Peritoneal Dialysis (PD) is a method of renal replacement therapy that utilizes the peritoneal membrane, lining the abdominal cavity, to cleanse the blood of waste products and excess water. However, prolonged exposure to dialysis fluid can lead to structural changes in the peritoneum, including angiogenesis—the formation of new blood vessels with abnormal structure, resulting in decreased PD efficiency. Angiogenesis is primarily stimulated by vascular endothelial growth factor (VEGF).

Previous studies have shown that the combined action of transforming growth factor β1 (TGF-β1) and tumor necrosis factor α (TNF-α) leads to increased production of VEGF by human peritoneal mesothelial cells (HPMC). However, new research suggests that VEGF-independent pathways may be equally crucial for angiogenesis. Based on the literature and preliminary research findings, we identified angiopoietin-like protein 4 (ANGPTL4) as a candidate angiogenic factor in the peritoneum. Pilot studies demonstrated that exposure to TGF-β1 results in increased secretion of ANGPTL4. Enhanced expression of ANGPTL4 was also observed at the gene level. Furthermore, HPMC was subjected to exposition to Peritoneal Dialysis Effluent (PDE) and the increased ANGPTL4 level was indicated in the supernatant.

Therefore, we propose to characterize the impact of TGF-β1 and other factors on ANGPTL4 production in the peritoneum. For this purpose, HPMC will be cultured *in vitro* and exposed to TGF-β1 selected factors. We will use molecular biology and immunochemical methods to determine the expression levels of genes and proteins involved in the adverse angiogenesis mechanism. These methods have been widely used in similar studies and are known for their accuracy and reliability.

The proposed studies are significant because of the increasing number of individuals suffering from kidney failure and undergoing dialysis therapy. Angiogenesis is a major cause of the loss of peritoneal filtration capacity in patients with PD. Additionally, understanding VEGF-independent angiogenesis mechanisms will indicate new targets for therapeutic intervention, not only in the context of dialysis therapy but also in other disease conditions.