Functional Effector Memory T Cells Enrich the Peritoneal Cavity of Patients Treated with Peritoneal Dialysis

Gareth W. Roberts,* Duncan Baird,† Kathleen Gallagher,‡ Rhiannon E. Jones,† Christopher J. Pepper,§ John D Williams,* and Nicholas Topley‡

*Institute of Nephrology and Departments of †Pathology, §Hematology, and ‡Infection, Immunity, and Biochemistry, School of Medicine, Cardiff University, Heath Park, Cardiff, Wales, United Kingdom

Despite advances in treatment, peritoneal infection remains one of the main causes of technique failure in peritoneal dialysis (PD) patients. There is a strong association between peritonitis (frequency and severity) and the loss of membrane function.1–3 In view of this, there has been considerable interest in understanding the basic processes that regulate peritoneal early responses to infection. Most of these studies have focused on the contribution of peritoneal macrophages or mesothelial cells to these processes.3–9 Despite representing up to 25% of the resident peritoneal leukocyte population and forming a significant proportion of the leukocyte population present in resolving peritonitis, the function and phenotype of human peritoneal T cells is poorly defined.10–12 Consequently we understand very little about the adaptive arm of the peritoneal immune response.

Recent developments in the field of immunology have greatly enhanced our understanding of T cell phenotype, activation status, differentiation, and tissue homing capacity. Many studies have highlighted the important role of T cells in providing long-term immunological memory.13–19 According to current definitions, memory T cells are distinguished from naive T cells (which are yet to encounter their cognate antigen) by the expression of CD45RO (rather than CD45RA).20 Within the memory T cell population, distinct functional subsets have been characterized based on the expression of lymph node homing signal CCR7.13–19 These subsets differ in both their tissue homing capability and in their response to antigenic stimulation.15,17,18 Central memory (T_{CM}) cells (CD45RO/CCR7+) are thought to migrate through lymph tissue, whereas effector memory (T_{EM}) cells (CD45RO /CCR7−), which lack lymph node homing signals, are thought to reside primarily in peripheral tissue.16,17 The T_{EM} subset rapidly produces effector cytokines such as IFN-γ and IL-4 and are thought to form a first line of defense against invading pathogens.

ABSTRACT

The frequency and severity of episodes of peritonitis adversely affect the structure and function of the peritoneal membrane in patients treated with peritoneal dialysis (PD), but the underlying mechanisms are not well understood. Alterations in the phenotype and function of resident peritoneal cells may contribute. Because effector memory T cells play a pivotal role in maintaining peripheral tissue immunity, we hypothesized that these cells may initiate or perpetuate the peritoneal inflammatory response. Here, we characterized the phenotype and effector function of peritoneal memory T cells. We found that functional effector memory T cells capable of mounting long-term recall responses enrich the peritoneal cavity of PD patients. Peritoneal T cells were able to mount a Th1-polarized response to recall antigens, and these responses were greater in peritoneal T cells compared with T cells in the peripheral blood. We also observed that the peritoneal T cells had altered telomeres; some cells had ultrashort telomeres, suggesting a highly differentiated local population. In summary, we describe a resident population of memory T cells in the peritoneum of PD patients and speculate that these cells form part of the first line of defense against invading pathogens.

Received October 30, 2008. Accepted June 3, 2009.
Published online ahead of print. Publication date available at www.jasn.org.
Correspondence: Dr. Gareth W. Roberts, Institute of Nephrology, School of Medicine, Cardiff University, Heath Park, Cardiff, CF144XN, United Kingdom. Phone: +44-29020-748446; Fax: +44-2920-748470; E-mail: Robertsgw1@cf.ac.uk
Copyright © 2009 by the American Society of Nephrology.


population, telomere lengths decrease from naïve through T<sub>CM</sub> through T<sub>EM</sub> cells, suggesting that the latter have undergone more cell divisions and are a more highly differentiated population.\(^{17,20}\)

Most of our current understanding of T cell memory is derived from murine data or from experiments performed on peripheral blood T cells. Because of the logistical difficulties involved in sample collection, there are very little data available regarding the phenotype and function of memory T cells in human peripheral tissue. The aim of our study was to characterize the phenotype, replicative history, and effector function of the peritoneal memory T cell population during steady-state (non-infected) PD.

Our results demonstrate that as compared with peripheral blood, the peritoneal cavity is enriched in cells displaying a T<sub>EM</sub> phenotype, with very few intra-peritoneal naïve T cells (Figure 1, A and B) (we found no significant difference in the proportion of T<sub>CM</sub> cells between blood and peritoneum). Subgroup analysis shows that neither time on PD nor recurrent peritonitis have a significant effect on the proportion of T<sub>EM</sub> within the peritoneal cavity, suggesting that T<sub>EM</sub> enrichment is a characteristic of the quiescent peritoneal cavity (Supplementary Figure 1). Further phenotypic analysis demonstrated increased expression of the proinflammatory chemokine receptor CCR5 on the T<sub>EM</sub> subset, but only low-level expression of the lymph node homing signal CD62L (Figure 1C).

To determine whether peritoneal memory cells retain effector function ex vivo, cells were stimulated for a short period with phorbol 12-myristate 13-acetate/ionomycin. As predicted from murine studies, the predominant early Th1 (IFN-γ-mediated) response to stimulation came from the T<sub>EM</sub> subset (Figure 2A). To examine the antigen specificity of this response, paired samples of peripheral blood and peritoneal T cells were exposed to the standardized recall antigens, including purified protein derivative from <i>Mycobacterium tuberculosis</i>, hemagglutinin antigen (HA) derived from influenza virus, and tetanus toxoid (TT). Our results demonstrate that peritoneal T cells are able to mount a Th1 polarized response to these recall antigens; moreover, these responses are increased in peritoneal T cells as compared with peripheral blood T cells (Figure 2B).

Because memory T cells are considered a highly differentiated population,\(^{17,20}\) we next examined the replicative history of the peritoneal T cells. Telomeres progressively shorten as a function of cell division, thus telomere length is a robust indicator of the replicative history of lymphocytes in vivo.\(^{20,21}\) To date, the two most widely applied methods for studying telomere length are terminal restriction fragment analysis and quantitative fluorescence in situ hybridization.\(^{21,22}\) Terminal restriction fragment analysis suffers from a low overall sensitivity and requires large cell numbers, whereas quantitative fluorescence in situ hybridization requires metaphase chro-
mosomes, limiting analysis to cells that are actively proliferating. In view of these restrictions, such methods are of limited value in the analysis of peritoneal T cells (in which cell numbers and proliferative capacity are low). Furthermore, these hybridization-based technologies become increasingly less efficient as telomere length diminishes and fail to detect the very short telomeres capable of triggering replicative senescence.

The development of single telomere length analysis (STELA) has emerged, which overcomes many of these limitations and allows accurate measurement of the full spectrum of telomere lengths from individual chromosomes. The robust nature of STELA allows detection of very short telomeres even when such telomeres are rare or present in a background of longer telomeres. This technology uniquely allows the accurate assessment of the mean telomere length (±SD) within a cellular population and can also identify subpopulations with longer or shorter telomeres. Using STELA, we were able to compare the telomere lengths of purified populations of peritoneal and peripheral blood T cells derived from the same patient. Our results show that as compared with peripheral blood from the same individual, peritoneal T cells have significantly shortened telomeres (mean 1 to 1.5 kb shorter, representing 15 to 20 population doublings, \( P < 0.05 \)) with some telomere lengths approaching the senescent range (1–2kb) (Figure 3). Because telomere lengths progressively shorten from naïve through TCM to TEM, these data correlate with our phenotypic analysis, confirming that the peritoneal cavity is enriched in highly differentiated TEM cells. It is important to point out here that in addition to the mean telomere lengths being significantly shorter in the peritoneal cavity T cells, a population of T cells with very short telomeres not represented in the paired peripheral blood samples was evident. This provides compelling evidence for a distinct resident population of T cells in the peritoneal cavity.

The above results collectively demonstrate that the peritoneal cavity is enriched in functional resident TEM cells. This observation is in agreement with the current paradigm of T cell memory that predicts that TEM cells reside primarily in peripheral tissues. The peritoneal homing of TEM cells is facilitated by the expression of proinflammatory chemokine receptors such as CCR5, the ligands for which (MIP-1 and RANTES) have been detected in the peritoneal effluent of PD patients. Our functional data support this “selective recruitment” hypothesis, because memory T cells formed in response to prior vaccination are present at an increased frequency within the peritoneal cavity. This peripheral homing of TEM cells may have evolved as a protective mechanism, ensuring that vulnerable peripheral tissues contain an abundance of “primed” effector cells.

Further insight into the dynamics of memory T cell trafficking was obtained from the analysis of T cell telomere lengths. Although the term “resident peritoneal cell” is often used to describe cells obtained in PD effluent, this term is misleading because cells recruited from the blood into the cavity then drained off minutes later are still classed as resident peritoneal cells.

### Table 1. Patient demographics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)</th>
<th>Peritonitis Episodes</th>
<th>Diabetes Mellitus (yes/no)</th>
<th>Glucose Exposure (g/d)</th>
<th>PD Vintage (mo)</th>
<th>Icodextrin (yes/no)</th>
<th>Etiology of End-Stage Renal Failure</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1</td>
<td>56</td>
<td>0</td>
<td>No</td>
<td>108</td>
<td>3</td>
<td>No</td>
<td>Hypertensive nephropathy</td>
</tr>
<tr>
<td>A2</td>
<td>58</td>
<td>0</td>
<td>No</td>
<td>108</td>
<td>4</td>
<td>No</td>
<td>Hypertensive nephropathy</td>
</tr>
<tr>
<td>A3</td>
<td>66</td>
<td>0</td>
<td>Yes</td>
<td>99.8</td>
<td>17</td>
<td>Yes</td>
<td>Systemic sclerosis</td>
</tr>
<tr>
<td>A4</td>
<td>66</td>
<td>0</td>
<td>Yes</td>
<td>127</td>
<td>37</td>
<td>No</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>A5</td>
<td>42</td>
<td>0</td>
<td>No</td>
<td>154.2</td>
<td>5</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>A6</td>
<td>59</td>
<td>0</td>
<td>No</td>
<td>127</td>
<td>86</td>
<td>Yes</td>
<td>Chronic pyelonephritis</td>
</tr>
<tr>
<td>A7</td>
<td>75</td>
<td>0</td>
<td>No</td>
<td>81.6</td>
<td>35</td>
<td>Yes</td>
<td>Reflux nephropathy</td>
</tr>
<tr>
<td>A8</td>
<td>66</td>
<td>0</td>
<td>No</td>
<td>108</td>
<td>13</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>B1</td>
<td>60</td>
<td>1</td>
<td>No</td>
<td>81.6</td>
<td>22</td>
<td>Yes</td>
<td>Unknown</td>
</tr>
<tr>
<td>B2</td>
<td>65</td>
<td>1</td>
<td>No</td>
<td>81.6</td>
<td>11</td>
<td>No</td>
<td>Reflux nephropathy</td>
</tr>
<tr>
<td>B3</td>
<td>62</td>
<td>1</td>
<td>No</td>
<td>154</td>
<td>4</td>
<td>No</td>
<td>Renovascular disease</td>
</tr>
<tr>
<td>B4</td>
<td>64</td>
<td>2</td>
<td>No</td>
<td>127</td>
<td>48</td>
<td>No</td>
<td>Unknown</td>
</tr>
<tr>
<td>B5</td>
<td>56</td>
<td>1</td>
<td>No</td>
<td>108</td>
<td>4</td>
<td>No</td>
<td>IgA GN</td>
</tr>
<tr>
<td>B6</td>
<td>79</td>
<td>2</td>
<td>Yes</td>
<td>81.6</td>
<td>15</td>
<td>Yes</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>B7</td>
<td>70</td>
<td>1</td>
<td>Yes</td>
<td>99.8</td>
<td>16</td>
<td>Yes</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>C1</td>
<td>66</td>
<td>3</td>
<td>No</td>
<td>113.6</td>
<td>30</td>
<td>Yes</td>
<td>Hypertensive nephropathy</td>
</tr>
<tr>
<td>C2</td>
<td>74</td>
<td>5</td>
<td>No</td>
<td>127</td>
<td>72</td>
<td>Yes</td>
<td>Hypertensive nephropathy</td>
</tr>
<tr>
<td>C3</td>
<td>71</td>
<td>5</td>
<td>Yes</td>
<td>81.6</td>
<td>24</td>
<td>Yes</td>
<td>Diabetic nephropathy</td>
</tr>
<tr>
<td>C4</td>
<td>57</td>
<td>5</td>
<td>Yes</td>
<td>93</td>
<td>89</td>
<td>Yes</td>
<td>Obstructive nephropathy</td>
</tr>
<tr>
<td>C5</td>
<td>64</td>
<td>6</td>
<td>No</td>
<td>163.4</td>
<td>60</td>
<td>No</td>
<td>Renovascular disease</td>
</tr>
<tr>
<td>C6</td>
<td>75</td>
<td>4</td>
<td>No</td>
<td>127</td>
<td>34</td>
<td>Yes</td>
<td>IgA nephropathy</td>
</tr>
</tbody>
</table>

### Table 2. Patients represented in each figure

<table>
<thead>
<tr>
<th>Figure</th>
<th>Patient</th>
</tr>
</thead>
<tbody>
<tr>
<td>1A</td>
<td>A2</td>
</tr>
<tr>
<td>1B</td>
<td>A1 to A8, B1 to B7,C1 to C6</td>
</tr>
<tr>
<td>1C</td>
<td>A2 to A4, A6, B3, B5, C3 to C6</td>
</tr>
<tr>
<td>2A</td>
<td>A5</td>
</tr>
<tr>
<td>2B</td>
<td>A5, A7, B2, C2</td>
</tr>
<tr>
<td>3A</td>
<td>B1</td>
</tr>
<tr>
<td>3B</td>
<td>C5, B1, A1</td>
</tr>
</tbody>
</table>

Table 1. Patient demographics

Table 2. Patients represented in each figure
It could be argued that resident peritoneal T cells do not in fact exist, and that cells obtained in PD effluent are cells that are continually trafficking between the peripheral circulation, the peritoneal cavity, and peritoneal lymphatics. Until now, it has been very difficult to disprove this argument because cell-labeling studies are logistically difficult to perform in humans. Our telomere data allow us to argue that there is in fact a truly resident peritoneal memory T cell population that resides and divides locally within the peritoneum. The evidence supporting this comes from the finding that T cells with very short telomere lengths were found only in the peritoneum but not in the peripheral circulation. Had these cells been recruited from the blood, then we would have seen a corresponding telomere band in the peripheral blood, but this is not in fact the case. Indeed, more detailed analysis of the STELA data suggests that there are two distinct T cell populations. One population has similar telomere lengths to peripheral blood T cells and is likely to represent recirculating TCM and naïve T cells, the other population has shorter telomere lengths and are likely to represent truly resident TEM cells. We speculate that these resident cells avoid being drained off during PD by adhering to the peritoneal membrane or trafficking to peritoneal milky spots, thus enabling long-lived memory responses. Some of these cells have ultrashort telomere lengths and may be approaching cellular senescence. Because senescent cells have a more catabolic, proinflammatory phenotype, the presence of even small numbers of such cells in the peritoneal cavity may contribute to the local proinflammatory milieu.

Figure 2. (A) Peritoneal leukocytes were stimulated with phorbol 12-myristate 13-acetate (500 ng/ml)/ionomycin (50 ng/ml) for 2 h. Cells were labeled with fluorescently conjugated monoclonal antibody directed against CD4/CD45RO/CCR7. Cells were subsequently fixed and permeabilized then stained with anti-IFN-γ. A combined gate was set on peritoneal T cells on the basis of CD4 expression and their FSC:SSC profiles. Further gates were plotted on the CD4 memory subsets (naïve/T<sub>CM</sub>/T<sub>EM</sub>). Results show the percentage of IFN-γ<sup>+</sup> cells within these memory subsets. Results are a representative example of experiments performed on four separate donors. (B) Paired samples of PBMCs and peritoneal leukocytes were collected from PD patients. ELISPOT plates were coated with 50 μl anti-IFN-γ antibody in sterile PBS (10 μg/ml) and incubated at 4°C for 180 min. Peritoneal leukocytes and PBMCs were plated out at 2 × 10<sup>5</sup> cells/well. Cells were incubated at 37°C for 16 h in the presence of purified protein derivative (PPD) (10 μg/ml), TT (5 μg/ml), or HA (5 μg/ml). The ELISPOT assay was developed according to the manufacturer’s instructions. Results show mean ± SEM of triplicate observations. See Tables 1 and 2 for patient demographics.

Figure 3. Samples of peritoneal leukocytes and PBMCs were obtained from PD patients. Further PBMC samples were obtained from healthy age-matched volunteers. Flow cytometry and cell sorting (FACS) were used to isolate highly purified (>98%) T cell populations. T cell telomere lengths were measured by STELA. (A) Representative example of STELA data from a PD patient. (B) Mean XpYp telomere lengths. The unpaired t test was used to compare means. See Tables 1 and 2 for patient demographics.
Of note, to standardize our telomere data we extended our study to include healthy age and sex-matched controls. We observed that (when compared with controls) PD patients had considerably shortened peripheral blood T cell telomeres (Figure 3). This telomere shortening may be secondary to the increased inflammatory burden that these patients have faced during the development of end-stage renal failure. This may have prognostic implications for PD patients, because previous population-based studies have shown that individuals with shortened peripheral blood telomeres have a 3-fold increase in cardiovascular mortality and an 8-fold higher mortality from infectious diseases.

In conclusion, we have shown for the first time that the peritoneal cavity hosts a population of functional resident TEM. Because these cells mount an immediate Th1 response, we speculate that they are important arbiters of the early immune response, aiding macrophage activation via the production of IFN-γ. Future work will focus on whether these cells can be primed to recognize components of the organisms that commonly cause peritonitis. Such work might allow the development of effective intraperitoneal vaccination conferring protection against recurrent peritonitis.

**CONCISE METHODS**

**Patient Selection**

Ethical approval was obtained from the South East Wales Ethics Committee (04WSE04/27). Consenting patients were recruited from the University Hospital of Wales PD Unit. Unless specifically stated, all patients were receiving a standard PD therapy of 4 exchanges per day. Before flow cytometry, cells were incubated with blocking buffer (25% normal rabbit serum, Dako-Cytomation, Ely, United Kingdom), 25% human AB serum (HD Supplies, Buckinghamshire, United Kingdom), and 50% PBS to prevent nonspecific binding.

**Leukocyte Isolation from PD Fluid**

PD effluent (mean drained volume 2187 ml, range 1585 to 3120 ml) was collected from patients after an overnight 8- to 10-h dwell. Samples were collected on ice to reduce adhesion of cells to the PD bag. After collection, the PD effluent was aliquoted into 50-ml tubes (Sarstedt AG, Nümbrecht, Germany) and centrifugated at 3000 rpm (2133 × g) at 4°C for 35 min (Minifuge T, Heraeus/Kendro Laboratory Products, Stevenage, United Kingdom). The cell pellets were resuspended in 50 ml PBS (Sigma-Aldrich, Kent, United Kingdom). The cell suspension was centrifuged at 4°C for 20 min at 3000 rpm (2133 × g). The supernatant was discarded, and the cell pellet was resuspended in lysis buffer and allowed to stand for 5 min at room temperature. The suspension was recentrifuged at 3000 rpm (2133 × g) at 4°C for 20 min and the pellet resuspended in PBS at 1 × 10⁶ cells/ml.

**Leukocyte Isolation from Peripheral Blood**

Venous blood was collected from consenting healthy laboratory volunteers/patients in an EDTA vacutainer tube (Becton Dickinson Ltd., Oxfordshire, United Kingdom) and centrifuged at 1300 rpm (400 × g) for 12 min. (Minifuge T, Heraeus/Kendro Laboratory Products, Stevenage, United Kingdom). After discarding the plasma, the remaining blood cells were resuspended in an equal volume of PBS. The cell suspension was layered onto Ficol-Paque (Amersham Biosciences Ltd., Bucks, United Kingdom) and centrifuged at 1300 rpm (400 × g) at 10°C for 35 min. The mononuclear cell layer (formed at the interface) was aspirated into a 50-ml tube and suspended in 10 ml of PBS at 10°C. The cell suspension was centrifuged at 10°C for 10 min at 1300 rpm (400 × g). The supernatant was discarded and the cell pellet resuspended in lysis buffer and allowed to stand for 5 min at room temperature. The suspension was recentrifuged at 1300 rpm (400 × g) at 10°C for 10 min and the pellet was washed 3 times before suspension in PBS at 1 × 10⁶ cells/ml.

**Antibodies and Flow Cytometry**

Before flow cytometry, cells were incubated with blocking buffer (25% normal rabbit serum, Dako-Cytomation, Ely, United Kingdom), 25% human AB serum (HD Supplies, Buckinghamshire, United Kingdom), and 50% PBS to prevent nonspecific binding.

Cells were labeled with FITC, phycoerythrin, phycoerythrin-Cy5.5, allophycocyanin-conjugated monoclonal antibodies directed against CD3, CD45RO, CD62L, CCR5 (BD Pharmingen, Oxford, United Kingdom), CCR7 (R&D Systems, Oxfordshire, United Kingdom), CD4 (Caltag, San Francisco, CA), and mouse IgG1 isotype controls (Bioscience, San Diego, CA). Flow cytometry was performed using an EPICS XL flow cytometer (Beckman Coulter, Fullerton, CA). Events were acquired and analyzed with CellQuest software (BD Biosciences, San Jose, CA).

**Telomere Length Analysis**

DNA was extracted using standard proteinase K, RNase A, and phenol/chloroform protocols. DNA was solubilized by digestion with EcoRI and quantified in triplicate with Hoechst 33258 fluorometry (BioRad, Hercules, CA). The genomic DNA was diluted to 10 ng/μl in 10 mM Tris- HCl, pH 7.5. Ten nanograms of DNA was fur-
ther diluted to 250 pg/μl in a volume of 40 μ
containing 1 μM Telor2ette linker and 1 mM
Tris-HCl, pH 7.5. Multiple PCRs (typically six
reactions per sample) were carried out for each
test DNA in 10-μl volumes containing 250 pg of
diluted DNA; 0.5 μM of the telomere-adjacent
and Telta1 primers; 75 mM Tris-HCl, pH 8.8;
20 mM ammonium sulfate; 0.01% Tween-20;
and 10:1 mixture of Taq (ABGene, Surrey, United
Kingdom) and Pwo polymerase (Roche, Hert-
fordshire, United Kingdom). The reactions were
cycled with an MJ PTC-225 thermocycler
fordshire, United Kingdom). The reactions
were cycled with an MJ PTC-225 thermocycler
DNA fragments were calculated using the Phoretix 1D quantifier (Non-
linear Dynamics, Newcastle, United Kingdom). The molecular weights of the DNA fragments were cal-
culated using the Phoretix 1D quantifier (Non-
linear Dynamics, Newcastle, United Kingdom).

Statistical Analysis
Statistical analysis was carried out using the SPSS statistical program (SPSS for Mac, Rel. 10.0.0, 1999, SPSS, Inc., Chicago, IL). A P value of less than 0.05 was considered statistically significant.

ACKNOWLEDGMENTS
This research was supported by the Welsh As-
sembly Government [Welsh Office of Re-
search and Development (WORD)].

DISCLOSURES
None.

REFERENCES
1. Davies SJ, Bryan J, Phillips L, Russell GI: Lon-
3. Williams JD, Craig KJ, Topley N, Von Ruhland C, Fallon M, Newman GR, Mackenzie RK, Wil-
lians GT: Morphological changes in the per-
toneal membrane of patients with renal dis-
4. Topley N, Mackenzie RK, Williams JD: Macro-
phages and mesothelial cells in bacterial peri-
5. Topley N, Mackenzie R, Jorres A, Coles GA, Davies M, Williams JD: Cytokine networks in continuous ambulatory peritoneal dialysis: Interactions of resident cells during inflam-
6. McGregor SJ, Topley N, Jorres A, Speeken-
brink AB, Gordon A, Ahal GIM, Junor BJ, Briggs JD, Brock JH: Longitudinal evaluation of peritoneal macrophage function and ac-
7. Mackenzie RK, Coles GA, Williams JD: The response of human peritoneal macrophages to stimulation with bacteria isolated from episodes of continuous ambulatory perito-
8. Betjes MG, Tuk CW, Struijk DG, Krediet RT, Arisz L, Beelen RH: Antigen-presenting ca-
10. Fricke H, Hartmann J, Sitter T, Fricke J, Rieber P, Schiffl H: Continuous ambulatory peritoneal dialysis: Maturity, cytokine secretion and ICAM-1 expres-
12. Braunr A, Hylander B, Jacobson SH, Mosh-
feigh A, Lundahl, J: Increased expression of
CD25 and HLA-DR on lymphocytes recruited into the peritoneal cavity in non-infected CAPD patients. Inflammation 25: 399–404, 2001
14. Masopust D, Veys V, Marzo AL, Lefrancosi L: Preferential localization of effector mem-
16. Lanzavecchia A, Sallusto F: Understanding the generation and function of memory T cell sub-
17. Sallusto F, Lenig D, Forster R, Lipp M, Lanza-
vecchia A: Two subsets of memory T lympho-
cytes with distinct homing potentials and ef-
18. Sallusto F, Lanzavecchia A: Exploring path-
19. Sallusto F, Langenkamp A, Geginat J, Lan-
20. Akbar AN, Beverley PC, Salmon M: Will telo-
mere erosion lead to a loss of T-cell mem-
23. Baird DM, Rowson J, Wynford-Thomas D, Kipling D: Extensive allelic variation and ul-
24. Kato S, Yuzawa Y, Tsuboi N, Maruyama S, Morita Y, Matsuuchi T, Matsu S: Endotoxin-
induced chemokine expression in murine peri-
25. Li FK, Davenport A, Robson RL, Loetscher P, Rothlein R, Williams JD, Topley N: Leu-
kocyte migration across human peritoneal mesothelial cells is dependent on directed chemokine secretion and ICAM-1 expres-
den Bom J, Zarei M: Omental milky spots in peritoneal pathophysiology (spots before your eyes), Perit Dial Int 25: 30–32, 2005
29. Cawthon RM, Smith KR, O'Brien E, Sivatch-
sion and a definition of the critical telo-