Docket #: S15-305

Novel AAV Capsids Resistant to Pre-existing Human Neutralizing Antibodies

Researchers in Prof. Mark Kay's laboratory have continued to develop novel recombinant adeno-associated viral (AAV) capsids via capsid gene shuffling that transduce human hepatocytes at high efficiency in vivo. The three new capsids were selected specifically for both human hepatocyte transduction from in vivo screens in humanized liver mice, as well as low immunogenicity on subsequent screens against pooled human immunoglobulins. The new capsid variants have highly favorable and importantly unique neutralization profiles compared to current capsids under consideration for liver clinical trials (AAV-3b, AAV-LK03). These unique antigen profiles are highly desirable in order to develop and offer gene therapy to a substantial proportion of the human population with pre-existing neutralizing antibodies against AAV-2, AAV-3b and AAV-LK03.

Related Research

Stanford Docket S11-298 describes the AAV-LK03 capsid mentioned above. Stanford Docket S15-415 describes AAV capsids designed for human muscle cell transduction.

Applications

- **Therapeutic:** human gene therapy
- **Research:** transduction of mouse or humanized mouse hepatocytes

Advantages

- **Unique and low immunogenicity:**

- created and selected specifically for low and unique neutralization profiles
- enables gene therapy in patients previously ruled out

Publications

- Paulk et al., Bioengineered AAV Capsids with Combined High Human Liver Transduction In Vivo and Unique Hu- moral Seroreactivity, Molecular Therapy (2017), https://doi.org/10.1016/j.ymthe.2017.09.021

Patents

- Published Application: 20170348433
- Published Application: WO2017143100
- Published Application: 20170360962
- Issued: 10,179,176 (USA)
- Issued: 10,532,111 (USA)

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