# Method for increasing gene expression in mammalian cells from transfected plasmids

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## Meet the Inventors

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## Department

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## External Link(s)

- From the lab of Dr. Bryan Cullen
- The SMC5/6 complex compacts and silences unintegrated HIV-1 DNA and is antagonized by Vpr (Cell host & microbe, 2021)
- Discovery of TAK-981, a First-in-Class Inhibitor of SUMO-Activating Enzyme for the Treatment of Cancer (Journal of Medicinal Chemistry, 2021)

## Unmet Need

Mammalian cell-based protein expression systems enable the production of mammalian proteins in the most native structure and activity. Thus, they have been commonly used for producing antibodies and therapeutic proteins, and more recently, for gene therapies. The global market size of mammalian cell expression systems was 760.1 USD million in 2020. Despite being one of the most used protein expression platforms, mammalian expression systems often exhibit unpredictable behavior and performance shortcomings, especially the low protein yield which limits large-scale protein production. There is a need for a strategy to boost gene expression in mammalian cells at a high yield.

## Technology

Duke inventors have developed a method of increasing gene expression in mammalian cells. This is intended to be used to boost expression of transfected expression plasmids for recombinant protein production or gene therapy. Specifically, the SMC5/6 heterooctamer complex induces silencing of unintegrated viral DNA by SUMOylation. Thus, either blocking the SUMOylation step using the drug TAK-981 or losing any one of the subunits of SMC5/6 rescues viral DNA expression.This has been demonstrated through expression level from a range of expression plasmids as well as lentiviral vectors in HEK293T cells, a human cell line widely used to produce important proteins. The expression plasmids contain various viral promoters (CMV, HIV-1) or a cellular promoter (EF-1$\alpha$). The results collectively show that treating a HEK293T cell line with partial knockout of the SMC5/6 complex or TAK-981 strongly boosts the expression of transfected expression plasmids.

## Advantages

- Significantly increase, as much as over 40 fold, the expression of transfected plasmids in mammalian cells
- Novel method of increasing efficiency for gene therapy and recombinant protein production
- Demonstrated to be effective for a range of plasmids and vectors, including lentiviral, retroviral, and AAV vectors