



## TECHNOLOGY OFFER

# UP-093: Modified AAV9 vectors for endothelial gene transfer

### Key Facts

- Adeno-associated virus (AAV) for efficient targeting of endothelial cells
- Highly increased transduction rate compared to wild type AAV9
- Reduced immunogenicity of the vector capsid

### The Technology

Adeno-associated virus (AAV) is a small virus which infects humans and other mammals. AAV is not currently known to cause human disease. AAV can infect both dividing and non-dividing cells and may incorporate its genome into that of the host cell. These features make AAV an attractive candidate for creating viral vectors for gene therapy.

Different serotypes of AAV have been shown to have different tropism inside the host body. AAV9 for example allows an efficient systemic gene transfer. However, as observed also with other serotypes, endothelial cells can be poorly transduced with AAV9 vectors. Vectors suitable for endothelial gene transfer would be highly valuable for target validation in vascular diseases such as atherosclerosis. In the long run, they could also enable novel gene therapeutic strategies against inherited and acquired vascular diseases such as atherosclerosis.

We engineered AAV9 vectors that can be targeted efficiently to endothelial cells *in vitro* and *in situ* by selection of a random AAV9 peptide library. These AAV libraries display the peptides in the context of the viral capsid. Besides a highly improved transduction rate of endothelial cells *in vitro* and *in situ*, modified AAV9 vectors also revealed a reduced immunogenicity.

### Background

The most common type of heart disease is the coronary artery disease (CAD), or ischaemic heart disease (IHD). Of an estimated 56 million deaths worldwide in 2001, more than 29% were due to cardiovascular disease, with over 12% attributed to ischaemic heart disease.

When atherosclerosis narrows or blocks the coronary arteries, depleting the oxygen-rich blood supply to the heart muscle, the muscle may malfunction or stop working altogether. Endothelial cells are the key to atherosclerosis, and underlying endothelial dysfunction is the central feature of this dreaded disease.

A number of preclinical studies have shown the adeno-associated virus (AAV) to be an efficient vehicle for gene therapy. Clinical studies successfully demonstrated its potential for *in vivo* gene transfer.

### Advantages

- non-pathogenic for humans
- long-term episomal transgene persistence
- robust transduction of tissues

### Commercial Opportunity

Target validation, Personalized therapy

### Development Stage

Ex vivo studies

### Inventors

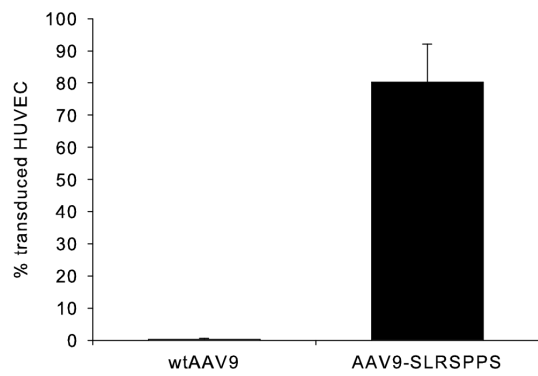
Oliver J. Müller, Karl Varadi, Jürgen A. Kleinschmidt and Hugo A. Katus,

### Intellectual Property

Patent application WO/2010/136549

### Reference:

Varadi et al. submitted.



**Figure:** Transduction of endothelial cells after vector administration on human umbilical veins *in situ*.

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