New approaches to molecular basis of Huntington's chorea: from disease targets to new treatments

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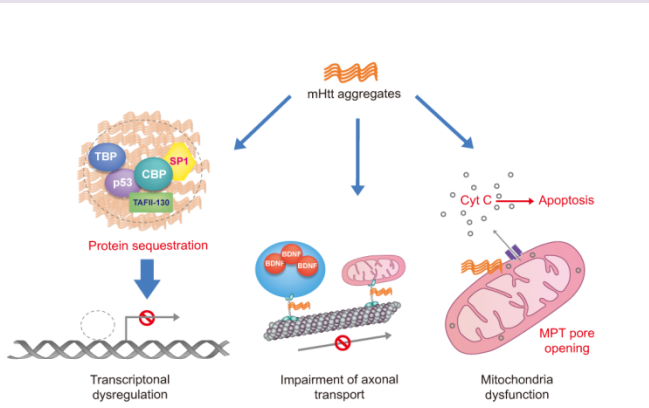
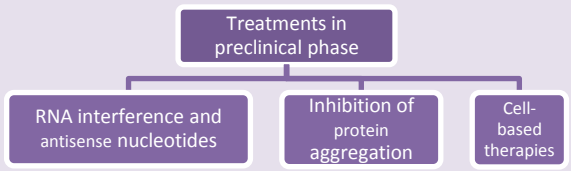
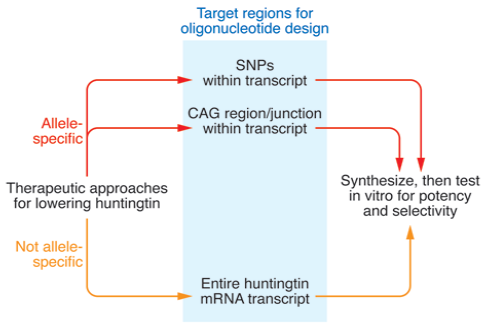
Huntington's disease (HD) is an autosomal dominant neurological disorder caused by a CAG repeat expansion in huntingtin gene. Mutated huntingtin (mHtt) is thermodynamically unfavorable misfolded what promotes the formation of inclusion bodies. Intermediary steps of mHtt aggregation evoke a progressive damage in striatum, cortex and hippocampus, what result in movement, cognitive and psychiatric disorders. There are basically three mechanisms of HD progression: trancrisptional dysregulation, impairment of axonal transport and mitochondria dysfunction.



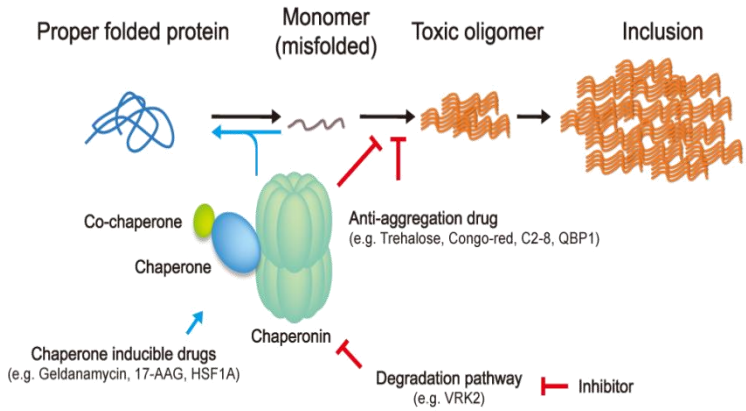
Molecular basis of Huntington's disease (1)

Nowadays, only palliative cures exist, therefore many treatments focused on several points of molecular progression of this disease are being developed. The aim of this study was to describe the pathogenic mechanisms involved in HD and novel therapeutic avenues to treat this disorder.

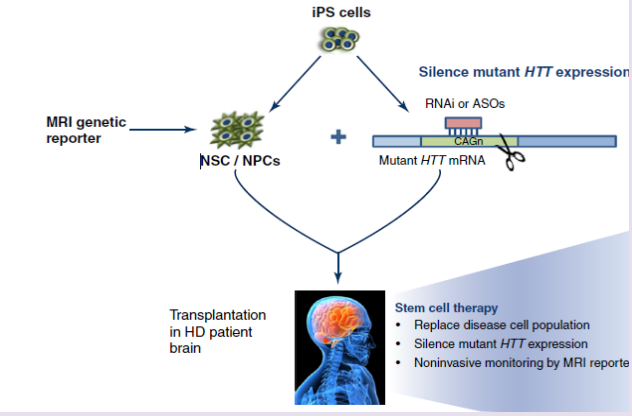




RNA interference and antisense nucleotides (2)



Inhibition of protein aggregation (1)



Cell-based therapies + RNA interferences and antisense nucleotides (3)

- **RNA interference and antisensenucleotides** block the expression of huntingtin by impairing its translation.
- **Inhibition of protein aggregation** can be achieved by chaperone inducible drugs, anti-aggregation drugs and inhibitors which impair chaperones activity.
- **Cell-based therapies** is focused on replenish lost neuronal population with induce-pluripotent stem cells (iPS cells) or embryonic stem cells (ES cells). This treatment would be specially suitable in advances stages of the disease.

Conclusions

Combining different therapies to stop the progression of the disease but also to reverse to the healthy situation may be the best option, e.g: cell-based therapies + RNA interference and antisense nucleotides.

References

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(2) Kim, S. K.-T. (2014). Therapeutic Approaches for Inhibition of Protein Aggregation in Huntington's Disease. *Exp. Neurobiol.* 23 (1):36-44.
(3) Yiju Chen, R. L. (2014). Cell-based therapies for Huntington's therapies. *Drug discovery today*, http://dx.doi.org/10.1016/j.drudis.2014.02.012.