

# IMPAIREMENT OF VITAMIN E INTESTINAL SECRETION IN PRIMARY HYPOBETALIPOPROTEINEMIAS : MECHANISTIC STUDIES IN A CELL MODEL

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## INTRODUCTION

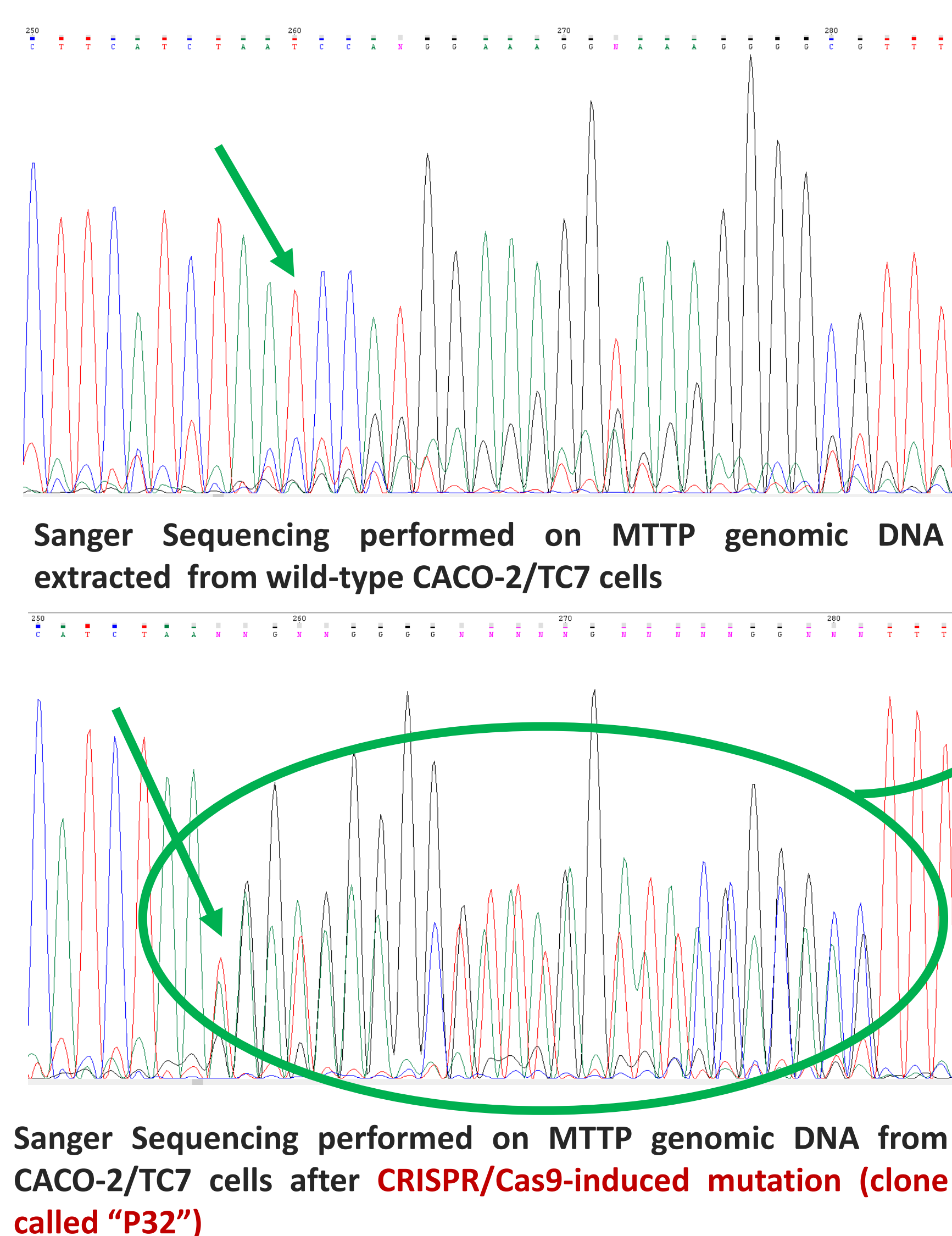
Chylomicron retention disease (CMRD) is a rare recessive inborn disorders of lipoprotein metabolism due to mutations in the **Microsomal Triglyceride Transfer Protein (MTTP)** gene. **Intestinal malabsorption of lipids and fat-soluble vitamins** (A, D, E, K) due to the lack of secretion of chylomicrons causes neurological complications. Supplementation in large doses is essential to prevent them. **However, serum vitamin E levels are never fully restored.** To understand these persistent low levels, previous studies were performed on **Mttp-KO mice**. Data showed a **reduced intestinal vitamin E accumulation** that was not consistent with the lipid accumulation observed.

## OBJECTIVES

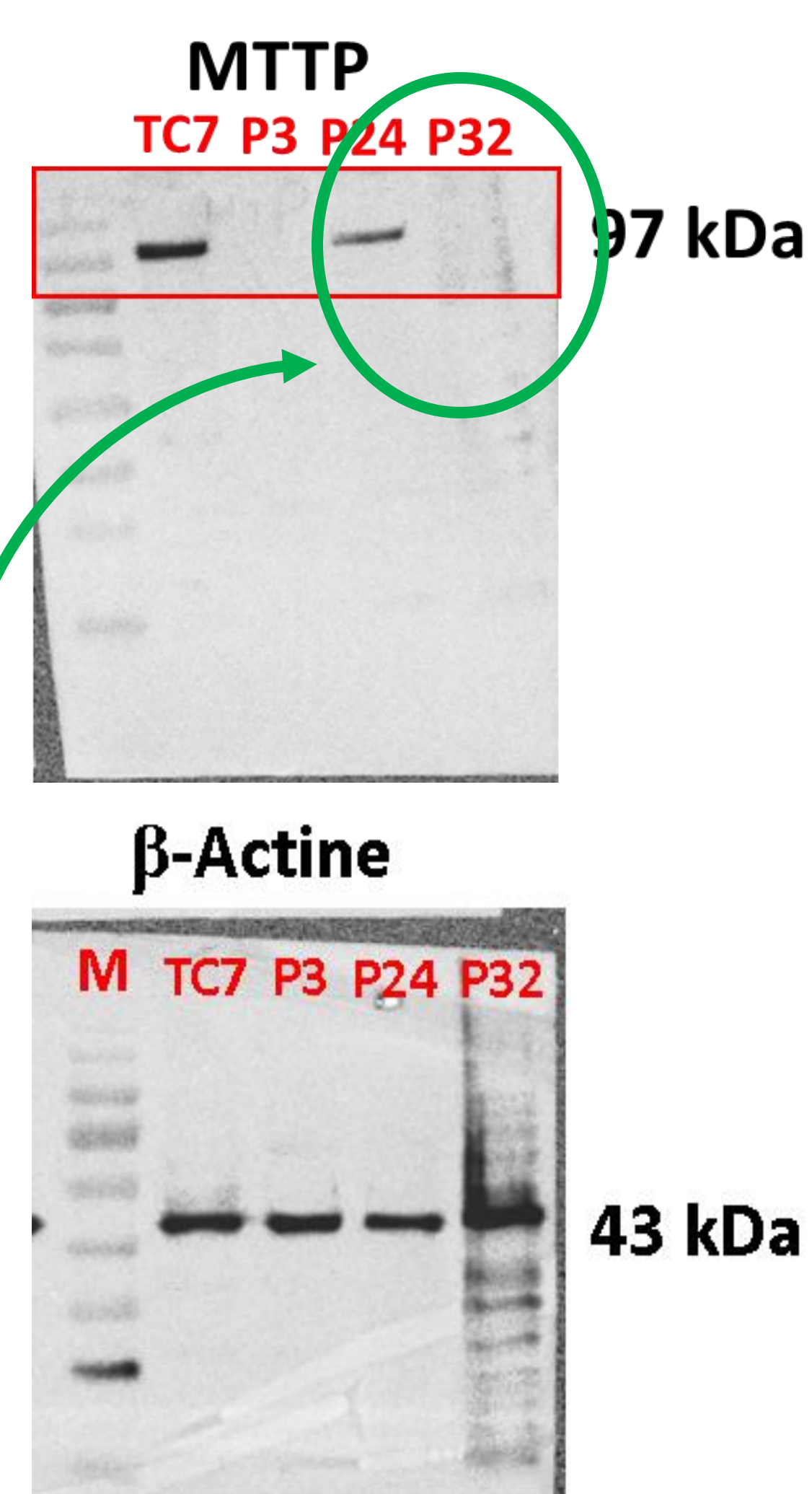
- Create a model of MTTP-knockdown-Caco-2/TC7 cells.
- Investigate the **mechanisms** underlying **reduced intestinal vitamin E accumulation**

## RESULTS

### DNA Sequencing confirmed mutation on MTTP gene

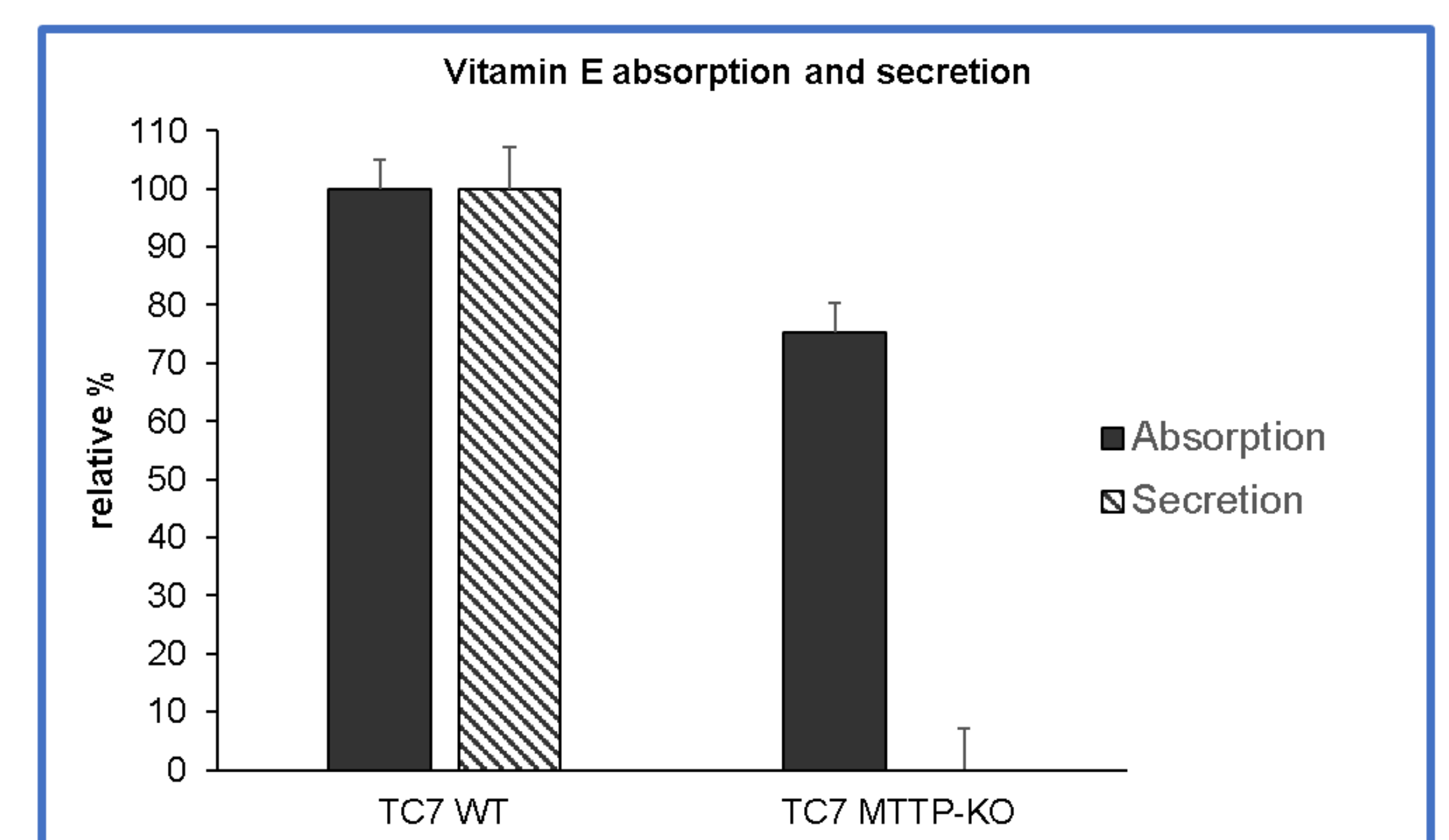


### Western-Blot confirmed MTTP knock-out



"TC7" → Wild-Type CACO-2/TC7 cells  
"P3", "P24", "P32" → Refers to 3 different cellular clones transfected with the CRISPR/Cas9 genome-editing system

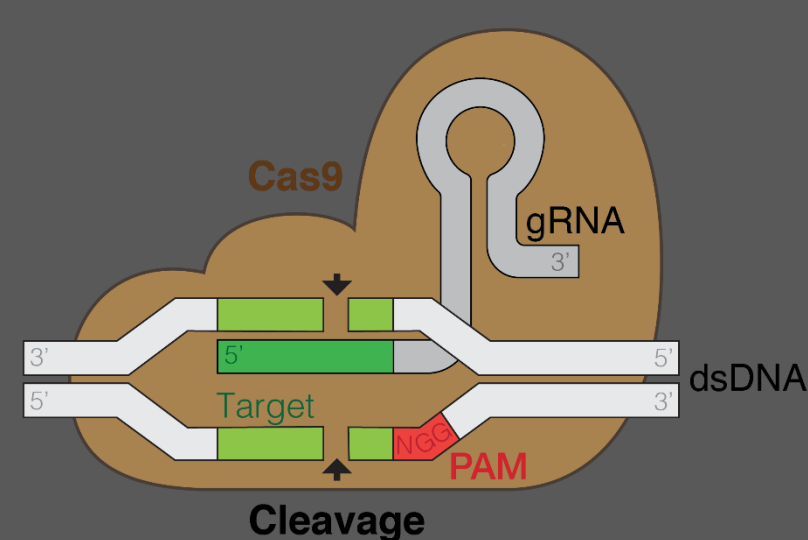
### Vitamin E assay performed on clone called "P32" show a drastic decrease in vitamin E basolateral secretion



## CONCLUSION

MTTP knock-out in Caco2 cells led to a **drastic decrease in vitamin E basolateral secretion** in Caco-2 TC7 cells. Further studies are needed to understand whether a degradation of vitamin E can occur in conditions mimicking those found in vivo, and to open **new therapeutic perspectives for these patients.**

## METHODOLOGY



- 1- **CRISPR/Cas9**-induced mutation on **MTTP gene**
- 2- DNA sequencing
- 3- Clone selection

- 4- Protein characterization
- 5- **Vitamin E absorption and secretion assays**
- 6- HPLC dosages