CFTR modulates membrane glycerol permeability in testicular cells – an intersection between cystic fibrosis and male infertility?

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The cystic fibrosis transmembrane conductance regulator (CFTR) is an anion channel that regulates fluid dynamics in the male reproductive tract. Recent studies suggested that CFTR may interact with other transmembrane proteins, namely aquaporins (AQPs), also known to play a critical role in male fertility. This interaction could have important implications for understanding the complex processes involved in male reproductive health. With this study, we aimed to investigate the impact of CFTR inhibition on AQP-mediated glycerol permeability in Sertoli cells (SCs). We employed a combination of RT-PCR, Western Blot, and immunofluorescence techniques to determine the expression/localization of CFTR, AQP3, AQP7, and AQP9 in SCs. Subsequentially, we treated the SCs a CFTR inhibitor to evaluate its effect on glycerol permeability using stopped-flow light scattering technique, to shed light on the complex interplay between these two key proteins in male reproductive health. Our study revealed that inhibiting CFTR caused a significant reduction in glycerol permeability in SCs. To further explore the relationship between CFTR and aquaglyceroporins, we employed a DUOLINK proximity ligation assay to investigate endogenous protein-protein interactions. The assay detected an interaction of CFTR with AQP3, AQP7, and AQP9, suggesting a potential physical modulation of AQP-mediated glycerol permeability in SCs by CFTR. Our study highlights that CFTR malfunction can result in an impairment of AQP-mediated glycerol permeability, potentially due to a physical interaction between the proteins, contributing to a better understanding of the complex mechanisms underlying glycerol permeability in male reproductive tract. Given that CFTR variants are responsible for the most common genetic disease in the European population, understanding the relationship between CFTR and AQPs may provide a crucial link between male infertility and cystic fibrosis (CF), and aid in identifying potential therapeutic targets.

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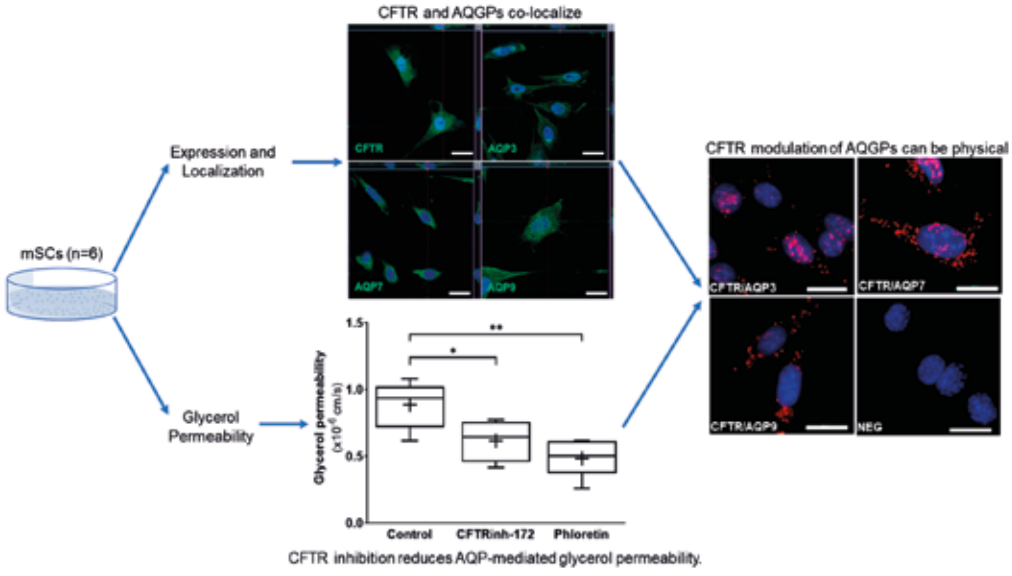

CFTR inhibition reduces AQP-mediated glycerol permeability.

FIGURE 1
Figure shows the impact of inhibiting cystic fibrosis transmembrane conductance regulator (CFTR) on aquaglyceroporin (AQGP)-mediated glycerol permeability. The results are presented as means with error bars representing standard deviation. Statistical significance is denoted as (*) for $p < 0.05$ and (**) for $p < 0.01$. The findings suggest a significant effect of CFTR inhibition on glycerol permeability through AQGP channels.