SMRT compounds abrogate cellular phenotypes of ataxia telangiectasia in neural derivatives of patient-specific hiPSCs.

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Public Summary:
Ataxia telangiectasia is a devastating neurodegenerative disease caused primarily by loss of function mutations in ATM, a hierarchical DNA repair gene and tumour suppressor. So far, murine models of ataxia telangiectasia have failed to accurately recapitulate many aspects of the disease, most notably, the progressive cerebellar ataxia. Here we present a model of human ataxia telangiectasia using induced pluripotent stem cells, and show that small molecule read-through compounds, designed to induce read-through of mRNA around premature termination codons, restore ATM activity and improve the response to DNA damage. This platform allows for efficient screening of novel compounds, identification of target and off-target effects, and preclinical testing on relevant cell types for the pathogenic dissection and treatment of ataxia telangiectasia.

Scientific Abstract:
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