

1. Department of Health Sciences, School of Medicine, University of Piemonte Orientale, Novara, Italy
2. Department of Pharmaceutical Sciences, University of Piemonte Orientale, Novara, Italy

## BACKGROUND

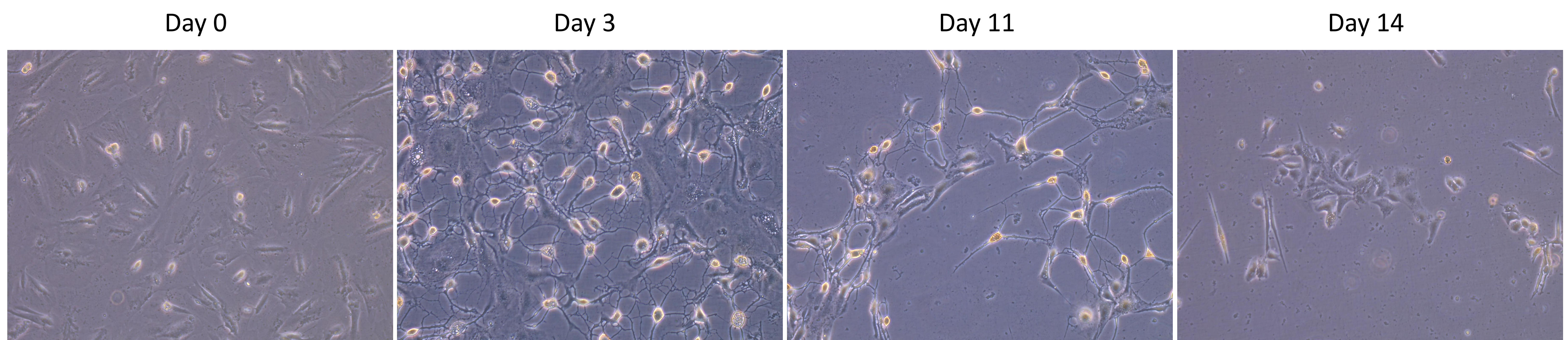
Ataxia telangiectasia (AT) is a rare multi-systemic neurodegenerative disease linked to the malfunction of the Ataxia Telangiectasia Mutated (ATM), which is a 350 KDa serine/threonine kinase. In response to DNA double-strand breaks (DBSs), ATM protein regulates cell cycle leading ultimately to the DNA repair.

## AIM

Current treatments are not able to improve the patients' life expectancy → it has become crucial to improve personalized cellular models to both deepen our knowledge in the pathophysiology of this rare disorder and to elaborate new therapies.

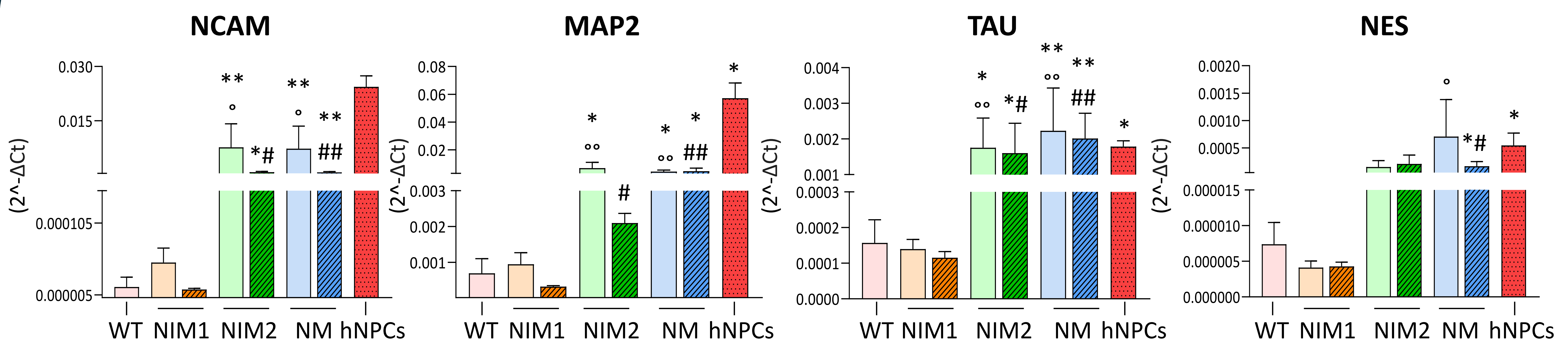
## METHODS and RESULTS

### Urine stem cells (USCs) were partly differentiated in neurons (USC-iNs)



**Fig 1. Neuronal differentiation of USCs.** Evocative phase-contrast microscopy images of USCs at day 0, day 3, day 11 and day 14, respectively, of the neuronal differentiation based on small molecules. Magnification: 200x.

### USC-iNs expressed typical neuronal markers



**Fig 2. Characterization of USC-iNs.** Gene expression analysis by qRT-PCR of USCs, USC-iNs and hNPCs of the indicated genes. Data are presented as histograms of the mean  $\pm$  SEM of  $2^{-\Delta C_t}$  values (n= at least 5 independent experiments).

\* p<0.05, \*\* p<0.01 vs WT; °p<0.05, °°p<0.01 vs NIM1; #p<0.05, ##p<0.01 vs NIM1 NAM.

□ NO NAM  
▨ NAM 10 mM

## LIMITATIONS

The **limited viability period** of USCs is one major issue common to all our experiments and RT-qPCR demonstrated that **USC-iNs don't achieve a complete neuronal development**, but rather a neural progenitor-like state.



## CONCLUSIONS

The objective of our research is the **generation of patient-specific and autologous cellular models** to deepen our knowledge of ATM pathogenetic pathways. At the moment the protocol based on the use of small molecules has only led to a partial neuronal model.