Despite major advancements in biopharmaceutical manufacturing, downstream processing remains one of the most costly and restrictive aspects of protein production. A driving factor is the cost of separating the product from the multitude of host cell proteins (HCPs). Boston Mountain Biotech (BMB) is directly tackling this challenge by developing a platform to identify the HCPs that exert the greatest burden on downstream processing, and then silence these genes in the production strain.

The Lotus platform is then implemented with gene modification methods to silence or reduce expression of the most burdensome contaminating proteins. This allows it to be readily incorporated into virtually any expression strain, offering a simple add-on to commercialized or proprietary production strains.

The Lotus platform will coordinately and completely turn off the expression of non-essential contaminating genes and finely tune expression of essential contaminating genes to improve target capture and purity while preserving cell growth. Lotus will represent a significant step toward a commercial product that could revolutionize how downstream processing is conducted in the expansive biopharmaceuticals industry.

How Can We Help You?
- **Identify:** host cell proteins (HCPs) that bind resin during the initial capture
- **Prioritize:** HCPs that have the biggest impact on column capacity and efficiency
- **Implement:** Silence or reduce the expression of high priority HCPs in the expression host
- **Optimize:** Provide higher efficiency chromatography due to reduced protein profile
- **Goal:** Provide affinity like specificity from non-affinity resins
Lotus® in E. coli cells – increased column capacity for anion exchange

The Lotus cells have been genetically modified to improved downstream purification of recombinant protein products without the reliance on affinity tags or costly resins. This is accomplished by reducing the host cell proteins produced by the cell by 14-17%.

Our proprietary analysis tools allow for modifications that will result in the highest column capacity improvement without compromising growth and expression.

- When both the Lotus cell line and wild-type MG1655 harboring plasmid for anti-fungal peptide (fused with GFP) were grown the cell lines showed similar growth indicating that the removed genes did not impair growth function. The data is from a fed-batch style growth. Lotus cells expressed AF-GFP in a 2:1 ratio to wild-type

As a proof of concept, the Lotus platform has been incorporated into an E. coli production strain. BMB is currently seeking industrial partners to expand the Lotus platform into CHO and yeast, as well as other production hosts.

Expression of target proteins in Lotus cells is maintained at wild-type expression level, if not better than expression in wild-type cells.

Anti-fungal peptide-GFP extracts were applied to columns (n=2) and RFU at exit were monitored. Area to the left of the breakthrough indicates amount adsorbed.

37% capture improvement in purification of anti-fungal peptide; currently working on other model therapeutics to test robustness of Lotus cell lines.