Viral vectors in Parkinson’s disease treatment
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INTRODUCTION
Parkinson’s disease is a neurodegenerative disorder, which is characterized by the loss of dopaminergic neurons in substantia nigra. Also, it is observed the presence of cytoplasmic inclusions (Lewy’s body or LB), made of α-synuclein, but also Lewy’s neurites (LN) formed by α-synuclein and ubiquitin. Despite environment play an important role in Parkinson development, there are also some genetic factors that can imply Parkinson’s disease. These genetic features are assembled in two groups, α-synuclein and recessive genes (parkin, DJ-1 and PINK1).
In this context, gene therapy has become in one of the most interesting fields due to the possibility to transfer corrected genes in affected cells or prevent cell death and stimulate dopaminergic neuronal proliferation. In this context, high efficiency and specificity of viral vectors make these the main alternative for delivery.

VIRAL VECTORS

- Adenoviral vectors [1]
  - Non-enveloped, icosaedral, DNA
  - Structural proteins: hexon, penton and fibre, IIIa, VI, VIII and IX (small proportion)
  - 4.5-30 kb DNA packaging capacity
  - Immunogenic
  - Long-term episomal expression
  - Different generations: less viral content on genome
  - Endosomal trafficking

- Lentiviral vectors [2]
  - Enveloped, spherical, RNA
  - Structural proteins: gag, pol, and env
  - Other proteins: rev, tat (regulatory), vpu, vpr, vif and nef (accessory)
  - 7-12 kb DNA packaging capacity
  - Long-term integrated expression
  - Different generations: LTR and U3 modified, viral genes elimination
  - RNA released on cytoplasm

- Adenoassociated vectors [3]
  - Non-enveloped, icosaedral, DNA
  - Structural proteins: VP1, VP2 and VP3
  - 4.7 kb DNA packaging capacity
  - Multiple serotypes (AAV1-12) and tropism
  - Low immunogenicity and non-pathogenic
  - Long-term episomal expression
  - Endosomal trafficking
  - Vector generation: rep and cap substitution by transgene

ACTUAL APPROACHES

Most of the studied genes code for neurotrophic factors that either promote neuroprotection or induce neuron growth, but also genes that code for different enzymes involved in dopamine synthesis. AAV-based vectors, which are non-pathogenic and non-immunogenic, are the most used vectors, also due to high neuron tropism.

**THERAPY** | **VECTOR** | **PHASE** | **ADMINISTRATION** | **DA SURVIVAL** | **UPDR IMPROVEMENT**
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GAD [4] | AAV2 | Phase 2 | Bilaterally injected into the STN | - | 8.1 points
AADC [5] | AAV2 | Phase 1 | Bilaterally injected into the putamen | 56% | 30-46%
AADC7TH/GCH [6] | AAV and LV | Preclinical | Injected into the striatum | - | 60%
NRN1 [7] | AAV2 | Phase 2 | Bilaterally injected into the putamen | 62% | 88%
GDNF [8] | Ad, LV and AAV2 | Preclinical | Injected into the striatum | 48,70% | -
VEGF [9] | AAV2 | Preclinical | Injected into the striatum | - | -
NUR7R/FOXa2 [10] | AAV2 and LV | Preclinical | Injected into the putamen | 69% | -

- Every therapy showed an evident improvement in Parkinson’s symptoms and neural characteristics.
- Any problem derived from viral vectors was observed.
- AAV2 are the most employed vectors.

CONCLUSION
1. Prevention of neurodegeneration
2. Improvement of symptoms: tremor and dyskinesia
3. Higher production of dopamine
4. High safety of vectors: AAVs as the best vectors
5. Modest results
6. Possible upgrades: different or new vectors or other administration via
7. Potential therapy

REFERENCES