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Intracellular Strategies for Gene Delivery into Mammalian Cells Using Bacteria as a Vector

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Abstract : E. coli has been engineered by our group and by others as a vector to deliver DNA into cultured human and animal cells. However, so far conditions to improve gene delivery using this vector have not been investigated, resulting in a major gap in our understanding of the requirements for this vector to function optimally. Our group recently published novel data showing that simple addition of the DNA transfection reagent Lipofectamine increased the efficiency of the E. coli vector by almost 3-fold, providing the first strong evidence that further optimization of bactofection is possible. This presentation will discuss advances that demonstrate the effects of several intracellular strategies that improve the efficiency of this vector. Conditions that promote endosomal escape of internalized bacteria to evade lysosomal destruction after entry in the cell, a known obstacle limiting this vector, are elucidated. Further, treatments that increase bacterial lysis so that the vector can release its transgene into the mammalian environment for expression will be discussed. These experiments will provide valuable new insight to advance this E. coli system as an important class of vector technology for genetic correction of human disease models in cells and whole animals.

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