

# **Non-Silencing Plasmid Vectors for Sustained High Level Expression of Transgenes**

Dr. Mark Kay and colleagues have created antibiotic-selectable, non-silencing plasmid vectors that can be prepared by conventional methods and provide persistent high levels of transgene expression. The introduction of exogenous DNA sequences into cells plays a major role in a variety of applications ranging from biological discovery to development of new therapeutics. In many applications it is desirable to have long term expression of the transgene, but in most plasmid DNA vectors the transgene is silenced after its initial high level of expression. Many types of DNA vectors have been generated in recent years in an attempt to overcome this problem, but these vectors all require special bacterial strains or complicated preparation procedures, limiting their practical use.

Based on their findings that the antibiotic-selectable marker can be optimized to prevent transgene silencing, the inventors have developed an alternative to conventional plasmid vectors. These non-silencing vectors, which use the optimized antibiotic-selectable markers, provide sustained elevated levels of transgene expression and can be produced using simple, well-established methods.

## **Stage of research**

The inventors have optimized the kanamycin resistance gene (Kan), a commonly used selectable marker, and shown that using the modified Kan marker transformed a silencing plasmid vector into a non-silencing plasmid vector that provided sustained high levels of transgene expression. Additional antibiotic resistance genes are also being optimized.

## **Applications**

- Gene expression in mammalian systems for:
  - Research
  - Therapeutic development

## Advantages

- Non-silencing plasmid vector
- Allows persistent high-level expression of transgenes *in vitro*, *ex vivo* or *in vivo*
- Allows transgene expression levels similar to minicircles
- Vectors can be prepared through conventional antibiotic selection and plasmid preparation methods:
  - No special bacterial strains required
  - No additional induction steps needed

## Publications

- Lu, J., Zhang, F., Fire, A. Z., and Mark A. Kay. "[Sequence-Modified Antibiotic Resistance Genes Provide Sustained Plasmid-Mediated Transgene Expression in Mammals.](#)" *Molecular Therapy*, 25(5):1187-1198, May 2017.

## Patents

- Published Application: [20160237454](#)
- Published Application: [WO2016130583](#)
- Published Application: [20180251783](#)
- Issued: [10,006,047 \(USA\)](#)
- Issued: [11,091,774 \(USA\)](#)

## Innovators

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