Utility of AAV Vectors Derived from Novel Serotypes

○Hiroaki Mizukami, Tsuyoshi Ogura, Takashi Okada, Takashi Matsushita, Masashi Urabe, Akihiro Kume, Keiya Ozawa
(Div. of Genetic Therapeutics, Center for Molecular Medicine, Jichi Medical Univ.)

AAV vector is derived from non-pathogenic virus, and possesses a number of attractive features as a vector for human gene transfer including safety, broad tissue specificity and low immunogenicity following gene transfer. Moreover, persistent transgene expression (for years) was demonstrated in multiple animal experiments. For these reasons, applications to a wide spectrum of diseases are expected and several clinical trials have been actually conducted. Although it is too early to conclude the outcome, the efficacy of treatment was not sufficiently substantiated in most of the trials despite the safety of the vector was consolidated. These results are primarily due to low levels of transgene expression. One of the approaches to improve this situation is a use of alternative serotypes of AAV. Traditionally, serotype 2 was considered as a prototype of AAV, and the majority of works including human clinical trials have been conducted using this serotype. On the other hand, there were five ‘classical’ serotypes, and several have been additionally discovered from tissues of primates including humans. These serotypes are now considered as precious resources for vector development to overcome shortcomings of serotype 2. In this presentation, we will focus on the difference in expression levels and tissue specificity of various serotype-derived vectors and will discuss about applications for the treatment of candidate diseases.