Evaluation of different AAV5 gene delivery methods to the central nervous system and application in rats

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General goal

Some important factors for CNS-targeting gene therapies are to determine whether the target cells or neurons are transducible, and to find the appropriate delivery route to efficiently transduce the affected regions of the brain and/or spinal cord. In the current study, we investigated:

1) Transduction of human iPSC-derived frontal brain like neurons (FBN), dopaminergic neurons (DPN), astrocytes (Astr) and motor neurons (MN) by adeno-associated viral vector serotype 5 (AAV5) expressing GFP by the synthetic CMV early enhancer/chicken β actin (CAG) promoter.

2) Biodistribution of AAV5 in the central nervous system upon administration in different structures of the brain in rats.

Conclusion

Our ex vivo data in iPSC-neurons confirm AAV5 as a useful vector for CNS disorders efficiently transducing different neuronal cell types found in the brain and/or spinal cord. Our in vivo data demonstrate that diseases with involvement of deep brain structures can be targeted by injection of AAV5 directly in the parenchyma of the striatum and thalamus. ICV administration of AAV5 could be more suitable for disorders where both brain and spinal cord needs to be targeted such as motor neuron diseases.

Thus, AAV5 has a broad neuronal tropism and has the potential to mediate gene transfer to the entire CNS dependent on the route of administration.

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