**Introduction**

DNA damage and repair is a critical domain of many neurodegenerative diseases. In this study, we focused on RpA1, a candidate key molecule in polyQ disease pathologies, and tested the therapeutic effect of adeno-associated virus (AAV) vector expressing RpA1 on mutant Ataxin-1 (Atxn1-KI) mice. We found significant effects on motor functions, normalized DNA damage markers (pH2AX and 53BP1), and improved Purkinje cell morphology, effects that lasted for 50 weeks following AAV-RpA1 infection. In addition, we confirmed that AAV-RpA1 indirectly recovered multiple cellular functions such as RNA splicing, transcription and cell cycle as well as abnormal morphology of dendrite and dendritic spine of Purkinje cells in Atxn1-KI mice. All these results suggested a possibility of gene therapy with RpA1 for SCA1.

**RpA1 effect in SCA pathology**

DNA damage and repair is a critical domain of many neurodegenerative diseases. In this study, we focused on RpA1, a candidate key molecule in polyQ disease pathologies, and tested the therapeutic effect of adeno-associated virus (AAV) vector expressing RpA1 on mutant Ataxin-1 (Atxn1-KI) mice. We found significant effects on motor functions, normalized DNA damage markers (pH2AX and 53BP1), and improved Purkinje cell morphology, effects that lasted for 50 weeks following AAV-RpA1 infection. In addition, we confirmed that AAV-RpA1 indirectly recovered multiple cellular functions such as RNA splicing, transcription and cell cycle as well as abnormal morphology of dendrite and dendritic spine of Purkinje cells in Atxn1-KI mice. All these results suggested a possibility of gene therapy with RpA1 for SCA1.

**Methods**

**Results**

**Conclusions**

The therapeutic effect of the RpA1 overexpression observed in the SCA1 fly model was observed also in the SCA1 mouse model.

- AAV-RpA1 recovers DNA damage.
- Dendritic shrinkage.
- Spine abnormalities.
- Motor dysfunction.

All these results suggested a possibility of gene therapy with RpA1 for SCA1.

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