SENESCENT PHENOTYPE AND DISTURBANCES IN AUTOPHAGY IN ATM-DEFICIENT NEURAL PRECURSOR CELLS

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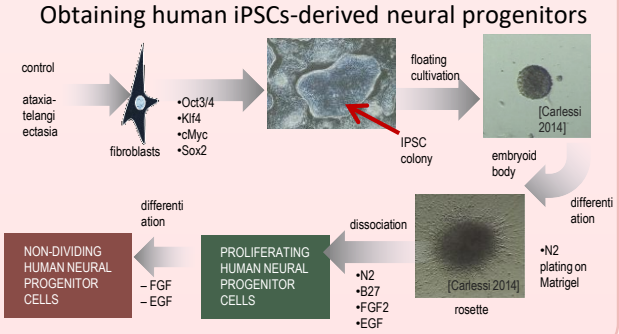
Background

- ATM is a kinase involved in DNA damage response (DDR), regulation of response to oxidative stress, autophagy and mitophagy. Mutations in the ATM gene in humans result in ataxia-telangiectasia disease (A-T) characterized by a variety of symptoms with neurodegeneration and premature ageing among them.
- Cellular senescence has been traditionally defined by proliferation arrest of dividing cells. Yet, some recent data suggest that more differentiated cells may enter a similar state. As we reported in previous studies, neurons in primary culture exhibit features of senescence, so do neurons in some areas of ageing brain, according to sparse data published on this topic.
- The aim of the study was to determine the phenotype of A-T neural progenitors in terms of senescence and to look at the role of ATM in this process. The study was conducted using human neural progenitors derived from induced pluripotent stem cells.

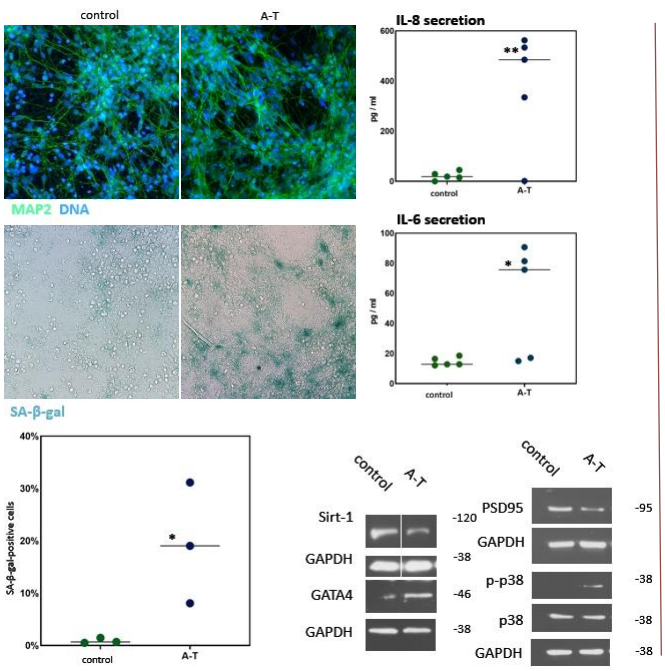
Material & Methods

Obtaining human iPSCs-derived neural progenitors

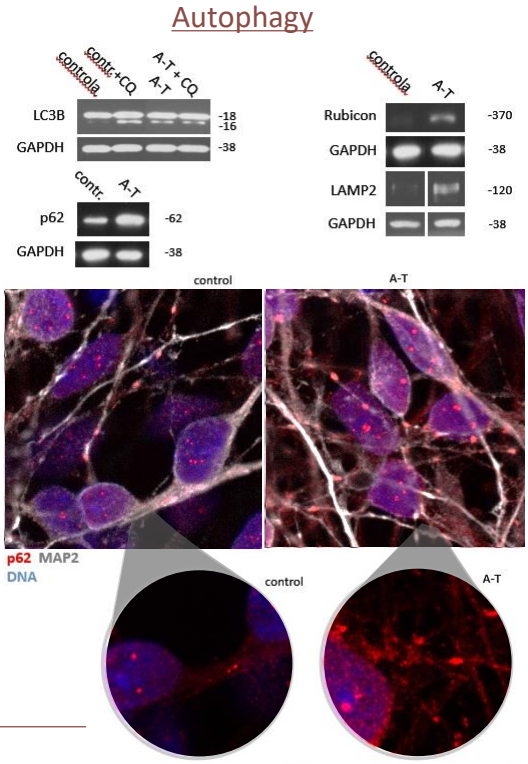


Results

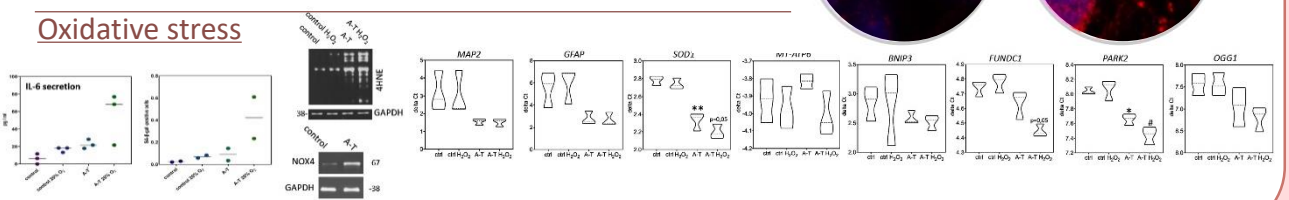
Cellular senescence



Autophagy



Oxidative stress



Conclusion

- ATM-deficient neural progenitors display markers of senescence and oxidative stress
- Autophagy and mitophagy are impaired in ATM-deficient neural progenitors
- External sources of oxidative stress partially aggravate the observed phenotype
- Ataxia-telangiectasia disease may have a component of neuronal senescence

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