Endometriosis: an inflammatory disease with a Th2 immune response component

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BACKGROUND: Efforts have been made to correctly characterize the role of the immune response in endometriosis. The objective of this study was to analyse the interaction between Th1 and Th2 immune response patterns and endometriosis by evaluating a panel of cytokines. METHODS: Between January 2004 and November 2005, 98 patients, classified into two groups according to the histologically confirmed presence (Group A) or absence of endometriosis (Group B), were evaluated. Interleukins (IL) 2, 4 and 10, tumour necrosis factor-alpha and interferon-gamma (IFN-gamma) were measured by flow cytometry in the peripheral blood and peritoneal fluid of all patients. RESULTS: IFN-gamma and IL-10 levels were significantly higher in the peritoneal fluid of patients with endometriosis compared to those without endometriosis (P<0.05). There was a significant alteration in the IL-4/IFN-gamma (P<0.001), IL-4/IL-2 (P=0.006), IL-10/IFN-gamma (P<0.001) and the IL-10/IL-2 ratios (P<0.001) in the peritoneal fluid of patients with endometriosis, with a predominance of IL-4 and IL-10, reflecting a shift towards Th2 immune response despite the increase in IFN-gamma concentrations. CONCLUSIONS: Endometriosis is an inflammatory disease involving a possible shift towards Th2 immune response component, as demonstrated by the relative increase in cytokines characteristic of this pattern of immune response.

Key words: cytokine/endometriosis/interleukin/interferon/tumor necrosis factor

Introduction

The importance of endometriosis is reflected in the growing number of studies published on the subject over the past 20 years in which particular emphasis has been given to investigating the pathogenesis of the disease. The most common hypothesis is the theory of retrograde menstruation, which consists of the implantation of endometrial cells originating from the reflux of menstrual blood through the Fallopian tubes to the abdominal cavity (Sampson, 1927). This implantation is believed to occur as a result of the influence of a favourable hormonal environment and immunological factors that result in failure to eliminate these cells from this inappropriate site (Missmer and Cramer, 2003).

In the mid-1980s, studies in mice demonstrated that effector lymphocytes could be divided into two types based on the pattern of cytokine secretion produced by these cells following stimulation. Th1 cells are secretors of cytokines denominated pro-inflammatory, principally interleukin (IL)-2 and interferon-gamma (IFN-gamma), whereas Th2 cells produce cytokines referred to as antiinflammatory, principally IL-4 and IL-10 (Mosmann et al., 1986). This concept was applied to the human immune system (Romagnani, 1991), creating the possibility of advancing knowledge of the pathogenesis and, consequently, the diagnosis and treatment of a series of diseases (Alviggi et al., 2006; Meiler et al., 2006; Xia et al., 2006).

In addition to the production of IL-2 and IFN-gamma, the Th1 immune response pattern triggers an immune cell process that involves the participation of natural killer cells, macrophages, CD8+ T-lymphocytes and secretion of other cytokines such as tumour necrosis factor-alpha (TNF-alpha), vascular endothelial growth factor and enzymes such as matrix metalloproteinase. On the other hand, Th2 response is characterized by its activation of B-lymphocytes, triggering a process that involves humoral immunity and includes the production of immunoglobulins and activation of eosinophiles, basophiles and tissue mastocytes. The two responses coexist and rarely fall into exclusive pro-Th1 or -Th2 patterns, but there is a predominance of one over the other that depends on a balance involving variables such as the type and quantity of the antigen involved and the site at which the immune response begins (Rizzo et al., 1995). The antagonistic activities of the cytokines secreted by the Th1 and Th2 lymphocytes have also been described (Benjamini et al., 2002).
Currently, these concepts are not considered absolute, and studies have been published in which questions have been raised with respect to the Th1/Th2 paradigm, such as the role of monocytes and dendritic cells as sentinels of the immune system, the diversity of cell interaction with the antigen presenting cells and principally the participation of the regulatory T-cells, with their own functional phenotypical characteristics fundamental to the immune response (Taylor et al., 2006).

With respect to endometriosis, various studies have analysed isolated cytokines or panels of cytokines, and divergent results have been reported (Wu and Ho, 2003; Seli et al., 2003), including alterations in B-lymphocyte activity, an increase in the levels of complement components C3 and C4 and the presence of greater circulating concentrations of auto-antibodies compared to women without endometriosis (Weed and Arquembourg, 1980; Mathur et al., 1990; Dmowski et al., 1995; Abrão et al., 1997; Mathur, 2000; Pasotto et al., 2005). The hypothesis was therefore made that endometriosis is an auto-immune disease since it involves a series of characteristics common to this type of condition, such as abnormalities in T- and B-cell function and the involvement of diverse organs (Gleicher et al., 1987; Nothnick, 2001).

Nevertheless, little information is available on the analysis of the interaction between the cytokines involved and the predominance of either type of immune response in patients with endometriosis, since, in general, the behaviour of the set of cytokines with respect to Th1 and Th2 response patterns has not been studied. Therefore, in the present study, recent technology has been applied to identify cytokines in small volume samples, to evaluate cytokines secreted in blood and in the peritoneal cavity, and their relationship with endometriosis, thus introducing the theory of Th1 and Th2 balance to this disease.

Methods

The study was carried out at the Endometriosis Clinic, Department of Gynecology, Teaching Hospital of the School of Medicine, University of São Paulo, between January 2004 and November 2005. The protocol was approved by the Internal Review Board of the institution (Approval no. 601/03). All patients read and signed the informed consent form.

Women with clinical complaints suggestive of endometriosis were evaluated by history and physical examination. In addition, evaluation was complemented with transvaginal ultrasonography and nuclear magnetic resonance, when appropriate, to look for ovarian endometriomas and/or deeply infiltrating disease. When the clinical and image data suggested the presence of these two types of endometriosis and when the patient’s clinical complaints could be compatible with peritoneal endometriosis, not identified by image complementary exams, there was indication of videolaparoscopy. Biopsies were performed during the surgical procedure to provide histological confirmation of the diagnosis of the disease.

Ninety-eight patients, attending consecutively at the endometriosis clinic, were evaluated and divided into two groups: Group A was composed of patients with endometriosis, whereas Group B comprised patients without the disease. Inclusion criteria for Group A were: age 18–40 years, histologically confirmed endometriosis, absence of autoimmune disease, eumenorheic patients with menstrual cycles of 26–32 days and no use of hormone therapy in the three months preceding the surgical procedure. For inclusion in Group B, patients had to have clinical signs of endometriosis and fulfil similar inclusion criteria as patients in Group A; however, in the case of Group B patients, the absence of endometriosis had to have been confirmed during surgery.

At the time of the surgical procedure, the day of the patient’s menstrual cycle was registered and 5 ml of peripheral blood was taken prior to initiation of the anaesthetic procedures. The patients were then submitted to laparoscopy at which time 2–10 ml of peritoneal fluid was collected from the anterior or posterior cul-de-sac. There was no peritoneal fluid in 12 patients during laparoscopy and we did not use peritoneal flushing to obtain fluid samples. The blood and the peritoneal fluid were centrifuged to, respectively, isolate cell-free serum and to remove cellular debris. The material was frozen at −80°C and was only thawed for cytokine measurement after all other data had been collected.

Endometriosis patients were classified according to the American Society for Reproductive Medicine (ASRM, 1997) stages 1 to 4.

The laboratory method used for the measurement of TNF-alpha, IFN-gamma, IL-2, IL-4 and IL-10 was the BD Cytometric Bead Array (CBA), catalogue no. 551809, manufactured by Pharmingen, Becton Dickinson, Co. (San Diego, California, USA) and carried out using a flow cytometer (BD FACSCalibur, Franklin Lakes, New Jersey, USA). The BD CBA system uses the sensitivity of amplified fluorescence detection by flow cytometry to measure the cytokines with a particle-based immunoassay. The specific capture beads were mixed with the phycoerythrin conjugated detection antibodies and then incubated with recombinant protein standards to form sandwich complexes. Following acquisition of sample data using the flow cytometer, the sample results were generated in graphical and tabular format using the BD CBA Analysis Software.

Figure 1 shows an example of a histogram of peritoneal fluid IFN-gamma concentration analysis per counted events and the standard curve of this cytokine obtained by flow cytometry. The mean fluorescent intensity obtained in the histogram is equivalent to a concentration measured in pg/ml.

The Mann–Whitney test was used in the statistical analysis to compare cytokine concentrations. With respect to the menstrual cycle, the 1st to the 14th days of the cycle were defined as the follicular phase, while the 15th to the last day of the cycle were defined as the luteal phase, and the chi-squared test was used to compare the groups. A P < 0.05 was considered statistically significant.

To establish the predominance of one type of immunological response, Th1 or Th2, an analysis of categorical data was carried out using MacNemar’s test with a significance level of 5%. Initially, a percentile proportional to the sample sizes was established for each cytokine measured in blood and peritoneal fluid, i.e. a percentile of 33/98 in which 33 is the number of patients without endometriosis and 65 the number of women with the disease. Therefore, a percentile was obtained for each cytokine and each result expressed as pg/ml was converted into 0 (if lower than the percentile) or 1 (if greater than the percentile), eliminating the comparison of absolute numbers. The number of zeros and ones was then calculated for each cytokine, comparisons were made and, from these, the relationship between the cytokines was obtained.

Results

Samples of blood and peritoneal fluid of 98 women were analysed, 65 of whom had endometriosis (Group A) and 33 of whom did not (Group B). The mean age of patients in Group A was 32.1 ± 5.4 years, which was not statistically
different from the mean age of patients in Group B of 32.9 ± 5.1 years (P > 0.05).

The comparison of cytokine levels found in the two groups is shown in Tables I and II. As seen in Table I, there appears to be no systemic change in the cytokine secretion pattern in patients with endometriosis. However, in Table II, a significant increase can be seen in IFN-gamma and IL-10 levels in the peritoneal fluid of patients with endometriosis compared with women in the control group. There were no statistical differences in cytokine levels between the two study groups when the phase of the menstrual cycle in which the samples had been collected was taken into consideration.

As shown in Figure 2, 13 of the 57 patients in Group A (with endometriosis) had detectable levels of IFN-gamma in peritoneal fluid compared to only 2/29 patients in Group B (without endometriosis).

The ASRM (1996) staging was applied for all patients with endometriosis and there were 28 patients in initial stages (1 and 2) and 37 patients in advanced stages (3 and 4). The cytokine concentrations were compared concerning this classification and we did not find any difference between the two groups.

Tables III and IV show the ratio between Th1 and Th2 responses based on the cytokine levels in blood and peritoneal fluid for each response. In this analysis, the highest measurements were compared and significance levels were described (P-values) for each cytokine ratio, i.e. IL-4/TNF-alpha, IL-4/IFN-gamma, IL-4/IL-2, IL-10/TNF-alpha, IL-10/IFN-gamma and IL-10/IL-2. Significant differences were found in the following ratios: IL-4/IFN-gamma, IL-4/IL-2, IL-10/IFN-gamma and IL-10/IL-2 in the peritoneal fluid of the group of patients with endometriosis, with IL-4 and IL-10 predominating over IFN-gamma and IL-2, reflecting a possible shift towards Th2 response in patients with endometriosis. When the phase of the menstrual cycle of the patients at the time of sample collection was compared, the patterns of these ratios remained the same, confirming that this variable had no effect on the secretion of the cytokines evaluated in this study. The same situation occurred with the ratios analysis.

**Table I.** Median cytokine levels (pg/ml) in the serum of patients with and without endometriosis (Group A, n = 65, and Group B, n = 33, respectively)

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>Group A, median (range)</th>
<th>Group B, median (range)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-alpha (Th1)</td>
<td>2.3 (0–9.6)</td>
<td>3.7 (0–10.4)</td>
<td>0.188</td>
</tr>
<tr>
<td>IFN-gamma (Th1)</td>
<td>1.6 (0–11.7)</td>
<td>2.1 (0–6.6)</td>
<td>0.571</td>
</tr>
<tr>
<td>IL-2 (Th1)</td>
<td>7.4 (0–34.1)</td>
<td>8.3 (0–26)</td>
<td>0.447</td>
</tr>
<tr>
<td>IL-4 (Th2)</td>
<td>1.9 (0–6.3)</td>
<td>2.0 (0–4.1)</td>
<td>0.731</td>
</tr>
<tr>
<td>IL-10 (Th2)</td>
<td>3.2 (0–12.9)</td>
<td>3.1 (0–7.5)</td>
<td>0.904</td>
</tr>
</tbody>
</table>

**Table II.** Median cytokine levels (pg/ml) in the peritoneal fluid of patients with and without endometriosis (Group A, n = 65, and Group B, n = 33, respectively)

<table>
<thead>
<tr>
<th>Cytokines</th>
<th>Group A, median (range)</th>
<th>Group B, median (range)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-alpha (Th1)</td>
<td>3.1 (0–30.3)</td>
<td>1.4 (0–20.7)</td>
<td>0.364</td>
</tr>
<tr>
<td>IFN-gamma (Th1)</td>
<td>0.5* (0–4.9)</td>
<td>0 (0–3.4)</td>
<td>0.039*</td>
</tr>
<tr>
<td>IL-2 (Th1)</td>
<td>0 (0–7.1)</td>
<td>0 (0–6.2)</td>
<td>0.072</td>
</tr>
<tr>
<td>IL-4 (Th2)</td>
<td>1.7 (0–121.3)</td>
<td>0 (0–66.3)</td>
<td>0.557</td>
</tr>
<tr>
<td>IL-10 (Th2)</td>
<td>28.6* (0–772.5)</td>
<td>25.7 (3.2–92.7)</td>
<td>0.035*</td>
</tr>
</tbody>
</table>

*Significant difference between groups, P < 0.05.
that also remained the same when ASRM endometriosis staging was considered.

Discussion

Various authors have attempted to clarify the role of the immunological system in endometriosis and several abnormalities have been detected in this association (Berkkanoglu and Arici, 2003). The principal path currently being followed updates the menstrual reflux theory by affirming that the endometrial cells invading the peritoneal cavity ought to be swept out by the components of the organism’s defence system. In women with endometriosis, this mechanism suffers a bias that allows the implantation and development of these cells in the peritoneal cavity (Harada et al., 2001).

In view of the inflammatory nature of the disease (Agic et al., 2006) and the importance of various cytokines produced by the immune system in distant cell implantation (Donskov and von der Maase, 2006), in this study we sought to identify the predominant cytokine profile associated with Th1 and Th2 responses in patients with endometriosis. Such an approach would confirm the participation of immunological alterations and encourage further research leading to the development of new therapeutic modalities for the treatment of this disease. It is important to emphasize that the laboratory method used in this study was flow cytometry, a technique that allowed the measurement of the cytokines studied to be carried out using one single 5 μl sample of blood and another 5 μl sample of peritoneal fluid in one single passage. This procedure offers certain advantages in relation to traditional evaluations of cytokine measurements using the enzyme-linked immunosorbent assay method because of the small quantity of fluid required to obtain the results. Moreover, in the latter method, each cytokine has to be measured separately (Cook et al., 2001).

There is some controversy with respect to whether there is any variation in cytokine measurement according to the phase of the menstrual cycle, i.e. if the production and secretion of these substances is affected by some type of hormone. In the present study, the measurements of each cytokine were compared in the follicular and in the luteal phases in the presence and absence of endometriosis and no statistically significant changes were found. In the literature, some studies have reported similar findings (Gazvani et al., 2000; Mahnke et al., 2000; Gazvani et al., 2001; Zhang et al., 2004), while some have reported progesterone-dependent variations (Tabibzadeh et al., 1989; Harada et al., 1997; von Wolff et al., 2000; Cheong et al., 2002; Arici et al., 2003) and others have defended estrogen-dependent variations in cytokines (Khan et al., 2002).

With the limited sample size of patients evaluated in this study, it was not possible to further subdivide the data into more phases of the menstrual cycle such as, for example, the early and late luteal phases, which would have permitted a more detailed data analysis. This study limitation may justify the lack of statistically significant differences in the analysis of this parameter.

Following the measurement of IL-2, IL-4, IL-10, TNF-alpha and IFN-gamma in serum and peritoneal fluid, these results

**Table III.** Levels of significance obtained from the ratios of serum cytokine concentrations for Th1 (TNF-alpha, IFN-gamma and IL-2) and Th2 response (IL-4 e IL-10) in patients in Groups A and B

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Group A, IL-4 (n = 65)</th>
<th>Group A, IL-10 (n = 65)</th>
<th>Group B, IL-4 (n = 33)</th>
<th>Group B, IL-10 (n = 33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-alpha</td>
<td>0.41</td>
<td>0.58</td>
<td>0.82</td>
<td>0.89</td>
</tr>
<tr>
<td>IFN-gamma</td>
<td>0.50</td>
<td>0.68</td>
<td>0.34</td>
<td>0.36</td>
</tr>
<tr>
<td>IL-2</td>
<td>0.39</td>
<td>0.59</td>
<td>0.85</td>
<td>0.85</td>
</tr>
</tbody>
</table>

**Table IV.** Levels of significance obtained from the ratios of cytokine concentrations in peritoneal fluid for Th1 (TNF-alpha, IFN-gamma and IL-2) and Th2 response (IL-4 e IL-10) in patients in Groups A and B

<table>
<thead>
<tr>
<th>Cytokine</th>
<th>Group A, IL-4 (n = 57)</th>
<th>Group A, IL-10 (n = 57)</th>
<th>Group B, IL-4 (n = 29)</th>
<th>Group B, IL-10 (n = 29)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TNF-alpha</td>
<td>0.89</td>
<td>0.32</td>
<td>0.68</td>
<td>0.50</td>
</tr>
<tr>
<td>IFN-gamma</td>
<td>&lt;0.001*</td>
<td>&lt;0.001*</td>
<td>0.09</td>
<td>0.06</td>
</tr>
<tr>
<td>IL-2</td>
<td>0.006*</td>
<td>&lt;0.001*</td>
<td>0.19</td>
<td>0.10</td>
</tr>
</tbody>
</table>

*P < 0.05.
were compared between patients with endometriosis and those without the disease. The patients with endometriosis were found to have higher concentrations of IFN-gamma and IL-10 in peritoneal fluid compared to patients without endometriosis. IFN-gamma measurements in peritoneal fluid were detectable in 13 of the 57 patients with endometriosis and only in 2 of the 29 patients without the disease, similar results to those found for IL-10. There are many conflicting reports in the literature on the action of each cytokine in endometriosis and the clinical application of the results obtained with the measurement of these cytokines for the laboratory diagnosis of endometriosis. Punnonen et al. (1996), Ho et al. (1997) and Tabibzadeh et al. (2003) also observed an increase in IL-10 in the peritoneal fluid of patients with endometriosis. On the other hand, in a study carried out in patients submitted to IVF, the authors concluded that IL-10 was higher in the control group comprised of fertile patients than in women with endometriosis and also in fertile patients than in women with infertility of apparent cause, proving that Th2 response facilitates trophoblastic implantation at the beginning of pregnancy (Ginsburg et al., 2005).

With respect to IFN-gamma, Khorram et al. (1993) failed to observe any changes in its concentrations in the peritoneal fluid of patients with endometriosis. The participation of this cytokine in the pathogenesis of endometriosis has already been described, specifically its ability to enhance resistance of endometrial cells to apoptosis, which would increase the chance of these cells to survive and be implanted outside the uterus (Nishida et al., 2005) and to stimulate the expression of cell adhesion molecules (e.g. ICAM-1), which would allow cells from retrograde menstruation to spread and invade other sites (Wu et al., 2004).

Regarding staging of endometriosis, no statistically significant differences were seen in our study with respect to cytokine measurement and Th1 and Th2 response patterns. There is no published specific data concerning this issue, however increased concentrations of TNF-alpha have already been described in relation to advanced stages (Richter et al., 2005), initial stages (Pizzo et al., 2002) and in cases in which no relationship could be made with the stage of endometriosis (Iwabe et al., 2002).

As an initial interpretation, the analysis of the data obtained in our study does not permit us to extrapolate the results of Th1 and Th2 activity, since an increase occurred in one cytokine of each response type: IFN-gamma of the Th1 response and IL-10 of the Th2 response. Nevertheless, the interpretation of these data depends on the relationship between the cytokines, i.e. an increase in the concentration of one cytokine in detriment to a reduction in another cytokine indirectly reflects the balance of the Th1 and Th2 responses.

The biological effects of each cytokine can certainly not be compared in absolute numbers, since IL-10, for example, is measured as concentrations of 10, 20 or 50 pg/ml while IFN-gamma has values 10 times lower, i.e. 1 or 2 pg/ml. If we were to compare the simple relationship between these two cytokines in absolute numbers, IL-10 would obviously be higher than IFN-gamma; however, these results would make no sense, since we would be comparing different reference levels. Therefore, analysis of the relationship between the cytokines is not based on the assumption that each one of these substances has the same biological action in relation to the others, and we know of no data in the literature supporting this affirmation. This bias was eliminated in the statistical analysis of the data.

Our results show that IL-4 measurements were higher in the peritoneal fluid of patients with endometriosis in relation to IFN-gamma and IL-2. Likewise, IL-10 behaved in a similar manner. Therefore, it is also possible to infer that Th2 response plays a role in the establishment of the disease. The test applied to analyse the ratio between the cytokines evaluates the absolute values of each substance and reflects the cytokine with the highest level in each patient, generating comparisons and statistical significance. In this study, it is not the activity of each individual cytokine that is being evaluated, but the presence and the relative concentration of each one of these substances analysed according to their participation in the Th1 or Th2 immune response pattern. These data should be evaluated in conjunction with data on the increase in IFN-gamma.

Examples of the cooperation between Th1 and Th2 cells have been shown in the literature, both with respect to the establishment of an antibody response and to increase in the survival of both cell types (Rizzo et al., 1995). Therefore, it may be suggested that endometriosis is a disease in which both arms of the immune response are involved. It should be emphasized that analysis of the ratio between the cytokines revealed no statistically significant change in the results when hormonal influences were taken into consideration, i.e. the changes observed remained the same irrespective of the phase of the menstrual cycle in which the samples were collected.

As mentioned, various studies have analysed a panel of cytokines and have reported results showing an increase or a decrease in a given cytokine. However, the most significant information refers to the relationship between the cytokines indicating a balance in the immune system that tends towards the Th2 arm. A study by Hsu et al. (1997) showed similar conclusions, albeit with the use of different methodology, and reported an increase in messenger RNA (mRNA) expression of IL-4 in the Th2 cells in peripheral blood and in the peritoneal fluid of patients with endometriosis.

Antsiferova et al. (2005) applied the two methods, flow cytometry and analysis of IL-2, IL-4 and IL-10 expression, using mRNA by RT–PCR to analyse cytokine synthesis and lymphocyte activation in peripheral blood and endometrial tissue (topic and ectopic) of 15 patients with endometriosis and 20 women without the disease. The results of this study showed that mRNA expression and intracellular synthesis of IL-4 and IL-10 were high in peripheral lymphocytes and the concentration of B lymphocytes was high in endometrial foci. The authors reached similar conclusions to those reported in the present study, affirming that ‘the development of endometriosis is accompanied by activation of the Th2 type of immune response at local and systemic levels’.

Endometriosis is a disease with different clinical presentations, and involves an abnormality in the immune response, as already demonstrated. The results of this study suggest
that endometriosis is a disease involving complex inflammatory behaviour with a clear Th1 component, as shown by the greater number of patients with detectable levels of IFN-gamma in peritoneal fluid, and also by the shift towards Th2 cytokine production.

This observation confirms that the human immune system is not comprised of only two types of immune response, and neither does one or other response exist in an absolute and exclusive form, i.e. when a Th1 response pattern is active, the Th2 pattern may also be present. Even diseases classically studied from the point of view of the immune system, such as rheumatoid arthritis and multiple sclerosis, have both inflammatory and auto-immune components in their etiopathogenesis (Kidd, 2003). These apparently conflicting data show that, both from an immunological and a clinical point of view, endometriosis has various facets and the continued studies of these associated with other variants, such as markers of immune response, are a promising path to be explored towards achieving a better understanding of the physiopathogenesis of the disease. Such studies may lead to alternative, perhaps more specific, therapies for each clinical type of endometriosis.

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References


Immune response and endometriosis

Tabibzadeh S, Becker JL and Parsons AK (2003) Endometriosis is associated with alterations in the relative abundance of proteins and IL-10 in the peritoneal fluid. Front Biosci 8,a70–a78.

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