Differentiated S100A7 expression in infected tonsils and tonsils from allergic individuals

Malin Bryborn1,2, Anne Månsson1, Lars Olaf Cardell2 & Mikael Adner3

1Laboratory of Clinical and Experimental Allergy Research, Department of Otorhinolaryngology, Malmö University Hospital, Lund University, Malmö, Sweden; 2Department of Otorhinolaryngology, Karolinska Institutet, Huddinge, Sweden; and 3The National Institute of Environmental Medicine, Karolinska Institutet, Solna, Sweden

Correspondence: Malin Bryborn, Laboratory of Clinical and Experimental Allergy Research, Department of Otorhinolaryngology, Malmö University Hospital, SE-205 02 Malmö, Sweden. Tel.: +46 40 33 12 65; fax: +46 33 62 29; e-mail: malin.bryborn@med.lu.se

Received 18 December 2007; revised 26 May 2008; accepted 28 May 2008. First published online 9 July 2008.

DOI:10.1111/j.1574-695X.2008.00444.x

Editor: Artur Ulmer

Keywords
S100A7 (psoriasin); palatine tonsil; bacterial infection; allergic disease.

Abstract

Palatine tonsils are continuously exposed to microorganisms and antigens and secrete antimicrobial peptides as a first line of defense. S100A7 is a protein with antimicrobial and chemotactic properties. Our aim was to investigate how the expression of S100A7 in human palatine tonsils is affected by inflammatory processes. Tonsils obtained from 109 patients undergoing tonsillectomy were divided into groups of infected and noninfected as well as allergic and nonallergic, based on the results from tonsillar core culture tests and Phadiatop analysis, respectively. Western blot and immunohistochemistry were used to assess protein expression and real-time PCR was used to quantify mRNA levels. To explore the induction of S100A7, tonsils were stimulated with lipopolysaccharide in vitro. The immunohistochemical staining for S100A7 was most intense in the tonsillar epithelium, but the protein was also detected in B- and T-cell regions, which was confirmed with Western blot on isolated B and T cells. The S100A7 expression appeared to be the highest in CD8+ T cells. Reduced mRNA levels of S100A7 were detected in infected tonsils as well as in tonsils from allergic individuals. In vitro stimulation of tonsils with lipopolysaccharide did not have any effect on the expression. The results suggest a role for S100A7 in recurrent tonsillitis and allergic disease.

Introduction

The respiratory tract mucosa is a primary site for deposition of different microorganisms, entering the body via inhaled air. The innate immune system constitutes the first line of defense against bacterial infections, capable of mounting a response within minutes after bacterial invasion (Basset et al., 2003). One important component of the innate immune system is secretion of antimicrobial peptides (AMPs) (Beisswenger & Bals, 2005). Several different types of AMPs have been identified in the airways (Travis et al., 2001; Wah et al., 2006) and apart from their direct antimicrobial function, many of them also exert functions as inflammatory mediators (Yang et al., 1999), providing a link between innate and adaptive immunity.

One AMP is S100A7, an 11-kDa large protein, which was first identified as a highly upregulated protein in skin from psoriatic patients (Madsen et al., 1991). S100A7, also called psoriasin, belongs to the S100 protein family, which consists of c. 20 different Ca2+-binding proteins of the EF-hand type (Marenholz et al., 2004). S100 proteins are involved in a number of different intracellular activities like Ca2+ homeostasis, protein phosphorylation, enzyme regulation and transcription factor interaction. Several S100 proteins, probably including S100A7, are also secreted into the extracellular compartment where they act on surrounding cells in a cytokine-like manner (Madsen et al., 1991; Donato, 2003). The extracellular functions of S100A7 are poorly understood, but there are studies suggesting both chemotactic and antimicrobial properties (Jinquan et al., 1996; Glaser et al., 2005). Recently, S100A7 has also been shown to activate neutrophils to produce a range of cytokines and chemokines (Zheng et al., 2008). High antibacterial activity for S100A7, preferentially against different Escherichia coli strains, has been described in the skin (Glaser et al., 2005) as well as the presence of S100A7 in the third trimester amniotic fluid, probably protecting the fetus against bacterial infections (Porre et al., 2005). It has also been shown that treatment of
keratinocytes with culture supernatants from different 
*E. coli* strains induces S100A7 expression (Glaser et al., 2005). These data suggest that S100A7 is involved in the first line of defense against bacterial infections. Recently, we described S100A7 in nasal lavage fluid (NFL), and reduced levels were found in individuals with ongoing allergic rhinitis (Bryborn et al., 2005).

The palatine tonsils are due to their anatomical location continuously exposed to inhaled bacteria and other airborne antigens (Nave et al., 2001). Tonsillitis is a common disease mostly caused by bacterial infections or viruses (Putto, 1987) and group A β-hemolytic streptococci have long been regarded as the most frequent causative agents of bacterial tonsillitis. However, there are studies also highlighting the pathogenic role of *Haemophilus influenzae* (Gaffney & Cafferkey, 1998). As secondary lymphoid organs, the palatine tonsils are able to mount an adaptive immune response involving T and B cells (Quiding-Jarbrink et al., 1995) but they are also involved in the innate immune system by secreting AMPs (Chae et al., 2001; Weise et al., 2002). Currently, very little is known about the effects of S100A7 on bacteria involved in tonsillar infections. Nonetheless, both *Pseudomonas aeruginosa* and *Staphylococcus aureus* are opportunistic respiratory pathogens (Lynch, 2001; Garau & Gomez, 2003) and S100A7 has, to some extent, been effective against these bacteria, albeit at rather high concentrations (Glaser et al., 2005). This suggests a potential role for S100A7 in respiratory tract infections. The purpose of this study was to investigate the appearance of S100A7 in human palatine tonsils and to evaluate whether the expression levels are affected by infectious stimulation and allergic predisposition.

**Materials and methods**

**Patients**

Palatine tonsils were obtained from 109 patients (54 females, 55 males) undergoing tonsillectomy at Malmö University Hospital (Malmö, Sweden). The mean age (range) of the patients was 15 (2–44) years. None of the patients displayed symptoms of acute infection at the time of surgery, and none of them had received any antibiotic treatment for at least 1 month before surgery. Apart from the tonsillar symptoms, all patients were healthy and did not receive any medication. The study was approved by the Ethics Committee of the Medical Faculty, Lund University, and written informed consent was obtained from all subjects.

**Tonsils**

Obtained tonsils were divided into two groups based on results from tonsillar core culture tests taken after tonsillectomy. Tonsils with positive core culture test for β-hemolytic streptococci (group A, C or G) and/or *H. influenzae* were considered infected (63 tonsils), whereas tonsils with a negative core culture test were considered noninfected (46 tonsils). The tonsils were also divided into allergic (41 tonsils) and nonallergic (68 tonsils) groups, based on the results from Phadiatop analysis, and subsequent test for specific IgE antibodies against a standard panel of allergens, including cat, dog, horse, birch, timothy, mugwort, *Parietaria officinalis*, *Olea europaea*, *Dermatophagoides pteronyssinus*, *Dermatophagoides farinae*, *Cladosporium* and *Alternaria* (Pharmacia Upjohn, Uppsala, Sweden). A positive Phadiatop test and class 2 for at least one allergen. These tonsils were not characterized according to infection and allergy status.

<table>
<thead>
<tr>
<th>Table 1. Division of tonsils according to infection and allergy status</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>-------------------</td>
</tr>
<tr>
<td><strong>Allergic</strong></td>
</tr>
<tr>
<td><strong>Nonallergic</strong></td>
</tr>
<tr>
<td><strong>Total</strong></td>
</tr>
</tbody>
</table>

*Positive core culture test for β-hemolytic streptococci (A, C or G) and/or *Haemophilus influenzae*.

Table 1. Division of tonsils according to infection and allergy status

**Cell separation**

Fresh tonsils were minced in complete medium consisting of RPMI 1640 (Sigma Aldrich, St Louis) supplemented with 0.3 g L⁻¹ l-glutamine, 10% fetal calf serum (FCS) (AH diagnostics, Aarhus, Denmark), 100 U mL⁻¹ penicillin and 100 μg mL⁻¹ streptomycin (Invitrogen, Carlsbad). The cell suspension was incubated with neuraminidase-activated sheep red blood cells (SRBC), followed by density gradient centrifugation with Ficoll-Paque (Amersham Bioscience, Uppsala, Sweden). T cells were obtained from the pellet after lysing the SRBCs with dH₂O and 1.4 M NaCl. Different subsets of T cells were further isolated using the MACS magnetic labeling system (Miltenyi Biotec, Cologne, Germany) according to the instructions of the manufacturer. Briefly, cells were incubated in 4°C with antibody-conjugated microbeads in buffer containing phosphate-buffered saline supplemented with 0.5% FCS and 2 mM EDTA, and separated on a large cell selection (LS) column placed on a
magnetic separator. Untouched CD8+ T cells were isolated by an indirect magnetic labeling system (CD8+ T Cell Isolation Kit II, Miltenyi Biotec) depleting non-CD8+ cells. Untouched CD4+ T cells were isolated in a similar manner (CD4+ T Cell Isolation Kit II, Miltenyi Biotec) by depletion of non-CD4+ cells.

For isolation of B cells, the interphase fraction, after density gradient centrifugation with Ficoll-Paque, was collected and washed in complete medium. Untouched CD19+ B cells were isolated using MACS B Cell Isolation Kit II (Miltenyi Biotec), by depletion of CD19+. For all protocols, the isolated cells routinely had a purity of >95% as determined by fluorescence-activated cell sorting. Freshly isolated B and T cells to be used in RNA experiments were lysed in RLT buffer (Qiagen) supplemented with 1% 2-mercaptoethanol and stored at −80°C until use. Cells for Western blot were lysed on ice for 5 min using Cell Lysis Buffer (Cell Signaling Technology, Danvers) supplemented with 1 mM phenylmethylsulfonyl fluoride. After homogenization, cells were centrifuged at 18,000 g for 10 min (5°C). Supernatants were mixed with sodium dodecyl sulfate (SDS) sample buffer and stored at 20°C until use.

Western blot

Pieces of whole tonsil were homogenized in SDS sample buffer. All samples were heated at 95–100°C for 5 min, centrifuged at 9,000 g for 10 min and loaded onto NuPAGE Bis-Tris 4–12% gel (Invitrogen), separated by electrophoresis (Mini vertical gel system, Thermo EC, Waltham) and blotted to Immobilon-P polyvinylidene difluoride membranes (Millipore, Billerica). Membranes were blocked in buffer 1 (Tris-HCl 10 mM pH 7.4, NaCl 0.9% and dry milk 5%) and then incubated overnight with primary antibody (1 μg mL−1) against S100A7 (mouse monoclonal) (Abcam, Cambridge, UK). Membranes were washed two times in buffer 1, followed by incubation for 2 h with horseradish peroxidase (HRP)-conjugated goat anti-mouse secondary antibody (50 ng mL−1). After two washes in buffer 2 (Tris-HCl 10 mM pH 7.4, NaCl 0.9% and Tween 20 0.05%), membranes were incubated for 5 min in SuperSignal West Pico solution (Pierce Biotechnology, Rockford). The chemiluminescence was detected using the MAN-X X-ray system (FUJIFILM Medical Systems, Stamford).

Immunohistochemistry

Formalin-fixed tissue preparations were embedded in paraffin, cut into 3-μm-thick sections, mounted on glass slides and stored at −80°C until use. Before visualization of proteins, the sections were treated with xylene to remove the paraffin and rehydrated using decreasing concentrations of ethanol. To facilitate binding of the antibody, the sections were treated with target retrieval solution (Dako, Glostrup, Denmark) for 20 min in a microwave oven, followed by 1% Triton X 100 for 20 min in order to increase the membrane permeability. To block endogenous peroxidase activity, sections were incubated in 0.03% hydrogen peroxide for 10–15 min. Thereafter, primary antibody against S100A7 (mouse monoclonal) (Abcam) was applied to the sections for 1 h. N-series Universal Negative Control Reagent (Dako) was used as a negative control. Subsequently, the sections were incubated with an HRP-labeled goat anti-mouse polymer for 30 min and then developed in 3,3’-diaminobenzidine (DAB) solution (Dako EnVision System-HRP kits) for 6 min. The DAB-stained sections were dehydrated with increasing concentrations of ethanol, rinsed in xylene and mounted in Pertex (Histolab, Gothenburg, Sweden). Tris-buffered saline (pH 7.6) supplemented with 0.05% Tween 20 was used for all washing steps.

Lipopolysaccharide stimulation of tonsils in vitro

Fresh tonsils were cut into smaller pieces, not larger than 3 × 3 × 3 mm, and placed into Dulbecco’s modified Eagle’s medium (DMEM) (PAA Laboratories, Pasching, Austria), supplemented with penicillin (100 U mL−1) and streptomycin (100 μg mL−1) (Invitrogen). The tonsil pieces were cultured for 6 h at 37°C in humidified 5% CO2 in air, in the absence or presence of different concentrations (1, 10, 100 and 1000 ng mL−1) of lipopolysaccharide from Salmonella minnesota R595 (Alexis Biochemicals, Lausen, Switzerland). After 6 h, the tonsil pieces were placed in RLT buffer (Qiagen) supplemented with 1% 2-mercaptoethanol and stored at −20°C overnight.

RNA extraction and reverse transcriptase PCR

Tonsil pieces were homogenized in RLT buffer (Qiagen) supplemented with 1% 2-mercaptoethanol using a TissueTearor™ (Biospec Products Inc., Bartlesville). Total RNA was extracted from isolated cells and homogenized tonsil using the RNeasy Mini Kit following the kit instructions (Qiagen). The purity and quantity of total RNA was measured by a spectrophotometer using the wavelength absorption ratio 260/280 nm. Reverse transcription of total RNA into cDNA was carried out using the Omniscript™ reverse transcriptase kit (Qiagen) with oligo(dT)16 (DNA Technology A/S, Aarhus) in a MASTERCYCLER personal PCR machine (Eppendorf AG, Hamburg, Germany). The reaction of reverse transcription was carried out at 37°C for 1 h in a final volume of 20 μL.

Real-time PCR

The quantitative real-time PCR was performed using the Quantitect SYBR® Green PCR kit (Qiagen) on a Smart Cycler (Cepheid, Sunnyvale). The reaction was performed in
a volume of 25 μL and carried out with heating to 95 °C for 15 min, followed by 46 PCR cycles of 94 °C for 30 s and 55 °C for 60 s (initially 66 °C, followed by a 2 °C decrease for the first six cycles). Melting curve analysis (60–95 °C) was performed in order to verify amplification of specific PCR products, and revealed a single peak in each sample for S100A7 and β-actin, respectively. The gene expression was assessed using the comparative cycle threshold (Ct) method. The relative amounts of mRNA for S100A7 were determined by subtracting the Ct value for the housekeeping gene β-actin from the Ct value for S100A7 (ΔCt). The amount of mRNA is expressed in relation to 100 mRNA molecules of β-actin (100 × 2−ΔCt) and presented as mean values ± SE of mean (SEM). These values were corrected for differences in amplification efficiency between S100A7 and β-actin.

All PCR primers (∼-actin forward: 5′-GCCAACCGCGAG AAGATG-3′, β-actin reverse: 5′-ACGGCCAGAGGCGTAC AG-3′, S100A7 forward: 5′-CGTGACGCTTCCCAGCTC-3′, S100A7 reverse: 5′-TCATCACGTCTGGTGTATTTGTGA-3′) were designed using PRIMER EXPRESS® 2.0 software (Applied Biosystems, Foster City, CA) and synthesized by DNA Technology A/S (Aarhus).

Statistics
Statistical analysis was performed using GraphPad Prism 4 (San Diego). All values are expressed as mean ± SEM. A nonparametric t-test (Mann–Whitney) was used to determine statistical differences for unpaired data. Repeated measures ANOVA was used for paired data. To test for interaction between allergy and infection, both an ordinary two-way ANOVA on the original data and a two-way ANOVA applied to ranked data were used. P-values of ≤ 0.05 were considered to be statistically significant.

Results
S100A7 is expressed in human palatine tonsils
A Western blot was performed in order to determine whether S100A7 is expressed in human palatine tonsils. The protein was detected as a distinct single band at c. 11 kDa (Fig. 1). Elucidation of the morphological distribution of S100A7 in tonsils was accomplished by immunohistochemical analysis (Fig. 2). The staining was more intense in the tonsillar epithelium (Fig. 2a), but the protein was also clearly detected in both germinal centers and in T-cell zones (Fig. 2b), indicating S100A7 expression in both epithelial cells as well as in B and T cells.

S100A7 expression in tonsillar B and T cells
To assess the expression of S100A7 in tonsillar B and T cells, CD19+ B cells, CD4+ T cells and CD8+ T cells were isolated from fresh tonsils. Quantitative real-time PCR was used to compare S100A7 mRNA levels in the different cell types and Western blot to measure corresponding protein levels. As the immunohistochemical pictures indicated, both B and T cells expressed S100A7 (Figs 3 and 4). The mRNA expression was significantly higher in CD8+ T cells (22.9 ± 5.5) as compared with both CD4+ T cells and CD19+ B cells (9.4 ± 2.1 and 6.5 ± 1.4, respectively) and the protein expression also appeared to be the highest in CD8+ T cells.

In vitro stimulation with lipopolysaccharide does not affect S100A7 expression
Because of the reported antimicrobial properties of S100A7, preferentially against the gram-negative bacteria E. coli, we wished to investigate whether in vitro stimulation with lipopolysaccharide, a cell wall component of gram-negative bacteria, could increase the mRNA expression of S100A7 in tonsils. However, after 6 h of culture there was no significant difference between tonsil pieces stimulated with lipopolysaccharide and control pieces (data not shown).

S100A7 mRNA expression is downregulated in infected tonsils
Tonsils are highly exposed to bacteria, and the secretion of AMPs from tonsils has been described previously as a part of the first line of defense against bacterial invasion. The
The present study shows that S100A7 is expressed in tonsils. Hence, to evaluate whether there was a difference in the S100A7 expression between infected and noninfected tonsils, the obtained tonsils were divided into two groups. Tonsils with a positive core culture test for β-hemolytic streptococci and/or Haemophilus influenzae were considered infected, while tonsils with a negative test were considered noninfected. The expression of S100A7 in the tonsils was quantified using real-time PCR. The infected group displayed lower S100A7 levels compared with the noninfected control group (264 ± 40 and 365 ± 49, respectively: Fig. 5).

**Altered S100A7 levels in allergic patients**

NLF from patients with allergic rhinitis contains reduced levels of S100A7 (Bryborn *et al.*, 2005). To investigate the pattern in tonsils, the tonsil material was divided into one group of tonsils obtained from allergic patients and one group obtained from nonallergic patients. When comparing mRNA levels of S100A7 in these groups, the same pattern as in NLF emerged. Tonsils from allergic patients expressed lower levels of S100A7 compared with tonsils from nonallergic individuals (212 ± 33 and 364 ± 45, respectively: Fig. 6).

Because the same tonsils were used when dividing the tonsils according to infection and allergy status, respectively, we also wanted to investigate whether there was an interaction between these two variables. However, neither the ANOVA on the original data ($P = 0.88$) nor the analysis of the ranked data ($P = 0.91$) gave any indication of an interaction.
Thus, the effects of allergy and infection appear to act in an additive manner.

**Discussion**

In the present study, S100A7 is described in human palatine tonsils. It is found in epithelial, B and T cells, and the expression in CD8⁺ T cells appears to be the highest among subsets of lymphocytes. A downregulation is noticed in infected tonsils as well as in tonsils from allergic patients, but in vitro stimulation with lipopolysaccharide does not affect the expression.

S100A7 was originally identified in the skin (Madsen et al., 1991), but has since been described in several other tissues (Madsen et al., 1991; Moog-Lutz et al., 1995; Celis et al., 1996). Although S100A7 lacks a signal peptide, it is probably secreted (Madsen et al., 1991), because the protein has been detected in different body fluids and secretions like amniotic fluid, vernix, urine and nasal secretion (Celis et al., 1996; Yoshio et al., 2003; Bryborn et al., 2005; Porre et al., 2005). In skin and vernix, S100A7 seems to function as an AMP (Yoshio et al., 2003; Glaser et al., 2005), and because palatine tonsils are highly exposed to bacteria, the high expression of S100A7 in this tissue suggests an antimicrobial role for S100A7 in this compartment as well. However, as mentioned before, there is not much described of the effects of S100A7 on bacteria colonizing the tonsils and further studies are needed to answer this question.

The immunohistochemical analysis indicates that S100A7 is present in tonsillar epithelial cells as well as in B and T cells. It is well known that airway epithelial cells secrete AMPs as a defense mechanism against infections (Bals, 2000), and evidence is now accumulating that these peptides are also expressed in airway immune cells like macrophages and lymphocytes (Wah et al., 2006). The role AMPs play in immune cells is not fully described but many AMPs are reported to act as inflammatory mediators, and because S100A7 is known to induce migration of CD4⁺ T cells and neutrophils (Jinquan et al., 1996), one can speculate that lymphocytes secrete S100A7 in order to recruit and activate other inflammatory cells. Respiratory tract lymphocytes expressing defensins are mainly CD8⁺ cells (Wah et al., 2006), in accordance with the role of this cell type in the acute defense against microorganisms. The same might be true for S100A7, explaining the higher expression of S100A7 in CD8⁺ T cells seen in this study.

Microorganisms are characterized by pathogen-associated molecular patterns recognized by the innate immune system through pattern recognition receptors (Janeway & Medzhitov, 2002). One important type of these receptors is the Toll-like receptors (TLRs) (Heine & Lien, 2003). Lipopolysaccharide is a gram-negative bacterial cell wall component interacting with TLR4 (Chow et al., 1999). TLR4 is expressed in human tonsillar tissue (Claeys et al., 2003; Mansson et al., 2006a,b), but in the present study in vitro stimulation of fresh tonsil pieces with lipopolysaccharide did not have any significant effect on the S100A7 mRNA levels. In a recent study, the TLR5 agonist flagellin and not lipopolysaccharide was shown to be the principal inducer of S100A7 in human epidermal keratinocytes exposed to the gram-negative bacterium, E. coli (Abtin et al., 2008). This might explain why there is no effect of the lipopolysaccharide stimulation in the present study.

Although in vitro stimulation with lipopolysaccharide did not have any effect on the S100A7 expression, a significant downregulation of S100A7 was detected in infected tonsils. This is in contrast to other studies concerning AMPs and tonsillar infection, where, in general, an increase of these proteins is described during infection (Song et al., 2006; Wah et al., 2006). Although S100A7 expression is induced in the skin in response to stimulation with bacterial products (Glaser et al., 2005), this does not seem to be the case in palatine tonsils, indicating that S100A7 may have tissuespecific functions. As mentioned previously, the functions of S100A7 are poorly understood and no receptor has been identified. Several S100 proteins bind to RAGE, the receptor for advanced glycation end products (Hofmann et al., 1999), but there are so far no studies describing an interaction between S100A7 and this receptor. There are at least two possible scenarios that can explain the reduced levels of S100A7 in infected tonsils. The first is that tonsillar infection causes a downregulation of S100A7, and the second is that individuals with low expression are more prone to develop recurrent infections. The reported antimicrobial properties of S100A7 support the latter.

A decreased S100A7 expression was also found in tonsils from allergic individuals. This finding is in line with our...
previous experiment, showing that S100A7 is decreased in NLF from allergic subjects (Bryborn et al., 2005). Because S100A7 has chemotactic properties (Jinquan et al., 1996), a decreased expression in allergic patients can result in an altered immunological response and possibly a loss of the T-helper type-1 (Th1) response, favoring Th2 activity, leading to an allergic response.

Microorganisms in our environment have strong immunomodulatory effects, which can be linked to development of allergic disease (Vandenbulcke et al., 2006). Patients with atopic eczema often have increased susceptibility to bacterial infections in the skin, due to inhibited AMP expression caused by Th2 cytokines (Ong et al., 2002; Nomura et al., 2003). The effects of Th2 cytokines on S100A7 expression are not known, but it is possible that high levels of Th2 cytokines in allergic individuals inhibit the expression of S100A7, as has been reported for other AMPs (Nomura et al., 2003). In contrast to this theory, there are data suggesting an upregulation of S100A7 in atopic skin lesions (Sugiura et al., 2005). It is, however, not known what causes this upregulation. The S100A7 gene that codes for S100A7 is situated in the epidermal differentiation complex on chromosome 1q21 (Mischke et al., 1996), and previous studies describe the involvement of S100A7 in keratinocyte differentiation (Martinsson et al., 2005). Is the observed upregulation of S100A7 in atopic dermatitis due to the atopic background or the disturbed keratinocyte differentiation associated with the disease? Further studies are needed to explore the effects of Th2 cytokines on the expression of S100A7. In addition to Th2 cytokines, IL-22 has been shown to regulate the expression of antimicrobial proteins, including S100A7 (Wolk et al., 2006). IL-22 is secreted from T cells, mainly Th1, and induces increased S100A7 expression in epithelial cells.

As a final point, it is worth noting that although we used in this study the same tonsils when dividing the tonsils according to infection and allergy status, respectively, the percentage infected tonsils in the allergic and nonallergic groups did not differ. In addition, we could not find an interaction between the two different conditions, allergy and infection. It thus seems like both infection and allergy affect the S100A7 expression in human palatine tonsils, but in an additive manner. In conclusion, the regulation of S100A7 found to be altered in inflammatory processes, such as tonsillar infection and allergic conditions. It is still not clear whether low levels of S100A7 contribute to the development of disease or whether they are a consequence of the disease. Still, the altered levels of S100A7 in this study suggest a role for S100A7 in recurrent tonsillitis and allergic disease.

Acknowledgements

This work was supported by the Swedish Medical Research Council, the Swedish Heart Lung Foundation, the Swedish Association for Allergology and the Swedish Foundation for Health Care Science and Allergic Research. The authors would like to thank Ingegerd Larsson and Ann Reutherborg for generous help with collecting the tonsil material, and Torbjörn Säll for helping with some of the statistical analysis.

References


