribonuclease, has demonstrated its power in RNA cleavage, editing, sensing, and imaging in various systems. It is a flexible tool for modifying and regulating coding and non-coding RNAs, with enormous potential for creating new cell functions. Compared to other RNA-level regulatory machinery, Cas13 has high RNA cleavage efficiency with little off-target effect, offering a better safety profile of regulation. However, the lack of control over Cas13 activity has limited its cell engineering capability.



Boston University researchers have developed the CRISTAL [Control of RNA with Inducible SpliT CAs13 Orthologs and Exogenous Ligands] platform which is powered by a collection (10 total) of orthogonal split inducible Cas13s that can be turned ON or OFF via small molecules in multiple cell types. This is a powerful platform for precisely regulating RNA dynamics to advance cell engineering and elucidate RNA biology.

Boston University is seeking licensing partners, R&D partnerships, or sponsored research to advance this technology.

Benefits

- Orthogonality, low leakiness, and high dynamic range of our inducible Cas13d and Cas13b
- Engineered Cas13 logic circuits that can respond to endogenous signaling and exogenous small molecule inputs
- Safer and reversible gene expression regulation on the RNA level
- Combinations of our inducible Cas13s can achieve simultaneous multiplexed control of multiple genes *in vitro* and in mice
- Validated high induced activity in mammalian cells and in mice
- Regulatory mechanism is orthogonal to endogenous cellular machinery and no genome modification required for effectiveness on endogenous targets

Market Applications

- ON/OFF switch for cell-based therapeutics (e.g. adoptive T cell therapy or stem cell therapy)
- Generation of animal models for study of genetic pathologies
- Genetic tools for investigating and manipulating genetic functions

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Keywords

CRISPR/Cas13

Gene therapy

Cell therapy

Synthetic genetic circuits

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Publications

Ding et al., "Orthogonal inducible control of Cas13 circuits enables programmable RNA regulation in mammalian cells." 2023 Mar 20;2023.03.20.533499. doi: 10.1101/2023.03.20.533499. Preprint

Patents

US Patent Application No. 17/381,780