Table 1: Types of vector and considerations in relation to placental directed gene therapy for FGR

Vector	DNA	Efficiency	Tropism	Advantages	Disadvantages	Placental gene therapy considerations
Non-viral DNA	no limit	+	Limited	Low toxicity Low immunogenicity	Low transduction efficiency	Expression may not last through gestation
Adenovirus	7.5kb	+++	Depends on serotype	Can grow to high titre Highly efficient gene transfer Clinical safety and efficacy data long term in adults	Short term expression & immunogenic	
Helper-dependent Adenovirus	35kb	+++	Broad	Low immunogenicity, high capacity, long-term expression in quiescent cells	Inefficient production	
Adeno-associated virus	4.7 kb generally	++	Depends on sub-type	Long term expression Low immunogenicity Very high titre Clinical safety and efficacy data long term in adults	Liver toxicity in adult trials due to anti-capsid T cells. Risk of hepatocellular cancer.	Some subtypes associated with miscarriage Low level integration into active genes so theoretical mutagenesis risk.
Retrovirus	10kb	+	Depends on pseudotyping	Long term gene transfer Clinical safety and efficacy data long term in neonates	Potential for insertional mutagenesis. Infect dividing cells only.	Risk of germ-line transmission and insertional mutagenesis
Lentivirus	10kb	++	Depends on pseudotyping	Long term gene transfer Infects dividing and non-dividing cells	Potential for insertional mutagenesis	Risk of germ-line transmission and insertional mutagenesis
Non-integrating lentivirus	10kb	++	Depends on pseudotyping	Insertional mutagenesis unlikely	Short term expression	Rapidly dividing placental cells may result in long term low transgenic protein expression