Chylomicron retention disease (CMRD) is a rare recessive inborn disorder 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.

**INTRODUCTION**

Chylomicron retention disease (CMRD) is a rare recessive inborn disorder 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-Caco2/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

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