TRANSCRIPTOME ALTERATIONS DURING PERITONEAL DIALYSIS TREATMENT

Parikova A.[1], Hruba P.[2], Krejcik Z.[3], Stranecky V.[4], Lavrikova P.[5], Franekova J.[5], Krediet R.T.[6], Viklicky O.[1]

1 Dept. of Nephrology, Institute for Clinical and Experimental Medicine, Prague, Czech Republic. 2 Transplant Laboratory, Institute for Clinical and Experimental Medicine, Prague, Czech Republic. 3 Institute of Haematology and Blood Transfusion, Prague, Czech Republic. 4 Institute of Inherited Metabolic Disorders, Prague, Czech Republic. 5 Dept. of Laboratory Methods, Institute for Clinical and Experimental Medicine, Prague, Czech Republic. 6 Dept. of Nephrology, Academic Medical Center University of Amsterdam, The Netherlands.

INTRODUCTION and AIM

Long-term peritoneal dialysis (PD) is associated with functional and structural alterations of peritoneal membrane. Inflammation may be the key moment in the development of peritoneal membrane changes. Consequently, fibrosis is the end result of chronic inflammatory reaction.

The CD24 gene encodes a sialoglycoprotein that is expressed on mature granulocytes and B cells, promotes proliferation of B-cells and prevents their terminal differentiation into antibody-forming cells. The glycoprotein CD24 is known to be involved in diverse biological processes. Recently has been shown that CD24 may play a regulatory role in several TGF-beta dependent pathways and may present a target to inhibit the unwanted development of myofibroblast caused extracellular matrix expansion.

The aim of the study was to identify genes potentially involved in peritoneal alterations during PD treatment by comparing transcriptome of peritoneal cells in short- and long-term PD patients.

METHODS

Peritoneal effluent of long-dwell (median 8, range 8-13 hours) of 33 stable PD patients was centrifuged to obtain peritoneal cells. Gene expression profiling of peritoneal cells of 20 patients treated less than 2 years (median 6, 2-21 months) and 13 patients treated more than 2 years (median 43, 24-68 months) was performed using Illumina Human HT-12 v4 Expression BeadChips. Differentially expressed genes were defined as those with a mean expression > 3.5, a fold change > 2 and a p value <0.05. A 4-hour 3,86% glucose peritoneal equilibration test (PET) including temporary drainage after 1 hour for assessment of free water transport was performed in all patients on the day after the long-dwell collection. The relationship between peritoneal transport characteristics and transcriptome was assessed. Based on microarray analysis 15 genes for RT-qPCR validation in cohort of 57 stable patients were chosen.

RESULTS

No differences were present in patient characteristics and transport parameters between short-term and long-term group.

In the long-term group 57 genes were up-regulated. In an enrichment analysis aimed to identify genes and pathways expressed differently between the short- and long-term group, genes involved in the immune system process (p= 1.70E-5), immune response (p=2,0E-3), cell activation (p= 1.3E-3) and leuko- and lymphocyte activation (p=2.6E-3) were found to be substantially up-regulated in the group treated more than 2 years (https://david.ncifcrf.gov/). RT-qPCR validation on the cohort of 57 patients showed higher expression of CD24 (CD24 molecule) (p=0.0001), LY9 (lymphocyte antigen 9) (p=0.004), TNFRSF4 (tumor necrosis factor receptor superfamily, member 4) (p=0.011), CD79A (CD79a molecule, immunoglobulin-associated alpha) (p=0.032), CCR7 (chemokine (C-C motif) receptor 7) (p=0.037), CEACAM1 (carcinoembryonic antigen-related cell adhesion molecule 1) (p=0.032) a IL2RA (interleukin 2 receptor, alpha) (p=0.041) in patients treated more than 2 years. CD24 expression was related to the duration of PD treatment (r=0.32, p<0.001) (Fig 1.). Furhermore, a positive correlation was found between the expression of CD24 and genes for both, Collagen Type I Alpha 1 Chain (COL1A1) and Collagen Type VI Alpha 3 Chain (COL6A3) (Fig.2).

Fig.1. **A positive correlation was present between CD- 24 gene expression and duration of PD treatment (r=0.32, P<0.001).**

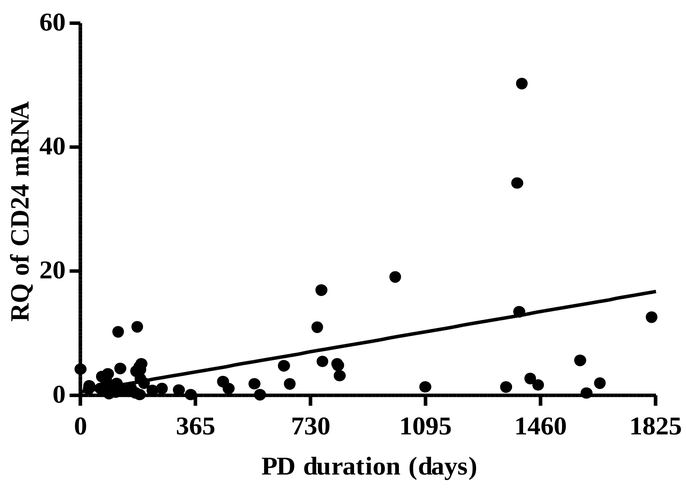
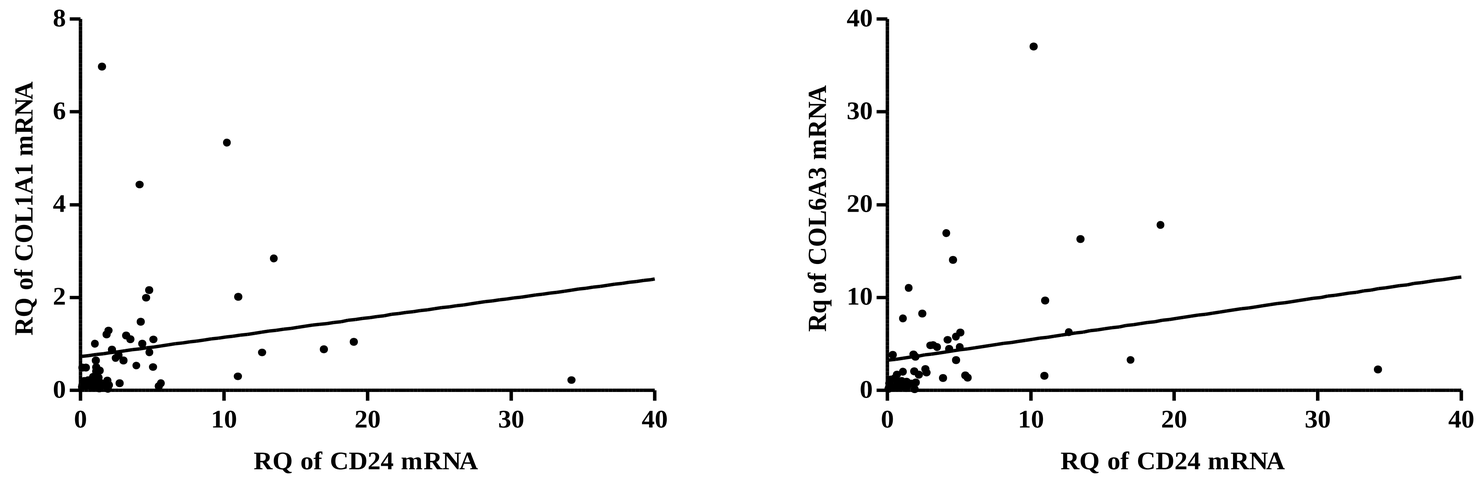


Fig.2**. Relationships between expression of CD24 and Collagen Type I Alpha 1 Chain (COL1A1) (r=0.51, P<0.001,) and between expression of CD24 and Collagen Type VI Alpha 3 Chain (COL6A3)(r=0.65, P<0.0001)**



CONCLUSION

Peritoneal dialysis treatment provokes activation of immune system response, especially B cell related transcript and some cytokines. B cell activity may be involved in long-term peritoneal membrane alterations. Whether this activity is associated with the alteration of peritoneal membrane function is the subject of ongoing research.

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