

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0272**

**Abstract Submission No. : APCN20250159**

### **Targeting SND1-Mediated CDC14B Splicing: A Novel Anti-Senescence Strategy Against PD-Associated Peritoneal Fibrosis**

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#### **Abstract**

##### **Introduction**

Alternative splicing represents a fundamental RNA processing mechanism that enhances transcriptomic complexity and proteomic diversity in fibrotic disorders. Accumulating evidence highlights the critical functional role of RNA-binding protein -regulated splicing variants during fibrogenesis. Staphylococcal nuclease and tudor domain-containing 1 (SND1), an RNA-binding protein previously linked to extracellular matrix remodeling, remains mechanistically uncharacterized in its regulatory role in peritoneal dialysis (PD)-associated peritoneal fibrosis and the associated splicing regulatory network.

##### **Methods**

Through single-cell RNA sequencing analysis of PD fluid from PD patients, SND1 was identified as a central regulator within fibrogenic niches. Bulk RNA-seq coupled with RNA-mediated alternative splicing analysis was employed to characterize SND1-mediated alternative splicing landscapes. The functional impact of SND1 on peritoneal mesothelial cell (PMC) senescence and peritoneal fibrosis was evaluated using an adeno-associated virus-mediated SND1 overexpression/knockdown mouse PD model, complemented by in vitro primary PMC cultures.

##### **Results**

SND1 expression was significantly downregulated in PMCs of peritoneal fibrosis models. Bulk RNA-seq revealed that SND1 knockdown in PMCs predominantly disrupted pathways associated with cellular senescence, cell cycle progression, extracellular matrix synthesis, and inflammatory responses. RNA-mediated alternative analysis identified 153 differential alternative splicing events in SND1-knockdown cells versus controls, with exon skipping being the most prevalent event type. Notably, cell division cycle 14B (CDC14B) was validated as a key downstream target of SND1. Reduced SND1 expression induced truncation of exon 2 in CDC14B transcripts, leading to decreased production of full-length CDC14B protein, cell cycle arrest, and subsequent senescence and fibrogenesis. In vivo studies demonstrated that SND1 overexpression attenuated peritoneal fibrosis, while SND1 knockdown exacerbated fibrotic severity.

##### **Conclusion**

This study demonstrates that SND1 in PMCs suppresses cellular senescence and fibrogenesis by regulating CDC14B alternative splicing. These findings elucidate a novel mechanistic pathway underlying PD-associated peritoneal fibrosis and position SND1 as a promising therapeutic target for preventing or alleviating peritoneal fibrosis.

**Keywords :** Peritoneal dialysis · Peritoneal fibrosis · Senescence · SND1 · Alternative Splicing

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0273**

**Abstract Submission No. : APCN20250209**

### **Acute Peritoneal Dialysis in a Neonate with Intra-Abdominal Pathology: Clinical and Ethical Reflections in a Case Report**

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#### **Abstract**

Neonatal acute kidney injury (AKI) is a major contributor to morbidity and mortality in critically ill neonates, particularly in the setting of sepsis, multi-organ dysfunction, and intra-abdominal pathology. When medical management fails to maintain fluid balance, electrolyte homeostasis, and metabolic clearance, kidney replacement therapy (KRT) becomes necessary. Peritoneal dialysis (PD) is preferred in neonates due to its gentler hemodynamic impact compared to hemodialysis (HD), technical feasibility, and suitability for low-birth-weight infants. However, the use of PD in neonates with intra-abdominal pathologies, such as necrotising enterocolitis (NEC), intestinal perforation, congenital gastrointestinal malformations, and post-surgical conditions, remains controversial. Concerns include dialysate leakage, peritoneal contamination, and peritonitis.

We report a 32-day-old term male neonate (39 weeks of gestation, birth weight 2.76 kg) who initially appeared well but developed NEC at 11 days of life, requiring hospitalization. After an apparent recovery, he presented again on day 30 of life with severe cardiorespiratory failure, sepsis and AKI, necessitating urgent kidney replacement therapy.

This case study highlights the successful application of PD in a neonate with NEC complicated with small bowel perforation and AKI, underscoring the importance of multidisciplinary management, adaptive PD strategies, compassionate communication and ethical considerations in clinical decision-making. With careful integration of ethical principles, clinicians navigated complex situations like PD in this critically ill neonate while prioritizing the best interests of the patient and family.

**Keywords :** Peritoneal dialysis, Intra-abdominal pathology, Neonate

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0274**

**Abstract Submission No. : APCN20250212**

### **Explore the Effects of Deleting Collagen Gene on Mesothelial Cells in Peritoneal Fibrosis**

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#### **Abstract**

##### **Introduction**

On healthy peritoneum, mesothelial cells express epithelial markers such as cytokeratin and present epithelial characteristics. Upon peritoneal fibrosis, the mesothelial cells were observed to produce collagen, one member of the extracellular matrix proteins, in murine models. However, the significance of this phenomenon remains unclear so far.

##### **Methods**

WT1-CreERT2; Colla1(f/f) mice were used to perform lineage tracing of WT1+ mesothelial cells and collagen deletion via the Cre/LoxP system. Colla1(f/f) and Colla1-GFPTg mice served as controls. Peritoneal fibrosis was induced using sodium hypochlorite according to our previous protocols. Severity of peritoneal fibrosis and expression of fibrotic-related proteins were analyzed in animals on day 0 and 7 post-injury.

##### **Results**

It was observed that the adhesions between peritoneal organs were significantly alleviated and the thickening of the peritoneum was markedly reduced in animals of the collagen-deletion group compared to controls. In addition, the immunofluorescence staining showed that the remaining number of mesothelial cells was higher and the infiltrating myofibroblasts were reduced on the peritoneum of mice in the collagen-deletion group when compared with controls.

##### **Conclusion**

In this study, we showed that the deletion of the Colla1 gene in mesothelial cells can improve the severity of peritoneal fibrosis, which suggests that the injured mesothelial cells also contribute to fibrosis by producing collagen. The underlying mechanisms of how the deletion of collagen production altered the formation of peritoneal fibrosis and whether it altered other pro-fibrotic characteristics of mesothelial cells should be further investigated.

**Keywords :** peritoneal fibrosis, mesothelial cell, Collagen

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0275**

**Abstract Submission No. : APCN20250270**

### **Dialysis Patient Support System II -Focus on Dietary Therapy Support -**

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#### **Abstract**

##### **[Introduction]**

The requirement to adhere to strict dietary guidelines can place a significant burden on hemodialysis patients, making adherence difficult. This also presents challenges for healthcare providers in accurately monitoring patients' eating habits. We are developing a community-based support system to assist dialysis patients with both exercise therapy and dietary therapy. We have added features to support the implementation and continuation of exercise (See, Dialysis Patient Support System I - Exercise Implementation and Continuation Support Using LINE app- ). Here, we introduce new features to the existing system to support dietary therapy.

##### **[Methods]**

Patients take a photograph of any meals or snacks prior to eating. The photograph is then uploaded to the enhanced community-based dialysis patient support system with the press of a single button. The risk of incorrect input is minimized because the system uses button-based input. Only one photograph is required per meal, and the patient can also optionally add a text description. The system also automatically records the time of food intake.

##### **[Results]**

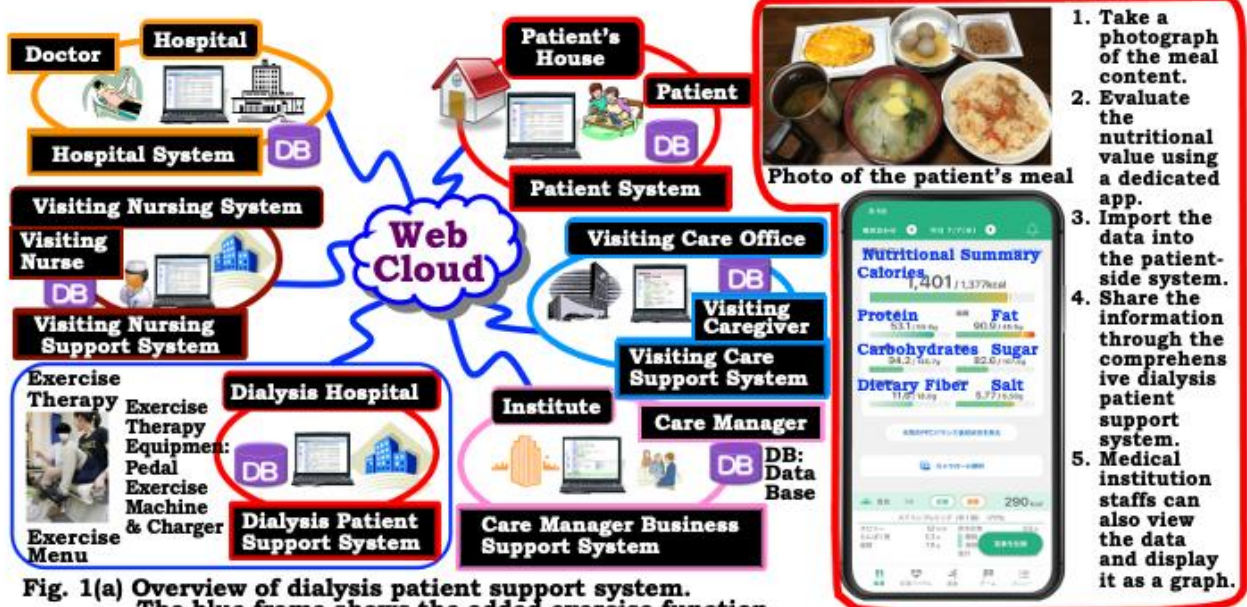
Figure 1(a) shows a schematic diagram of the community-based dialysis patient support system. Figure 1(b) presents an example of the display of nutrient calculation results from the added diet monitoring function. The patients could easily upload photographs of meals and snacks to the community-based dialysis patient support system with a single button press. The text input function also allowed patients to record not only the contents of meals but also the portion size. Through the system, medical staff at medical institutions can access patients' dietary records and share information. In addition, the system can be used to provide nutritional guidance to patients.

##### **[Conclusion]**

By incorporating a dietary management feature into the support system developed in this study, dialysis patients could share meal details with healthcare providers with a single button press. This ability to continuously upload meal records enabled patients to manage their nutrition independently. This system allows healthcare providers to accurately monitor patients' dietary habits, including meal contents and timing. The system is expected to enhance the effectiveness of dietary monitoring and nutritional guidance, thereby improving support for dietary therapy in dialysis patients.

This research was partially supported by a grant from the Japan Society for the Promotion of Science (JP20H03982).

**Keywords :** Dialysis rehabilitation, QOL, Dialysis support system, Exercise therapy, diet therapy



**Fig. 1(a) Overview of dialysis patient support system.**  
 The blue frame shows the added exercise function  
 & the red frame shows the added meal function.

**Photo of the patient's meal**

1. Take a photograph of the meal content.
2. Evaluate the nutritional value using a dedicated app.
3. Import the data into the patient-side system.
4. Share the information through the comprehensive dialysis patient support system.
5. Medical institution staffs can also view the data and display it as a graph.

**Fig. 1(b) Display of nutrient calculations**



## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0276**

**Abstract Submission No. : APCN20250271**

### **Dialysis Patient Support System I – Exercise Implementation and Continuation Support Using LINE app –**

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#### **Abstract**

##### **[Introduction]**

Exercise plays a crucial role in the rehabilitation of dialysis patients. However, many patients are unable to maintain regular exercise as they find it “troublesome” or “lack motivation”. We have developed a community-based dialysis patient support system to assist dialysis patients with both exercise therapy and dietary therapy (see, Dialysis Patient Support System II -Focus on Dietary Therapy Support- ). The support system includes a “reward” function to encourage consistent exercise and allows patients to easily track their activity using the LINE app. Here, we explain how we have developed a system to encourage dialysis patients to start and continue exercising.

##### **[Methods]**

To support dialysis patients in performing and maintaining regular exercise, we incorporated a “reward” function into the support system. For this purpose, we enhanced the ergometer and developed the “Ergo-Storage Device”, which converts rotational energy from the ergometer into electrical energy for use in charging mobile devices. A newly developed LINE app was also integrated into the system to allow patients to easily log their exercise volume and thus continuously track their exercise over time.

##### **[Results]**

Patients used the Ergo-Storage Device to perform and sustain exercise, while also charging their electronic devices. They could easily log their exercise volume using the LINE app, and these data could also be viewed at their medical institution, allowing monitoring of changes in each patient’s exercise volume alongside their medical records. Figure 1(a) shows a schematic diagram of the developed system. Figure 1(b) shows the device added to support the implementation and continuation of exercise, while Figure 1(c) presents an example of the input screen using the LINE app.

Healthcare staff were able to visualize changes in each patient’s exercise volume by graphing the entered data.

##### **[Conclusion]**

We added a “reward” function to an existing dialysis patient support system to encourage patients to sustain regular exercise regardless of location or dialysis schedule. The patients could easily log their exercise volume using the LINE app, and were motivated to maintain their daily exercise activity to earn rewards. This function encourages dialysis patients to continue exercising regardless of location and on both dialysis and non-dialysis days. Changes in the amount of exercise could be visualized on graphs, allowing patients and medical professionals to track their progress.

This study was partially supported by the Japan Society for the Promotion of Science (JP20H03982).

**Keywords** : Dialysis rehabilitation, QOL, Dialysis support system, Exercise therapy, diet therapy

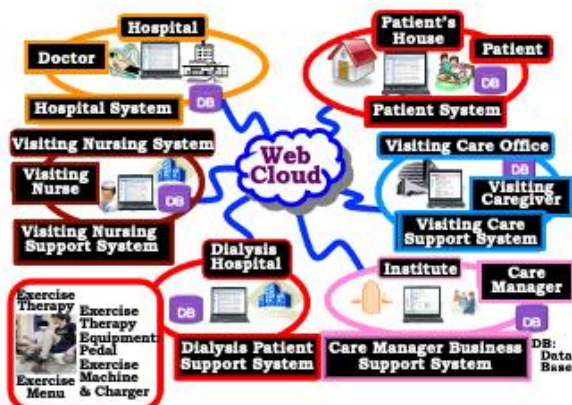


Fig. 1(a) Schematic diagram of the developed dialysis patient support system. The red frame shows the added exercise function.



Fig. 1(b) The ergo-storage device developed in this study to promote exercise implementation and continuation.



Fig. 1(c) The input screen using the additional features of the LINE app.

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0277**

**Abstract Submission No. : APCN20250277**

### **Establishment of a Mouse Model for Peritoneal Fibrosis in Adenine-Induced Chronic Kidney Disease**

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#### **Abstract**

##### **Introduction**

Peritoneal fibrosis is a complication in end-stage renal disease patients undergoing peritoneal dialysis. It primarily results from prolonged exposure to peritoneal dialysis solution, leading to chronic inflammation and fibrosis, ultimately resulting in peritoneal function failure. It is noteworthy that, even before exposure to peritoneal dialysis solution, chronic kidney disease patients already exhibit structural alterations in the peritoneum, including thickening, increased submesothelial fibrosis, and collagen deposition. However, most studies on peritoneal fibrosis utilize animals with normal renal function. Therefore, this study aims to establish a murine model of peritoneal fibrosis in adenine-induced chronic kidney disease.

##### **Method**

6-week-old C57BL/6 mice were fed a diet containing 0.2% adenine for 6 weeks to induce chronic kidney disease. Peritoneal fibrosis was induced by administering a single intraperitoneal injection of 0.05% Sodium hypochlorite (NaClO). After 7 days of NaClO injection, mice were euthanized, and plasma was collected for renal function assessment. The adhesion score evaluated the severity of peritoneal fibrosis. The thickness of the peritoneal membrane was measured using Masson's trichrome stain and the measurement scale function in Photoshop software. The peritoneal equilibration test was performed by injecting 2 mL of 2.5% peritoneal dialysis solution for 30 minutes to assess the peritoneal solute transport rates and ultrafiltration volume.

##### **Results**

In the adenine-CKD group, each mouse consumed an average of 3.14 g of food daily, equivalent to 6.28 mg of adenine per day. Blood urea nitrogen and creatinine levels were markedly increased in this group. After NaClO injury, peritoneal adhesion scores were increased in both the normal and adenine groups, especially in the adenine group. In this group, peritoneal adhesions were particularly observed in the intestines and omentum. Thickening of the parietal and visceral peritoneal membrane was observed in NaClO-injured mice, with no differences between the two dietary groups. The peritoneal equilibration test showed that NaClO-injured mice absorbed more glucose from the dialysate, consequently reducing ultrafiltration.

##### **Conclusion**

NaClO-induced peritoneal fibrosis resulted in thickened, adhesive peritoneal membranes and a loss of the osmotic gradient, reducing water removal. Although the adenine group showed higher adhesion scores, the decline in renal function did not influence membrane thickening, peritoneal solute transport, and ultrafiltration. This model is relevant to human patients suffering from peritoneal fibrosis and impaired renal function.

**Keywords :** Peritoneal fibrosis, Chronic kidney disease, Adenine diet

## **Poster Presentation : Peritoneal Dialysis and Telehealth**

**Poster No. : B0278**

**Abstract Submission No. : APCN20250508**

### **Targeting Yes-Associated Protein to Mitigate Peritoneal Dialysis-Induced Fibrosis**

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#### **Abstract**

##### **Introduction:**

Peritoneal dialysis is a widely used renal replacement therapy, but is often limited by progressive peritoneal fibrosis. This pathological process, driven by chronic inflammation and the activation of fibroblasts, compromises dialysis efficacy. The yes-associated protein (YAP), a core effector of the Hippo pathway, has been implicated in fibrosis across multiple organs. However, its role in peritoneal fibrosis remains unclear.

##### **Methods:**

We examined the function of YAP using both in vitro and in vivo models. Fibroblast-to-myofibroblast transition (FMT) was induced in NIH/3T3 and primary mouse fibroblasts with transforming growth factor-beta (TGF- $\beta$ ). YAP expression was suppressed using siRNA or the pharmacologic inhibitor verteporfin. In vivo, a murine model of peritoneal dialysis-induced fibrosis was developed. Conditional knockout of YAP in Gli1-expressing cells was achieved using Gli1-CreERT2; YAP<sup>f/f</sup> mice.

##### **Results:**

TGF- $\beta$  enhanced YAP expression and nuclear translocation, promoting the expression of myofibroblast markers, including  $\alpha$ -smooth muscle actin, collagen 1A1, and connective tissue growth factor. YAP knockdown or verteporfin treatment suppressed FMT and downstream Smad2/3 phosphorylation. In the peritoneal fibrosis model, Gli1<sup>+</sup> cells were enriched and co-expressed YAP and markers of fibrosis. Conditional deletion of YAP in Gli1<sup>+</sup> cells and verteporfin administration significantly attenuated peritoneal thickening, collagen deposition, and profibrotic signaling.

##### **Conclusion:**

YAP promotes peritoneal fibrosis by mediating fibroblast transdifferentiation via TGF- $\beta$  signaling in Gli1<sup>+</sup> cells. Targeting YAP through genetic deletion or pharmacological inhibition represents a promising therapeutic strategy for mitigating fibrosis in patients undergoing long-term peritoneal dialysis.

**Keywords :** Peritoneal Fibrosis, Fibroblast-To-Myofibroblast Transition, Yes-Associated Protein, Gli1, Verteporfin

## Poster Presentation : Peritoneal Dialysis and Telehealth

Poster No. : B0279

Abstract Submission No. : APCN20250625

### The Impact of Nutritional Education for Peritoneal Dialysis Patients in Mongolia

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#### Abstract

**Introduction:** Peritoneal dialysis treatment has developed instantly in Mongolia for past five years. Currently, more than 120 patients undergo PD nationwide. These patients lack nutritional education, which predisposes them to protein deficiency and further impair their quality of life. However, there is no study which is conducted among those about their dietary in Mongolia. Therefore, integrated nutrition information and educating them about dietary patterns to follow are an urgent needed for PD patients.

**Methods:** This study aimed to evaluate the effectiveness of structured nutrition education in CAPD patients 18 to 60 years at Medvic dialysis center in Ulaanbaatar, focusing on improved dietary knowledge and compliance. A total of 45 patients were randomly assigned into three groups (n=15 per group):

Group A (Group Education Sessions)

Group B (Online Education Sessions)

Group C (Control Sessions)

Each group received a total of five educational interventions over a period of five weeks. The educational content covered essential topics including fluid, electrolyte management, protein intake, phosphorus and potassium control, and food label reading. The nutrition education is assessed by interview based on a validated questionnaire. In addition, a biochemical blood test and 24-hour dietary recall methods are used for an nutrition assessment.

**Results:** Base line: The rate of mildly-to-moderately malnutrition were at 48.8% among research participants. All patient's energy intake was significantly lower /1328±304kcal/ than the energy requirement. Only 14.2% met the recommended dietary protein intake.

Educational intervention: The average knowledge assessment score improved from 8.2 /pre-intervention/ to 11.4 /post-intervention/. The proportion of participants scoring ≥10 increased markedly in group A /33.3% - 93.3%/ and moderately in the group B /20.0% - 46.7%/, while the group C showed minimal change.

Correlation analysis between nutrition knowledge scores and biochemical parameters revealed a statistically significant relationship with phosphorus /r = -0.473, p < 0.01/ and calcium /r = 0.696, p < 0.01/ levels. Increased nutrition knowledge was associated with lower serum phosphorus and higher calcium levels. Biochemical indicators also showed notable improvements with total protein levels increased significantly /p=0.01/, and creatinine levels decreased /p=0.05/ in the group A.

**Conclusion:** This study demonstrated that providing nutrition education to patients led to noticeable improvements in their dietary habits and health status. However, the findings also highlight the need for continuous learning and sustained application of the acquired knowledge. Ongoing support and adherence to nutrition guidelines are essential to maintain these positive changes over time.

**Keywords :** Keywords: peritoneal dialysis, malnutrition, nutritional education, nutritional status

## Poster Presentation : Peritoneal Dialysis and Telehealth

Poster No. : B0280

Abstract Submission No. : APCN20250791

### Trichosporon PD-related Peritonitis in a Filipino Female: A case report

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#### Abstract

We present the case of a 35-year-old Filipino female from Benguet with end-stage renal disease secondary to chronic glomerulonephritis, maintained on continuous ambulatory peritoneal dialysis (CAPD) since 2018. She initially presented with sharp, episodic left lower quadrant abdominal pain and was diagnosed with bacterial peritonitis. She was treated with intraperitoneal antibiotics and discharged improved.

Two weeks later, she returned with persistent abdominal pain unrelieved by analgesics. There were no associated systemic symptoms. An abdominal ultrasound done at a local facility revealed loculated fluid collections, and she was started on Heparin. A week prior to admission, her pain persisted, prompting further consultation and symptomatic treatment with mefenamic acid, which provided no relief. She then sought consult at our institution for ongoing symptoms.

On examination, she was hemodynamically stable but had a flabby abdomen with generalized tenderness and dullness on percussion. The peritoneal catheter exit site was dry with intact dressing. Gram stain of peritoneal effluent revealed blastospores and hyphae, and culture confirmed *Trichosporon asahii*. Intraperitoneal Fluconazole and intravenous Amphotericin B were initiated on hospital day 4. On day 12, repeat culture of PD effluent grew methicillin-resistant *Staphylococcus aureus* (MRSA), and intravenous Vancomycin was added. PD catheter removal was performed on hospital day 18. The patient's condition improved with the completion of antifungal and antibiotic therapy, and she was transitioned to hemodialysis.

#### Discussion

Fungal peritonitis, though uncommon, is a serious complication in CAPD patients, particularly following recent antibiotic therapy for bacterial peritonitis. *Trichosporon* spp., part of the normal flora of the GI tract, skin, and lungs, can cause invasive infections in immunocompromised individuals or those with indwelling devices. Though rare, *T. asahii* has been identified as a pathogen in CAPD-related peritonitis, with few documented cases in Southeast Asia and none found in the Philippine literature. Previous reports noted favorable outcomes with early antifungal treatment and catheter removal—similar to our patient's course.

#### Conclusion

This case highlights the importance of considering *Trichosporon asahii* as a potential cause of fungal peritonitis in CAPD patients, especially those with prior antibiotic exposure. Prompt initiation of antifungal therapy and timely PD catheter removal are critical to improving clinical outcomes.

**Keywords** : Peritonitis, Fungal peritonitis, *Trichosporon asahii*



## Poster Presentation : Peritoneal Dialysis and Telehealth

Poster No. : B0281

Abstract Submission No. : APCN20250882

### Sildenafil Mitigates Peritoneal Fibrosis via Metabolic Reprogramming and Myofibroblast Inhibition

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#### Abstract

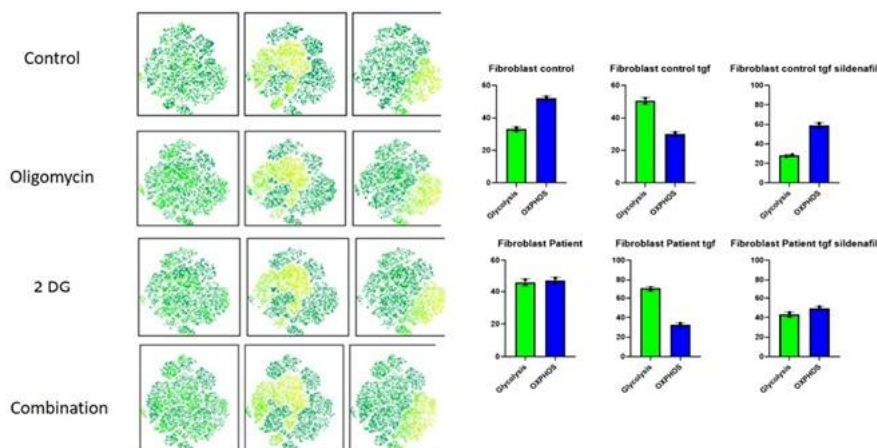
**Background and Objective:** Peritoneal fibrosis (PF), a major cause of technique failure in peritoneal dialysis (PD) patients, is driven by the excessive deposition of extracellular matrix (ECM) proteins, primarily mediated by the activation of fibroblasts into myofibroblasts. This activation is associated with a metabolic reprogramming from oxidative phosphorylation (OXPHOS) to glycolysis, particularly under profibrotic stimuli such as TGF- $\beta$ 1. This study investigated the anti-fibrotic potential of sildenafil, a phosphodiesterase-5 inhibitor, in modulating metabolism and inflammation in human peritoneal fibroblasts (HPFBs).

**Methods:** HPFBs isolated from long-term PD patients (n = 8) and controls (n = 8) were treated with TGF- $\beta$ 1 (10 ng/mL), alone or in combination with sildenafil (10  $\mu$ M), SB204741 (1  $\mu$ M), or both using pre- and post-treatment strategies. Metabolic analysis was performed using the SCENITH assay via flow cytometry. Gene expression was assessed by qPCR, and cytokines were quantified using ELISA.

**Results:** SCENITH analysis showed a non-significant increase in basal glycolytic dependency in patient-derived fibroblasts (32%) compared to controls (26%). However, TGF- $\beta$ 1 stimulation significantly enhanced glycolysis in patient fibroblasts (87%) versus controls (51%). This metabolic shift coincided with upregulation of glycolytic enzymes (GLUT1, LDHA, Hexokinase II) and profibrotic markers ( $\alpha$ -SMA, fibronectin, collagen I). Sildenafil treatment effectively reduced glycolytic dependency (to 52.5% in patients and 39% in controls) while promoting OXPHOS (67%–73%). Furthermore, sildenafil significantly downregulated glycolytic and profibrotic gene expression (p < 0.001) and decreased pro-inflammatory cytokines, while upregulating IL-10, supporting an anti-inflammatory shift.

**Conclusion:** Sildenafil attenuates peritoneal fibrosis by inhibiting fibroblast activation through metabolic reprogramming and immune modulation. These findings highlight the therapeutic potential of sildenafil in preventing PF and preserving peritoneal membrane function in PD patients.

**Keywords :** Peritoneal Dialysis, Sildenafil, Metabolic reprogramming, Fibroblasts, Myofibroblasts



## Poster Presentation : Peritoneal Dialysis and Telehealth

Poster No. : B0282

Abstract Submission No. : APCN20250888

### Immune-Metabolic Crosstalk in Peritoneal Dialysis: A Central Role for T Cell Bioenergetics in Fibrosis Progression

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#### Abstract

**Introduction:** Peritoneal dialysis (PD), a life-saving renal replacement therapy, is often complicated by peritoneal fibrosis, which limits long-term efficacy. Emerging evidence suggests that immune cells, particularly T cells, play a pivotal role in driving this fibrotic response. In this study, we explore the increased T cell infiltration and altered bioenergetics in the peritoneum of PD patients, shedding light on immune-metabolic pathways that may contribute to fibrosis and identifying potential therapeutic targets to improve PD outcomes.

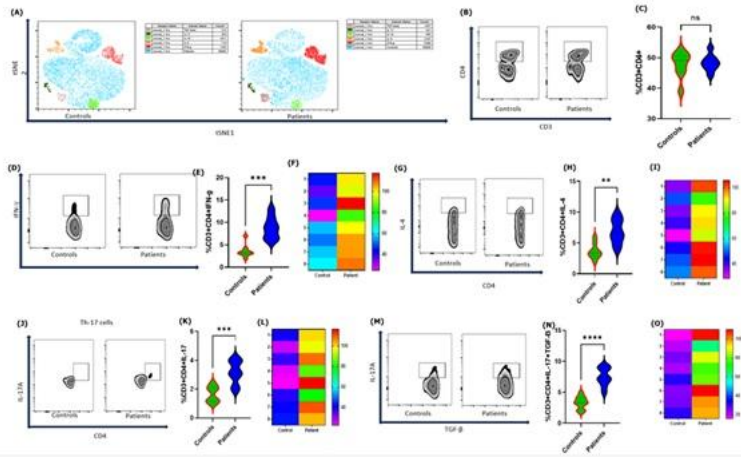
**Methods:** Peritoneal biopsy tissue was obtained from ESRD patients on PD (n=8) undergoing catheter replacement or removal after renal transplantation. The peritoneal tissue for the control population (n=8) of the study was taken from persons with normal renal function during laparoscopic donor nephrectomy. T cell profiling and Bioenergetics studies using Flow Cytometry. Expression levels of key pro- and anti-fibrotic genes were measured by quantitative PCR (qPCR), and cytokine concentrations in culture supernatant were quantified using ELISA.

**Results:** Flow cytometric analysis revealed a significant increase in the percentage of Th1, Th2, and Th17 cells and their functional markers in PBMCs of peritoneal dialysis patients compared to controls (P<0.001). Cytokine analysis showed increased levels of IFN- $\gamma$ , IL-4, TGF-beta and IL-17 in patients samples, SCENITH analysis demonstrated that T cells from PD patients exhibited enhanced bioenergetics (glycolysis 84%, OXPHOS 27%), suggesting a metabolic reprogramming that supports their heightened proliferative and effector functions. This metabolic shift correlates with increased expression of key transcription factors (T bet, GATA3, FOXP3, ROR Gamma T, p<0.001) and cytokines involved in T cell activation and differentiation (IFN-gamma, IL-17, IL4 p<0.0001). The gene expression of the key transcription factor was increased in PD patients PBMCs as compared to controls (p<0.0001)

**Conclusion:** Targeting T cell metabolism may offer novel therapeutic avenues to mitigate fibrosis and improve the longevity of peritoneal dialysis.

**Keywords :** Peritoneal Fibrosis, Bioincompatible PD solutions, Peritoneal Fibrosis, Serotonin, T cells, Bioenergetics

Figure 1: T cell phenotype in Patients and Controls



## **Poster Presentation : Peritoneal Dialysis and Telehealth**

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### **Synergistic Inhibition of PDE5 and 5-HT<sub>2B</sub> Receptor Signalling: A Promising Anti-Fibrotic Strategy to Suppress Peritoneal Fibroblast Activation in Peritoneal Dialysis Patients**

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#### **Abstract**

##### **Introduction**

Peritoneal fibrosis (PF) results in ultrafiltration failure in peritoneal dialysis (PD) patients. 5-hydroxytryptamine (5-HT; serotonin) induces extracellular matrix (ECM) proteins synthesis in fibroblasts in a transforming growth factor beta 1 (TGF- $\beta$ 1) dependent manner. TGF- $\beta$ 1, trans-differentiate fibroblasts into peritoneal myofibroblasts characterized by increased alpha-smooth muscle actin ( $\alpha$ -SMA) expression, ECM proteins production. Here we evaluate anti-fibrotic efficacy of phosphodiesterase-5 (PDE-5) inhibitor, Sildenafil, and 5-HT<sub>2B</sub> inhibitor, SB204741, in combination on human peritoneal fibroblasts (HPFBs) isolated from parietal peritoneum biopsy (PB) of PD patients.

##### **Methods**

PB from controls (n=10)/PD patients (n=8) excised during laparotomy was incubated overnight in dispase (2.4 U/mL)/37°C [3]. HPFBs, incubated with TGF- $\beta$ 1 (10ng/ml) for 1 hour and later with TGF- $\beta$ 1 (10ng/ml) [Sildenafil (10 $\mu$ M) or SB204741 (1 $\mu$ M)] and their combination for 24 hours (Post-treatment strategy). In pre-treatment strategy, HPFBs pre-treated with [Sildenafil (10 $\mu$ M) or SB204741 (1 $\mu$ M)] and combination of the two for 1 hour and later with only TGF- $\beta$ 1 (10ng/ml) for 24 hours. Real time PCR for pro-fibrotic (COL1A1, COL1A2, ACTA2, CTGF, FN1, TGFB1) and anti-fibrotic genes (MMP2/TIMP1) expression was performed. Levels of cytokines IFN- $\gamma$ , IL-4, IL-17, IL-1 $\beta$ , IL-6, TNF- $\alpha$  proinflammatory and IL-10 (anti-inflammatory) in culture supernatant of HPFBs were determined by ELISA. Type-1 collagen/ $\alpha$ -SMA were examined by immunoblotting.

##### **Results**

In this study, anti-fibrotic effect of combination of Sildenafil and SB204741 was greater than that of each drug alone. In TGF- $\beta$ 1 stimulated HPFBs, upregulated expression of pro-fibrotic genes was observed. Expression of pro-fibrotic genes reduced with almost complete amelioration of ACTA2. Ratio of anti-fibrotic genes (MMP2/TIMP1) was restored. Expression of  $\alpha$ -SMA/type 1 collagen was decreased (table 1). Production of proinflammatory cytokines also reduced with increase in IL-10 levels.

##### **Conclusion**

Combination of Sildenafil and SB204741 may be efficacious in treating PF in its active phase by near complete attenuation of conversion of resident fibroblasts to MFBs.

**Keywords :** Peritoneal Fibrosis, TGF- $\beta$ 1, Sildenafil, SB204741, ACTA2, Inflammation

**Table 1. Effect of Sildenafil, SB204741 and their combination on TGF-β1 induced pro-fibrotic/anti-fibrotic genes mRNA expression along with Type-1 Collagen and α-SMA protein expression in cultured HPFBs**

	TGF-β1 treatment (Fold change in comparison to media+ cells only)	TGF-β1+ Sildenafil + SB204741 (Fold change in comparison to TGF-β1 stimulation)
<b>Post-treatment strategy</b>		
*COL1A1	Reference ( <u>5.3 fold</u> increase)	( <u>1.5 fold</u> decrease)
*COL1A2	Reference ( <u>4.1 fold</u> increase)	( <u>1.1 fold</u> decrease)
*ACTA2	Reference ( <u>4.7 fold</u> increase)	( <u>2.2 fold</u> decrease)
*CTGF	Reference ( <u>8.9 fold</u> increase)	( <u>4.3 fold</u> decrease)
*FN1	Reference ( <u>5.4 fold</u> increase)	( <u>1.1 fold</u> decrease)
*MMP2	Reference ( <u>0.4 fold</u> decrease)	( <u>0.6 fold</u> increase)
*TIMP1	Reference ( <u>3.1 fold</u> increase)	( <u>1.3 fold</u> decrease)
*MMP2/TIMP1	Reference ( <u>0.3 fold</u> decrease)	( <u>0.5 fold</u> increase)
*Type 1 collagen protein	Reference ( <u>3.4 fold</u> increase)	( <u>1.5 fold</u> decrease)
*α-SMA protein	Reference ( <u>2.8 fold</u> increase)	( <u>1.2 fold</u> decrease)
<b>Pre-treatment strategy</b>		
*COL1A1	Reference ( <u>5.3 fold</u> increase)	( <u>3.2 fold</u> decrease)
*COL1A2	Reference ( <u>4.1 fold</u> increase)	( <u>2.2 fold</u> decrease)
*ACTA2	Reference ( <u>4.7 fold</u> increase)	( <u>3.9 fold</u> decrease)
*CTGF	Reference ( <u>8.9 fold</u> increase)	( <u>6.6 fold</u> decrease)
*FN1	Reference ( <u>5.4 fold</u> increase)	( <u>3.0 fold</u> decrease)
*MMP2	Reference ( <u>0.4 fold</u> decrease)	( <u>1.3 fold</u> increase)
*TIMP1	Reference ( <u>3.1 fold</u> increase)	( <u>2.5 fold</u> decrease)
*MMP2/TIMP1	Reference ( <u>0.3 fold</u> decrease)	( <u>1.1 fold</u> increase)
*Type 1 collagen protein	Reference ( <u>3.4 fold</u> increase)	( <u>2.0 fold</u> decrease)
*α-SMA protein	Reference ( <u>2.8 fold</u> increase)	( <u>2.3 fold</u> decrease)
Experiments were performed in (n=5) independent series. Significance was determined by paired student's t test.		
*Values marked with asterix indicate those attaining statistical significance (p<0.05)		