stable biofilms, positive biofilm cultures and a high incidence of catheter loss. Recently, examination by electron microscopy of catheters of patients who experienced PD peritonitis revealed biofilm formation; however, no biofilm formation was found in PD catheters removed from patients without infection [3]. The risk associated with administering cefazolin continuously (in every PD bag) is that the organisms survive and continue dividing in biofilms. Our current antimicrobial protocols may not permit adequate dosing to penetrate the biofilm and be a reason for recurrent episodes of peritonitis. To evaluate the differences in the antibiotic sensitivity patterns of CNS, minimum inhibitory concentrations (MIC) and minimum biofilm eradication concentration (MBEC) assays were compared in CNS isolates from patients with PD-associated peritonitis in a study [4]. In the PD effluent sample from patients with repeat infection, the rate of first-generation cephalosporin (FGC) or gentamicin or both resistances was higher. MBEC results were higher than those with standard MIC assays. Although no vancomycin resistance was observed with MIC assays, a small number of cases were identified with MBEC assays. There was no resistance when a vancomycin/rifampin 1:1 combination was used. All patients with repeat infections had high degrees of FGC resistance, and infection cycles were terminated when their treatment protocol included vancomycin. In conclusion, we assume that adequate antibiotic levels will be achieved within the catheter-contained biofilm with a single dose of vancomycin of 2 g at the end of the treatment course that will prevent recurrent peritonitis and catheter loss. These results are difficult to compare because patient numbers are small. In our opinion, this observation should be confirmed by other investigators.

Conflict of interest statement. None declared.

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Biocompatibility of peritoneal dialysis solutions determined by genomics of human leucocytes: a cross-over study

Sir,

Peritoneal dialysis (PD) is based on passive movement of water and soluble molecules across the peritoneum. In continuous ambulatory peritoneal dialysis (CAPD), the patient's abdomen is filled with a dialysate fluid introducing an osmotic gradient driven by electrolytes and glucose, or macromolecules such as icodextrin. Biocompatibility of PD fluids is the most important criterion to enable long-term dialysis without introducing clinically significant changes in the functional characteristics of the peritoneum and systemic inflammatory effects [1]. The effects of biocompatibility on clinical outcome include changes in the physiology of cell populations constituting the peritoneal cavity (leucocyte, mesothelial and endothelial cells, and fibroblasts) and the gene expression of peripheral blood mononuclear cells (PBMCs) triggering alterations in cytokine, chemokine and growth factor networks, upregulation of proinflammatory and profibrotic pathways, and induction of carbonyl and oxidative stress [2–4].

Our study objective was to compare the genome-wide gene expression signature of PBMCs of PD patients using glucose-based (GBF) and icodextrin-based peritoneal fluids (IBF) to allow a direct comparison of biocompatibility relevant intracellular processes with respect to the PD fluid used. This pilot study should give us first insights into the alterations in gene expression of leucocytes triggered by different PD fluids and should provide an informative basis for future research.

Therefore, we conducted a random cross-over study in five stable ESRD patients being treated with CAPD between 4 and 18 months (demographic data are provided on our laboratory homepage in Table 1 (http://www.meduniwien.ac.at/nephrogene/data/pd/)). Blood samples (10 ml) were collected immediately after a 4- to 6-h dwell of GBF (Physioneal® 40, Glucose 2.27% w/v, 395 mOsmol/l) and an overnight dwell of IBF (Extraneal®, icodextrin 7.5%, 284 mOsmol/l) [study approved by the local Institutional review board (Ethical Committee # EK-318/06, see http://ohrp.cit.nih.gov/search/asearch.asp)]. Oligoarrays were obtained from the Stanford University Functional Genomics core facility. All microarray experiment protocols can be found on the Stanford University webpage at http://cmgm.stanford.edu/pbrown/protocols/index.html. Stratagene Universal human reference RNA was used as a reference. Raw data files as well as the MIAME checklist are available at our laboratory webpage.

A paired *t*-test ($P < 0.05$) of log-transformed expression values was used to evaluate differences between IBF and GBF treatment. Differentially expressed genes (DEGs) were hierarchically clustered and graphically represented using the MultiExperiment Viewer (MeV) (Pearson correlation, complete linkage) [5]. DEGs were furthermore analysed with respect to their molecular functions, biological processes and interaction partner using gene ontology terms

Table 1. Biological processes separating IBF- and GBF-treated patient groups as derived on the level of PBMC differential gene expression

Biological process	Gene symbols	*P*-value
DEGs up-regulated by IBF treatment		
Immunity and defence	CIITA, UNQ3033, SCGB1C1, CLEC1B, CTSW, CLEC4E, TNFRSF7, CLEC10A	<0.001
Natural killer cell-mediated immunity	UNQ3033, CLEC1B, CTSW	<0.001
T-cell-mediated immunity	CIITA, CTSW, TNFRSF7	0.001
Cell communication	UNQ3033, SCGB1C1, CLEC1B, STAT4, CLEC10A	0.008
Other neuronal activity	SP110, RASGRP2	0.009
Macrophage-mediated immunity	CLEC4E, CLEC10A	0.010
Ligand-mediated signalling	STAT4, UNQ3033, SCGB1C1	0.010
Other immune and defence	SCGB1C1, CLEC4E	0.012
Glucose haemeostasis	STAT4	0.021
Signal transduction	LST1, STAT4, UNQ3033, SCGB1C1, RASGRP2, CLEC1B, TNFRSF7, CLEC10A	0.022
MHC I-mediated immunity	CTSW	0.023
Cytokine- and chemokine-mediated signalling pathways	STAT4, TNFRSF7	0.029
MHC II-mediated immunity	CIITA	0.036
Glycolysis	HK3	0.048
DEGs up-regulated by GBF treatment		
Ectoderm development	CELSR2, FOXA2, HLF, KRT80, TNFRSF21, COBLL1, NTN4, CRABP1, NLGN2, FGFR3, THSD3	<0.001
Signal transduction	FRAS1, DOC1, CELSR2, MGP, RND3,CGA, GNG4, RAB23, FOXA2, AXL, CAP2, CDH13, INPP5F, TACSTD2, TNFRST21, MFAP4, DIRAS1, CRABP1, NLGN2, SFRP2, THSD3, GPR161, FGFR3, NTN4	<0.001
Neurogenesis	CELSR2, FOXA2, HLF, TNFRSF21, COBLL1, NTN4, NLGN2, FGFR3, THSD3	<0.001
Cell communication	FRAS1, CELSR2, MGP, CGA, FOXA2, CAP2, CDH13, MFAP4, NTN4, CRABP1, NLGN2, SFRP2, THSD3	<0.001
Oncogenesis	DOC1, AXL, CDH13, MAGEA12, NTN4, MLF1, FGFR3, THSD3	<0.001
Developmental processes	DOC1, CELSR2, MGP, FOXA2, HLF, KRT80, TTK, MAGEA12, EFHD1, TNFRSF21, COBLL1, NTN4, CRABP1, NLGN2, FGFR3, THSD3	0.001
Other oncogenesis	MAGEA12, FGFR3, THSD3	0.002
Cell proliferation and differentiation	DOC1, FOXA2, AXL, TACSTD2, C9orf58, UHRF1, NTN4, MLF1, GINS2, FGFR3	0.002
Cell structure	DLG5, CELSR2, COL7A1, FOXA2, KRT80, PHLDB1, TJP1	0.006
Cell structure and motility	DLG5, CELSR2, COL7A1, FOXA2, KRT80, PHLDB1, TJP1, RND3, CAP2	0.011
DNA replication	DOC1, CDC2, GINS2	0.014
Homeostasis	CGA, HEPH, FSTL1	0.025
Stress response	MOCOS, C9orf58, GPX3	0.026
Other cell cycle process	UHRF1	0.028
DNA metabolism	DOC1, CDC2, DNTT, GINS2	0.028
Other receptor-mediated signalling pathway	FOXA2, TACSTD2, TNFRSF21	0.030
Proteolysis	DOC1, DGC, C1R, MMP15, CAP2, SERPINA5, TIMP3	0.033
Cell surface receptor-mediated signal transduction	CELSR2, RND3, GNG4, FOXA2, AXL, TACSTD2, TNFRSF21, FGFR3, THSD3, GPR161	0.035
Other steroid metabolism	SC5DL	0.041
Cell cycle	DOC1, CDC2, FOXA2, TTK, C9orf58, UHRF1, GINS2	0.042
Sex determination	TTK	0.044
Cell cycle control	DOC1, CDC2, FOXA2, C9orf58	0.045
Neurotransmitter release	STXBP1, EHD2	0.046
Cell adhesion	CELSR2, COL7A1, CDH13, MFAP4, NLGN2	0.049

Categories are ranked by the *P*-value (comparison of expected number of genes and observed number of genes in each biological process) indicating the relevance of a particular process.

(GO-Terms), PANTHER (Protein ANalysis THrough Evolutionary Relationships) ontologies and Online Predicted Human Interaction Database (OPHID).

A total of 124 genes (fold change over two, 34 up-regulated and 90 down-regulated in the IBF group) were identified as being significantly differentially expressed in PBMCs comparing patients under IBF and GBF usage (Figure 1 online on our homepage).

A total of 27 up-regulated genes assigned to IBF treatment and 81 up-regulated genes associated with GBF treatment could be classified according to PANTHER ontologies (Table 1). A number of the genes up-regulated in the course of IBF usage were found to be involved in immune response and inflammatory processes. Genes up-regulated by GBF usage in contrast are found to be assigned to development and signal transduction processes.

Our study provides full genome differential gene expression profiles of PBMCs after peritoneal dialysis on a genome-wide scale comparing GBF and IBF peritoneal dialysis fluids confirming the differential involvement of inflammation. A limitation of our study is the small sample

size of five CAPD patients. Therefore, we used a random cross-over design and computed a paired *t*-test.

These pilot data suggest reduced inflammation and consequently an improved biocompatibility of GBF peritoneal fluids compared with IBF fluids. Certainly, further evaluation in larger studies is needed.

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Crescentic glomerulonephritis in a patient with advanced lung cancer during erlotinib therapy

Sir,

Erlotinib (Tarceva®), an epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor, has been shown to improve survival of previously treated non-small cell lung cancer (NSCLC) [1]. The common adverse effects of this agent include diarrhoea and anorexia [1], which may cause severe dehydration and renal failure, although their incidence has been low [2]. Here, we report a case of pauci-immune crescentic glomerulonephritis (CrGN) and acute renal failure in a patient with advanced NSCLC treated with erlotinib.

Table 1. Result of blood test on admission

White blood count	11.6×10^9/L
Haemoglobin	8.4 g/dL (84 g/L)
Platelets	156×10^9/L
Blood urea nitrogen	37.8 mmol/L
Serum creatinine	1,228 μmol/L
Serum protein, total	61 g/L
Serum albumin	21 g/L
Glycosylated haemoglobin A_{1c}	5.4%
C-reactive protein	131 mg/L
Immunoglobulin (Ig)-G	12.8 g/L
IgA	8.7 g/L
IgM	0.5 g/L
C3	1.0 g/L
C4	0.4 g/L
Antinuclear antibody (ANA)	<1:40
Cryoglobulin	Negative
MPO-ANCA	Negative
PR3-ANCA	Negative
Anti-GBM antibody	Negative
pH	7.18
$PaCO_2$	30.8 mmHg
Bicarbonate	11.3 mmol/L

Case

In May 2009, a 72-year-old man with advanced NSCLC was admitted to our department because of acute renal failure. In July 2007, he underwent a pulmonary lobectomy for NSCLC. Because of intrapulmonary recurrence, he received multiple chemotherapies between November 2007 and December 2008, including carboplatin, docetaxel, paclitaxel, irinotecan and gemcitabine. In February 2009, erlotinib (150 mg daily) was started due to the progression of intrapulmonary lesions.

When erlotinib was started, serum creatinine (sCr) was 88 μmol/L and urinalysis showed only slight proteinuria without haematuria. During erlotinib treatment, diarrhoea and acneiform eruptions were transiently observed. Six weeks later, microhaematuria and 2+ proteinuria were detected. Over 1 month, proteinuria progressed to 3+ and sCr rose to 141 μmol/L.

On admission, he presented with anorexia, diarrhoea and severe dehydration. Although he was almost anuric, urine test revealed 3+ proteinuria and microscopic haematuria. Marked renal dysfunction and metabolic acidosis were noted (Table 1). The onset of microhaematuria and progressive renal failure and proteinuria suggested the possibility of rapidly progressive glomerulonephritis. However, he was critically ill and a renal biopsy was considered dangerous. In addition, acute tubular necrosis following pre-renal azotaemia was also probable. Thus, erlotinib was discontinued and supportive therapy with haemodialysis was started. Despite adequate fluid replacement, anuria persisted, and 1 month later, he died of pneumonia. By an autopsy, pauci-immune CrGN was diagnosed (Figure 1). No vasculitic lesion was found in other organs.

Discussion

Acute renal failure with nephritic urine sediment is an atypical manifestation during erlotinib therapy. As for