

## Gene Section Review

### SLPI (secretory leukocyte peptidase inhibitor)

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#### Abstract

Secretory Leukocyte Peptidase Inhibitor (SLPI) functionality in health and disease: Secretory Leukocyte Peptidase Inhibitor (SLPI) is a serine protease inhibitor of cathepsin G, trypsin and chymotrypsin, but primarily against neutrophil elastase. Its major function is to inhibit inflammation by blocking the proteolytic activity of these proteinases released by leukocytes and also through down-modulation of several cytokines. The anti-inflammatory activity is also mediated by inhibition of the activation of the transcription nuclear factor NF- $\kappa$ B. Some studies localized the molecule within the cytosol and in secondary granules of neutrophils. Because of this, it is believed that neutrophil-derived SLPI may regulate the protease/antiprotease balance at sites of tissue inflammation. In relation with the adaptive immune system, it was suggested that SLPI modulates the cellular and humoral immune response, by decreasing the T cell proliferation and reducing the class switching. Also, it is known that this polycationic non-glycosylated peptide, displays anti-microbial properties against bacteria, viruses (in particular HIV) and fungus. In summary, the SLPI is a pleiotropic molecule, implicated in physiological and pathological events, such as wound healing, pregnancy, chronic obstructive pulmonary disease, cancer, ischemia reperfusion injury and stroke, among others. Their detection in serum and biological fluids may be useful as a biomarker to diagnosis and prognosis for certain diseases.

#### Keywords

SLPI, antimicrobial activity, anti-inflammatory activity, anti-tumoral activity.

#### Identity

**Other names:** ALK1, ALP, HUSI, HUSI-I, BLPI, MPI, WAP4, WFDC4

**HGNC (Hugo):** SLPI

**Location:** 20q13.12 chr20:43,881,055- 43,883,184 (reverse strand)

#### DNA/RNA

##### Description

SLPI belongs to the whey acidic protein four-disulfide core family of proteins. The human SLPI gene is localized on chromosome 20q12-13.2 (Kikuchi et al. 1998). The SLPI gene consists of four exons and three introns, it spans approximately 2.6 kb (Kikuchi et al. 1998; Stetler et al. 1986). The SLPI gene is stable and seems to be nonpolymorphic (Abe et al. 1991). Though, it has the potential to be modulated at both the transcriptional and post-transcriptional levels (Abe et al. 1991). Up to date, it has not been detected a state of SLPI deficiency. However, patients with severe congenital neutropenia (a primary immunodeficiency syndrome characterized by mutations in at least 6 different genes) were found to have strongly reduced SLPI levels, being SLPI a key factor for the neutrophil differentiation in the bone marrow (Klimenkova et al. 2014).

## Transcription

The SLPI gene is actively transcribed in mucosal cells, being the half-life of the transcripts of approximately 12 h. Close to the exon 1, SLPI gene has four potential binding sites for transcription factor AP-1, three for AP-2 and one for C/EPB (Klimenkova et al. 2014). Also, Kikuchi et al., describes that SLPI has a promoter region which has a recognition sequence for two transcription factors, one of which is highly expressed in lung cell lines, and the other in nonlung cell lines (Kikuchi et al. 1997).

## Protein

### Description

SLPI is an 11,7 kDa molecular weight non-glycosylated protein composed by 132 amino acids (Stolk et al. 1999). The amino acid sequence of SLPI generates a highly polycationic peptide with two highly homologous domains. These two domains (COOH and NH<sub>2</sub> terminal domains) share around a 35% homology (Vogelmeier et al. 1996). Each domain contains eight cysteine residues that form four disulfide bonds, which helps to stabilize the structure of the molecule (Grutter et al. 1988). These cysteine rich domains are also called WAP domains (Whey Acid Protein). Domain 2 was initially described to bind and inhibit the serine proteases such as trypsin and elastase, while the domain 1 was probably not inhibitory (Eisenberg et al. 1990; Meckelein et al. 1990). It has been proposed that this last domain helps in the stabilization of the complexes "SLPI:elastase". Also, it is believed that the domain 1 mediates binding to heparin, and thus increases its antiprotease activity, probably as a result of a conformational change of the molecule (Faller et al. 1992).

### Expression

SLPI was first isolated from bronchial secretions (Hochstrasser et al. 1972; Ohlsson et al. 1976). Then the SLPI was characterized by two groups of researchers, whom purified the molecule from the urine and (Seemuller et al. 1986) and the parotid gland secretions (Thompson et al. 1986). SLPI is located in both, the extracellular matrix and the intracellular compartments, suggesting that it could exert autocrine and paracrine effects (Taggart et al. 2005).

The expression of SLPI is constitutive as well as modulated by different factors. Constitutively SLPI can be found in serum and in extravascular mucosal fluids. Thus, it is found around of 40 (26.1-65.0) ng/ml in serum, 72 (0.4-250) ng/ml in bronchial lavage fluid (Hollander et al. 2007), in exhaled breath condensate (2.82 - 0.58 pg/ml) (Tateosian et al. 2012) and saliva (0.3-3.2 ug/ml) (Shugars et al.

2001). However, concentrations of the molecule vary depending on age and gender of the individual tested. In vivo, it is produced in the lung by tracheal serous glands and by clear bronchial cells. In male (Ohlsson et al. 1995) and female (Moriyama et al. 1999) genital tracts, SLPI is located in seminal plasma and cervical mucosa, respectively. Furthermore, it is produced by the parotid glands, intestinal epithelial cells (Si-Tahar et al. 2000), renal tubule cells (Ohlsson et al. 2001), keratinocytes (Wiedow et al. 1998), beta cells of the pancreas (Nystrom et al. 1999) and immune cells like neutrophils and alveolar macrophages (Sallenave et al. 1997; Mihaila et al. 2001; Guerrieri et al. 2011). The SLPI expression is modulated by different molecules. It has been shown that SLPI is up-regulated by LPS, IL-1beta, TNF-alpha, neutrophil elastase, alpha-defensins, surfactant protein A, corticosteroid and progesterone (Sallenave et al. 1994; Reid et al. 1999; Maruyama et al. 1994; Abbinante-Nissen et al. 1995; King et al. 2003; Velarde et al. 2005; van Wetering et al. 2000; Ramadas et al. 2009). Finally, apoptotic cells can upregulate SLPI production by macrophages (Odaka et al. 2003).

In contrast, few factors can downmodulate the expression of SLPI. Among them, the most significant are IFN-gamma and TGF-beta (Jaumann et al. 2000; Jin et al. 1997).

Although, the structure of SLPI seems to be stable, it could be cleaved and inactivated by chymase (Belkowski et al. 2008), cathepsins B, L, S (Taggart et al. 2001), lipid peroxidation products (Tomova et al. 1994) and Host dust mite 1 allergen (Brown et al. 2003), among others (Weldon et al. 2009).

### Function

**Antiprotease activity:** The inhibition of protease activity was described for C-terminus domain against elastase, cathepsin G, trypsin, chymotrypsin, tryptase and chymase (Williams et al. 2006). Thus, SLPI major function is inhibit inflammation by blocking the proteolytic activity of serine proteinases released by leukocytes and also through blocking the LPS effects, such as the upregulation of several cytokines like TNF-alpha, MCP-1 and IL-6 (Yang et al. 2005; Jin et al. 1998; Taggart et al. 2005; Ashcroft et al. 2000). SLPI acts locally to maintain a protease/antiprotease balance thereby preventing protease mediated tissue destruction (Vogelmeier et al. 1990). In the lungs, the disturbance of this balance is responsible for various lung diseases, many of which are initiated and maintained by the recruitment and activation of neutrophils (Birrer et al. 1994; Suter 1989).

**Anti-inflammatory activity:** SLPI has anti-inflammatory activities not necessarily related to its

ability to inhibit extracellular proteases. The anti-inflammatory activity is also mediated by inhibition of proteolytic degradation of I $\kappa$ B, an inhibitor of the nuclear factor NF- $\kappa$ B (Ashcroft et al. 2000; Samsom et al. 2007).

It has been shown that over-expression of SLPI inhibits NF- $\kappa$ B, which is a transcription factor of several pro-inflammatory mediators in pulmonary inflammation (Henriksen et al. 2004). Currently, there are some evidence that SLPI is rapidly taken up by cells and is localized in the nucleus and cytoplasm (Taggart et al. 2002). In the cytoplasm, SLPI prevents degradation of several key proteins in the regulated activation of NF- $\kappa$ B, as I $\kappa$ B $\alpha$ , I $\kappa$ B $\beta$  and IRAK (IL-1-receptor-associated kinase) through the ubiquitin-proteasome mechanism (Greene et al. 2004; Taggart et al. 2002), that follows the activation of NF- $\kappa$ B by LPS or LTA (lipoteichoic acids). Also it has been proposed that SLPI acting in the nucleus can bind to NF- $\kappa$ B consensus region of target genes (Taggart et al. 2005). The entering into the nucleus occurs through a mechanism in which SLPI may traverse membranes, due to its cationic nature (favored by the high content of arginine and lysine) by interaction with the negatively charged membrane. Independently of the mode of action, in vivo experiments have demonstrated anti-inflammatory / pro-apoptotic activities in the lung, and in a variety of other organs.

Microbicidal activity:

- Against Bacteria:

SLPI displays anti-microbial properties in vivo and in vitro (Sallenave 2002; Gomez et al. 2009). It has been recently reported that mouse and even human SLPI shows anti-bacterial activity against mycobacteria and it constitutes a pattern recognition receptor (PRR), that not only kills the microorganism, but also facilitates their phagocytosis by murine and human macrophages (Nishimura et al. 2008; Gomez et al. 2009). Either the antimicrobial activity or PRR ability depends on the COOH terminal domain where the inhibitory activity of serine proteases resides. The WAPs domains of the molecule are involved, and this is due to cationic residues that allow the disruption of the membranes of target organisms (Verma et al. 2007; Gomez et al. 2009; Nishimura et al. 2008). The antimicrobial activity of human SLPI has been described for various bacteria such as *Pseudomonas aeruginosa*, *Staphylococcus aureus*, *Staphylococcus epidermidis* (Wiedow et al. 1998; Wingens et al. 1998), *Mycobacterium tuberculosis* (Gomez et al. 2009), and *Escherichia coli* (Williams et al. 2006). Therefore this activity is against Gram negative and Gram positive bacteria and is part of the defense system of the mucosa.

- Against Viruses:

SLPI has been suggested as the main soluble factor responsible for the HIV inhibitory effect of saliva. It

is well-established that human saliva inhibits HIV infectivity in vitro (McNeely et al. 1995; Nagashunmugam et al. 1997; Shugars et al. 2001; Malamud et al. 1992; Fultz 1986). The infection of adherent primary monocytes with HIV-1 was significantly suppressed in the presence of human saliva [76-80]. Four in vitro studies have demonstrated that SLPI has anti-HIV-1 activity in cells that included peripheral blood mononuclear cells, purified primary T cells, and SupT1 cells, a lymphocyte-derived tumor cell line (Fultz 1986; Hocini et al. 2000; Shugars et al. 1997; Skott et al. 2002).

Evidence suggests that SLPI blocks HIV-1 internalization in a dose-dependent manner (McNeely et al. 1997). McNeely et al. found that SLPI inhibits a step of viral infection that occurs after virus binding but before reverse transcription. In a co-precipitation experiment, it was described a 55-kDa cell surface protein from monocytes by using anti-SLPI antibodies. For some authors, the interaction between HIV and CCR5 could be the main target of SLPI (Naif et al. 1998). Other authors showed that SLPI interferes with HIV fusion with the T-cell plasma membrane through binding to scramblase 1, a membrane protein that interacts with CD4 and controls the movement of the phospholipid bilayer of the plasma membrane (Shugars et al. 1999). It was also demonstrated that in myeloid cell, SLPI blocks viral entry/fusion as a result of binding to annexin II (Ohlsson et al. 2001; Ma et al. 2004; Drannik et al. 2011). This molecule is a macrophage receptor that binds to phosphatidylserine moiety that HIV carries on its outer layer on exiting from an infected cell (Ohlsson et al. 2001; Drannik et al. 2011; Ma et al. 2004). Furthermore, the elastase inhibiting activity of SLPI was not essential for their anti-HIV-1 activity (McNeely et al. 1997).

- Against Fungi:

*C. albicans* and *Aspergillus fumigatus* were sensitive to the antimicrobial activity of recombinant SLPI. This activity was localized to N-terminal domain of the molecule (Tomee et al. 1997).

**Wound healing activity:** The role of SLPI in tissue repair was suggested by the observation that in human, epithelial expression of SLPI is increased in damaged skin (Wingens et al. 1998). Studies in SLPI deficient mice demonstrated that SLPI has an essential role in wound healing (Ashcroft et al. 2000). In the absence of SLPI, the animals presents a delay in cutaneous wound healing, which is attributed to an increased and prolonged inflammatory response during the repair process, and a delay in the accumulation of the matrix. The altered inflammatory profile involves enhanced activation of local TGF- $\beta$  (Ashcroft et al. 2000).

**Immunomodulatory activity in adaptive immune response:** The effect of SLPI seems not to be limited to innate immune response but also to the cellular

and humoral adaptive immune response. In fact, the high SLPI expression was found in dendritic cells of mucosal lymph node and it was suggested that these dendritic cells regulate cellular activation to microbial products and maintain the tolerance threshold (Samsom et al. 2007).

Also, we have observed that SLPI decreases lymphocyte proliferation, a phenomenon which depends on the presence of monocytes (Guerrieri et al. 2011). However, it is not possible to rule out a direct effect of SLPI on lymphocytes since it is able to bind the receptors phospholipid scramblases 1 and 4 on CD4 T cells (Py et al. 2009). On tonsillar cells, SLPI inhibits B cells expressing activation-induced cytidine deaminase, an enzyme involved in class switching.

Thus, the overall idea is that SLPI is a tolerogenic factor, that it is able to down modulate the innate and adaptive immune response. Moreover, recently it has been shown that the hyporesponsiveness of human buccal epithelium to microbial stimulation is a phenomenon that depends on SLPI expression. (Menckeberg et al. 2015).

Recently, it has been also described that SLPI, in conjunction of neutrophil DNA or cathepsin G and human neutrophil elastase, induced a marked production of type I interferon by plasmacytoid dendritic cells (Skrzeczynska-Moncznik et al. 2012; Skrzeczynska-Moncznik et al. 2013).

On the other hand, it was found that SLPI inhibits the formation of neutrophil extracellular traps; structures that are involved in the elimination of microorganisms, and also in the presentation of autoantigens (Zabieglo et al. 2015). These findings suggest a role of SLPI in autoimmune diseases.

## Implicated in

### Cancer

The invasiveness of tumors occurs through infiltration of tumor cells into healthy tissue and by angiogenesis, which is modulated by proteases and antiproteases released from tumor cells that carry out tissue remodeling.

Many studies have shown that SLPI expression is modulated in cancer. However, there has been reported an increased or decreased expression profile of the protein depending on the type of tumor.

For example, SLPI expression is increased in pancreatic (Iacobuzio-Donahue et al. 2003), thyroid (Jarzab et al. 2005), cervix (Rein et al. 2004), endometrial (Zhang et al. 2002), ovarian (Israeli et al. 2005) and gastric cancer (Cheng et al. 2008).

In contrast, it is weakly expressed in nasopharyngeal carcinoma (Sriuranpong et al. 2004; Huang et al. 2012), bladder tumors (Liang et al. 2002) and some breast carcinomas (Hu et al. 2004). As we mentioned above, in ovarian cancer, SLPI is over-expressed and is thought to have a carcinogenic function (Hough et

al. 2001; Clauss et al. 2005; Devoogdt et al. 2009) independent of its antiprotease activity (Simpkins et al. 2008). However, in Lewis lung cancer cells, the pro-tumoral activity was shown to be dependent on its protease inhibitor activity (Devoogdt et al. 2003). Also, it was described that SLPI plasma levels were elevated in lung cancer patients (Zelvyte et al. 2004). More recently, low level of SLPI was detected in oral squamous cell carcinoma compared with normal oral epithelium (Wen et al. 2011). Moreover, an inverse correlation was also reported between SLPI and histological parameters associated with tumor progression (Wen et al. 2011). Interestingly, SLPI reduced the hepatic lung carcinoma metastasis (Wang et al. 2006). In breast tumors, the mRNA expression of SLPI either increases or decreases depending on the case (Kluger et al. 2004; Stoff-Khalili et al. 2005). Also in a breast tumor cell line, the SLPI overexpressing cells did not develop tumors in mice (Amiano et al. 2013). This effect was specific for this type of cell line, since colon tumor cells overexpressing SLPI, developed faster tumors than control cells. Moreover, the breast cancer cell line that overexpresses SLPI showed a decrease in E-cadherin expression, pro-apoptotic effects and cell cycle arrests. (Rosso et al. 2014). Interestingly, the administration of these SLPI transfected cells, which do not develop tumor in immunocompetent mice, inhibited the tumor growth and increased the survival of mice that were inoculated with mock transfected control cells. (Amiano et al. 2011).

In ovarian cancer SLPI inhibits cell growth through an apoptotic pathway (Nakamura et al. 2008), while, it has been also described that over-expression of SLPI is capable of producing a more aggressive ovarian cancer in vitro and in vivo models (Devoogdt et al. 2009). In fact, it was suggested that SLPI could be a useful diagnostic and prognostic tool in ovarian cancer (Carlson et al. 2013).

The SLPI gene and the protein expression are significantly lower in metastatic "head and neck squamous cell carcinoma" compared with non-metastatic ones. Also, an inverse significant correlation with HPV status was found for this kind of tumor (Hoffmann et al. 2013). Therefore, overall these data suggests us that it is not possible to generalize the findings related to SLPI expression and function in only a unique type of tumor, since its expression and modulation seems to be tumor specific.

### Pregnancy

SLPI among others antimicrobial peptides seems to play a role in pregnancy. SLPI is produced by amnion epithelium and deciduas (King et al. 2007). High levels of SLPI were found in the cervical mucus plug during human pregnancy. The SLPI mRNA expression was higher in the second and the third trimester when compared with the first one



(Itaoka et al. 2015). Thus, in amniotic fluid, its concentration increases according to the period of pregnancy and the highest levels is reached on the onset of labor (Denison et al. 1999). As SLPI is a natural antimicrobial molecule, it may be involved in the prevention of uterine infection during pregnancy and labor, and be a modulator of inflammation in this stage.

### **Autoimmunity**

High levels of SLPI have been observed in several autoimmune diseases. For example, it was observed in: i) inflamed joint tissues in a rat model of arthritis (Song et al. 1999); ii) patients with primary Sjögren's syndrome (Maruyama et al. 1998); iii) immune cells infiltrating the corpus in autoimmune gastritis (Hritz et al. 2006); iv) macrophages, activated microglia, neuronal cells and astrocytes during experimental autoimmune encephalomyelitis (Mueller et al. 2008).

In contrast, the administration of systemic SLPI or microencapsulated SLPI has proven to reduce the injury found in tissues of different autoimmune models (Guazzone et al. 2011; Song et al. 1999). Overall, these results highlight the *in vivo* immunosuppressive effect of SLPI. However, it has been also implicated in the pathogenesis of other autoimmune diseases such as psoriasis. As we mentioned above, Nestle et al. have demonstrated that the IFN $\alpha$ , produced by plasmacytoid dendritic cells in response to DNA structures, containing the neutrophil serine protease cathepsin G (CatG) and SLPI was important in the development of psoriatic skin lesions (Skrzeczynska-Moncznik et al. 2013). In fact, the neutralization of SLPI reduces the severity of experimental autoimmune encephalitis (Muller et al. 2012).

### **Tuberculosis**

Exposure of murine peritoneal macrophages to *Mycobacterium tuberculosis* led to an increase in SLPI protein secretion (Ding et al. 2005) which seems to be a pattern recognition receptor for micobacterias and inhibits the growth of them (Nishimura et al. 2008; Gomez et al. 2009). In plasma of tuberculosis patients, the SLPI and IFN- $\gamma$  levels were significantly higher compared with the levels found in healthy subjects. Moreover, a direct association between SLPI levels and the severity of tuberculosis was detected. The main protective cytokine in tuberculosis, IFN- $\gamma$ , decreased the expression of SLPI in healthy subjects but not in tuberculosis patients, probably because of the low expression of IFN- $\gamma$  detected in these patients (Tateosian et al. 2014).

### **Chronic obstructive pulmonary disease (COPD)**

Emphysema may be due to an imbalance in protease-antiprotease activity. Patients with COPD show high levels of SLPI compared with healthy subjects (Hollander et al. 2007). Conversely, SLPI levels are decreased during COPD exacerbations produced by bacterial infection or rhinovirus (Mallia et al. 2012).

### **Ischemia reperfusion injury**

It has been described a protective effect of SLPI in different ischemia/reperfusion injury models, such as heart and liver (Amberger et al. 2002; Lentsch et al. 1999). We have also observed a beneficial effect of SLPI in kidney ischemia reperfusion injury (unpublished result). Interestingly, in cardiac transplantation, null mice for SLPI had an impaired function after cold ischemia unlike the wild type (Schneeberger et al. 2008). Moreover, when SLPI was added to the preservation solution, myocardial contraction was restored to normal.

### **Central Nervous System Ischemia**

In two rat models, one of focal cerebral ischemia (Wang et al. 2003) and the other of spinal injury, it was observed high levels of SLPI. The same was seen in ischemic stroke in humans (Ilzecka et al. 2002). Interestingly, the administration of SLPI has been shown to be neuroprotective in both models of injury in rats (Wang et al. 2003; Hannila et al. 2013). Taking into account that the SLPI can promote axonal regeneration, plus the evidence of their neuroprotective effects, we could consider this molecule as potential therapeutic tool for different nervous system diseases (Hannila 2014).

### **Biomarker**

It has been found that the determination of serum SLPI levels could be useful as a marker of several diseases, such as disease activity in systemic sclerosis with interstitial lung disease (Aozasa et al. 2012). Also, it has been suggested that a form of cleaved SLPI can reflect the disease activity of patients with allergic rhinitis and asthma (Belkowski et al. 2009). It was also been proposed as a biomarker in ovarian and gastric cancer (Devoogdt et al. 2009; Cheng et al. 2008), or to identify subjects at risk of infections and malignant transformation due to HIV infection (Nittayananta et al. 2013). Recently, it was proposed as a biomarker for acute kidney injury after transplantation (Wilflingseder et al. 2014). However, until now none of these assays have been introduced in the clinical settings.

## **References**

Abbinante-Nissen JM, Simpson LG, Leikauf GD. Corticosteroids increase secretory leukocyte protease

- inhibitor transcript levels in airway epithelial cells. *Am J Physiol*. 1995 Apr;268(4 Pt 1):L601-6
- Abe T, Kobayashi N, Yoshimura K, Trapnell BC, Kim H, Hubbard RC, Brewer MT, Thompson RC, Crystal RG. Expression of the secretory leukoprotease inhibitor gene in epithelial cells. *J Clin Invest*. 1991 Jun;87(6):2207-15
- Amberger A, Schneeberger S, Hernegger G, Brandacher G, Obrist P, Lackner P, Margreiter R, Mark W. Gene expression profiling of prolonged cold ischemia and reperfusion in murine heart transplants. *Transplantation*. 2002 Nov 27;74(10):1441-9
- Amiano N, Reiteri RM, Costa MJ, Tateosian N, Chuluyan HE. Immunotherapy with SLPI over-expressing mammary tumor cells decreases tumor growth. *Cancer Immunol Immunother*. 2011 Jun;60(6):895-900
- Amiano NO, Costa MJ, Reiteri RM, Payés C, Guerrieri D, Tateosian NL, Sánchez ML, Maffia PC, Diamant M, Karas R, Orqueda A, Rizzo M, Alaniz L, Mazzolini G, Klein S, Sallenave JM, Chuluyan HE. Anti-tumor effect of SLPI on mammary but not colon tumor growth. *J Cell Physiol*. 2013 Feb;228(2):469-75
- Aozasa N, Asano Y, Akamata K, Noda S, Masui Y, Tamaki Z, Tada Y, Sugaya M, Kadono T, Sato S. Clinical significance of serum levels of secretory leukocyte protease inhibitor in patients with systemic sclerosis *Mod Rheumatol* 2012 Aug;22(4):576-83
- Ashcroft GS, Lei K, Jin W, Longenecker G, Kulkarni AB, Greenwell-Wild T, Hale-Donze H, McGrady G, Song XY, Wahl SM. Secretory leukocyte protease inhibitor mediates non-redundant functions necessary for normal wound healing *Nat Med* 2000 Oct;6(10):1147-53
- Belkowski SM, Boot JD, Mascelli MA, Diamant Z, de Garavilla L, Hertzog B, Polkovitch D, Towers M, Batheja A, D'Andrea MR. Cleaved secretory leukocyte protease inhibitor as a biomarker of chymase activity in allergic airway disease *Clin Exp Allergy* 2009 Aug;39(8):1179-86
- Birrer P, McElvaney NG, Rådeberg A, Sommer CW, Liechti-Gallati S, Kraemer R, Hubbard R, Crystal RG. Protease-antiprotease imbalance in the lungs of children with cystic fibrosis *Am J Respir Crit Care Med* 1994 Jul;150(1):207-13
- Brown A, Farmer K, MacDonald L, Kalsheker N, Pritchard D, Haslett C, Lamb J, Sallenave JM. House dust mite Der p 1 downregulates defenses of the lung by inactivating elastase inhibitors *Am J Respir Cell Mol Biol* 2003 Sep;29(3 Pt 1):381-9
- Carlson AM, Maurer MJ, Goergen KM, Kalli KR, Erskine CL, Behrens MD, Knutson KL, Block MS. Utility of progranulin and serum leukocyte protease inhibitor as diagnostic and prognostic biomarkers in ovarian cancer *Cancer Epidemiol Biomarkers Prev* 2013 Oct;22(10):1730-5
- Cheng WL, Wang CS, Huang YH, Liang Y, Lin PY, Hsueh C, Wu YC, Chen WJ, Yu CJ, Lin SR, Lin KH. Overexpression of a secretory leukocyte protease inhibitor in human gastric cancer *Int J Cancer* 2008 Oct 15;123(8):1787-96
- Clauss A, Lilja H, Lundwall A. The evolution of a genetic locus encoding small serine proteinase inhibitors *Biochem Biophys Res Commun* 2005 Jul 29;333(2):383-9
- Denison FC, Kelly RW, Calder AA, Riley SC. Secretory leukocyte protease inhibitor concentration increases in amniotic fluid with the onset of labour in women: characterization of sites of release within the uterus *J Endocrinol* 1999 May;161(2):299-306
- Devoogdt N, Rasool N, Hoskins E, Simpkins F, Tchabo N, Kohn EC. Overexpression of protease inhibitor-dead secretory leukocyte protease inhibitor causes more aggressive ovarian cancer in vitro and in vivo *Cancer Sci* 2009 Mar;100(3):434-40
- Ding A, Yu H, Yang J, Shi S, Ehrt S. Induction of macrophage-derived SLPI by *Mycobacterium tuberculosis* depends on TLR2 but not MyD88 *Immunology* 2005 Nov;116(3):381-9
- Drannik AG, Henrick BM, Rosenthal KL. War and peace between WAP and HIV: role of SLPI, trappin-2, elafin and ps20 in susceptibility to HIV infection *Biochem Soc Trans* 2011 Oct;39(5):1427-32
- Eisenberg SP, Hale KK, Heimdal P, Thompson RC. Location of the protease-inhibitory region of secretory leukocyte protease inhibitor *J Biol Chem* 1990 May 15;265(14):7976-81
- Faller B, Frommherz K, Bieth JG. Heparin interferes with the inhibition of neutrophil elastase by its physiological inhibitors *Biol Chem Hoppe Seyler* 1992 Jul;373(7):503-8
- Fultz PN. Components of saliva inactivate human immunodeficiency virus *Lancet* 1986 Nov 22;2(8517):1215
- Gomez SA, Argüelles CL, Guerrieri D, Tateosian NL, Amiano NO, Slimovich R, Maffia PC, Abbate E, Musella RM, Garcia VE, Chuluyan HE. Secretory leukocyte protease inhibitor: a secreted pattern recognition receptor for mycobacteria *Am J Respir Crit Care Med* 2009 Feb 1;179(3):247-53
- Grütter MG, Fendrich G, Huber R, Bode W. The 2.5 Å X-ray crystal structure of the acid-stable proteinase inhibitor from human mucous secretions analysed in its complex with bovine alpha-chymotrypsin *EMBO J*
- Greene CM, McElvaney NG, O'Neill SJ, Taggart CC. Secretory leukocyte protease inhibitor impairs Toll-like receptor 2- and 4-mediated responses in monocytic cells *Infect Immun* 2004 Jun;72(6):3684-7
- Guazzone VA, Guerrieri D, Jacobo P, Glisoni RJ, Chiappetta D, Lustig L, Chuluyan HE. Micro-encapsulated secretory leukocyte protease inhibitor decreases cell-mediated immune response in autoimmune orchitis *Life Sci* 2011 Jul 18;89(3-4):100-6
- Guerrieri D, Tateosian NL, Maffia PC, Reiteri RM, Amiano NO, Costa MJ, Villalonga X, Sanchez ML, Estein SM, Garcia VE, Sallenave JM, Chuluyan HE. Serine leukocyte proteinase inhibitor-treated monocyte inhibits human CD4(+) lymphocyte proliferation *Immunology* 2011 Aug;133(4):434-41
- Hannila SS. Secretory Leukocyte Protease Inhibitor (SLPI): Emerging Roles in CNS Trauma and Repair *Neuroscientist* 2014 Aug 12
- Hannila SS, Siddiq MM, Carmel JB, Hou J, Chaudhry N, Bradley PM, Hilaire M, Richman EL, Hart RP, Filbin MT. Secretory leukocyte protease inhibitor reverses inhibition by CNS myelin, promotes regeneration in the optic nerve, and suppresses expression of the transforming growth factor-signaling protein Smad2 *J Neurosci* 2013 Mar 20;33(12):5138-51
- Henriksen PA, Hitt M, Xing Z, Wang J, Haslett C, Riemersma RA, Webb DJ, Kotelevtsev YV, Sallenave JM. Adenoviral gene delivery of elafin and secretory leukocyte protease inhibitor attenuates NF-kappa B-dependent inflammatory responses of human endothelial cells and macrophages to atherogenic stimuli *J Immunol* 2004 Apr 1;172(7):4535-44

- Hochstrasser K, Reichert R, Schwarz S, Werle E. [Isolation and characterisation of a protease inhibitor from human bronchial secretion] *Hoppe Seylers Z Physiol Chem* 1972 Feb;353(2):221-6
- Hocini H, Becquart P, Bouhlal H, Adle-Biassette H, Kazatchkine MD, Bélec L. Secretory leukocyte protease inhibitor inhibits infection of monocytes and lymphocytes with human immunodeficiency virus type 1 but does not interfere with transcytosis of cell-associated virus across tight epithelial barriers *Clin Diagn Lab Immunol* 2000 May;7(3):515-8
- Hoffmann M, Quabius ES, Tribius S, Hebebrand L, Görögh T, Halec G, Kahn T, Hedderich J, Röcken C, Haag J, Waterboer T, Schmitt M, Giuliano AR, Kast WM. Human papillomavirus infection in head and neck cancer: the role of the secretory leukocyte protease inhibitor *Oncol Rep* 2013 May;29(5):1962-8
- Hollander C, Westin U, Wallmark A, Piitulainen E, Sveger T, Janciauskiene SM. Plasma levels of alpha1-antichymotrypsin and secretory leukocyte proteinase inhibitor in healthy and chronic obstructive pulmonary disease (COPD) subjects with and without severe alpha1-antitrypsin deficiency *BMC Pulm Med* 2007 Jan 29;7:1
- Hough CD, Cho KR, Zonderman AB, Schwartz DR, Morin PJ. Coordinately up-regulated genes in ovarian cancer *Cancer Res* 2001 May 15;61(10):3869-76
- Hritz I, Kuester D, Vieth M, Herszenyi L, Stolte M, Roessner A, Tulassay Z, Wex T, Malfertheiner P. Secretory leukocyte protease inhibitor expression in various types of gastritis: a specific role of *Helicobacter pylori* infection *Eur J Gastroenterol Hepatol* 2006 Mar;18(3):277-82
- Hu Y, Sun H, Drake J, Kittrell F, Abba MC, Deng L, Gaddis S, Sahin A, Baggerly K, Medina D, Aldaz CM. From mice to humans: identification of commonly deregulated genes in mammary cancer via comparative SAGE studies *Cancer Res* 2004 Nov 1;64(21):7748-55
- Huang C, Tang H, Zhang W, She X, Liao Q, Li X, Wu M, Li G. Integrated analysis of multiple gene expression profiling datasets revealed novel gene signatures and molecular markers in nasopharyngeal carcinoma *Cancer Epidemiol Biomarkers Prev* 2012 Jan;21(1):166-75
- Ilkayak Z, Zecka J, Stelmasiak Z. Increased serum levels of endogenous protectant secretory leukocyte protease inhibitor in acute ischemic stroke patients *Cerebrovasc Dis* 2002;13(1):38-42
- Iacobuzio-Donahue CA, Ashfaq R, Maitra A, Adsay NV, Shen-Ong GL, Berg K, Hollingsworth MA, Cameron JL, Yeo CJ, Kern SE, Goggins M, Hruban RH. Highly expressed genes in pancreatic ductal adenocarcinomas: a comprehensive characterization and comparison of the transcription profiles obtained from three major technologies *Cancer Res* 2003 Dec 15;63(24):8614-22
- Israeli O, Goldring-Avram A, Rienstein S, Ben-Baruch G, Korach J, Goldman B, Friedman E. In silico chromosomal clustering of genes displaying altered expression patterns in ovarian cancer *Cancer Genet Cytogenet* 2005 Jul 1;160(1):35-42
- Itaoka N, Nagamatsu T, Schust DJ, Ichikawa M, Sayama S, Iwasawa-Kawai Y, Kawana K, Yamashita T, Osuga Y, Fujii T. Cervical Expression of Elafin and SLPI in Pregnancy and Their Association With Preterm Labor *Am J Reprod Immunol* 2015 Jun;73(6):536-44
- Jarzab B, Wiench M, Fijarewicz K, Simek K, Jarzab M, Oczko-Wojciechowska M, Wloch J, Czarniecka A, Chmielik E, Lange D, Pawlaczek A, Szpak S, Gubala E, Swierniak A. Gene expression profile of papillary thyroid cancer: sources of variability and diagnostic implications *Cancer Res* 2005 Feb 15;65(4):1587-97
- Jaumann F, Elssner A, Mazur G, Dobmann S, Vogelmeier C. Transforming growth factor-beta1 is a potent inhibitor of secretory leukoprotease inhibitor expression in a bronchial epithelial cell line *Munich Lung Transplant Group Eur Respir J*
- Jin F, Nathan CF, Radzioch D, Ding A. Lipopolysaccharide-related stimuli induce expression of the secretory leukocyte protease inhibitor, a macrophage-derived lipopolysaccharide inhibitor *Infect Immun* 1998 Jun;66(6):2447-52
- Jin FY, Nathan C, Radzioch D, Ding A. Secretory leukocyte protease inhibitor: a macrophage product induced by and antagonistic to bacterial lipopolysaccharide *Cell* 1997 Feb 7;88(3):417-26
- Kikuchi T, Abe T, Hoshi S, Matsubara N, Tominaga Y, Satoh K, Nukiwa T. Structure of the murine secretory leukoprotease inhibitor (Slpi) gene and chromosomal localization of the human and murine SLPI genes *Am J Respir Cell Mol Biol* 1998 Dec;19(6):875-80
- King AE, Kelly RW, Sallenave JM, Bocking AD, Challis JR. Innate immune defences in the human uterus during pregnancy *Placenta* 2007 Nov-Dec;28(11-12):1099-106
- King AE, Morgan K, Sallenave JM, Kelly RW. Differential regulation of secretory leukocyte protease inhibitor and elafin by progesterone *Biochem Biophys Res Commun* 2003 Oct 17;310(2):594-9
- Klimenkova O, Ellerbeck W, Klimiankou M, Ünal M, Kandabarau S, Gigina A, Hussein K, Zeidler C, Welte K, Skokowa J. A lack of secretory leukocyte protease inhibitor (SLPI) causes defects in granulocytic differentiation *Blood* 2014 Feb 20;123(8):1239-49
- Kluger HM, Kluger Y, Gilmore-Hebert M, DiVito K, Chang JT, Rodov S, Mironenko O, Kacinski BM, Perkins AS, Sapi E. cDNA microarray analysis of invasive and tumorigenic phenotypes in a breast cancer model *Lab Invest* 2004 Mar;84(3):320-31
- Lentsch AB, Yoshidome H, Warner RL, Ward PA, Edwards MJ. Secretory leukocyte protease inhibitor in mice regulates local and remote organ inflammatory injury induced by hepatic ischemia/reperfusion *Gastroenterology* 1999 Oct;117(4):953-61
- Liang G, Gonzales FA, Jones PA, Orntoft TF, Thykjaer T. Analysis of gene induction in human fibroblasts and bladder cancer cells exposed to the methylation inhibitor 5-aza-2'-deoxycytidine *Cancer Res* 2002 Feb 15;62(4):961-6
- Müller AM, Jun E, Conlon H, Sadiq SA. Inhibition of SLPI ameliorates disease activity in experimental autoimmune encephalomyelitis *BMC Neurosci* 2012 Mar 21;13:30
- Ma G, Greenwell-Wild T, Lei K, Jin W, Swisher J, Hardegen N, Wild CT, Wahl SM. Secretory leukocyte protease inhibitor binds to annexin II, a cofactor for macrophage HIV-1 infection *J Exp Med* 2004 Nov 15;200(10):1337-46
- Malamud D, Friedman HM. HIV in the oral cavity: virus, viral inhibitory activity, and antiviral antibodies: a review *Crit Rev Oral Biol Med* 1993;4(3-4):461-6
- Mallia P, Footitt J, Sotero R, Jepson A, Contoli M, Trujillo-Torralbo MB, Keadze T, Aniscenko J, Oleszkiewicz G, Gray K, Message SD, Ito K, Barnes PJ, Adcock IM, Papi A, Stanciu LA, Elkin SL, Kon OM, Johnson M, Johnston SL. Rhinovirus infection induces degradation of antimicrobial peptides and secondary bacterial infection in chronic

- obstructive pulmonary disease *Am J Respir Crit Care Med* 2012 Dec 1;186(11):1117-24
- Maruyama M, Sugiyama E, Hori T, Murayama R, Nakazaki S, Yamashita N, Kobayashi M. Increased serum concentrations of secretory leukoprotease inhibitor in patients with primary Sjögren's syndrome *In Vivo* 1998 Sep-Oct;12(5):535-8
- McNeely TB, Shugars DC, Rosendahl M, Tucker C, Eisenberg SP, Wahl SM. Inhibition of human immunodeficiency virus type 1 infectivity by secretory leukocyte protease inhibitor occurs prior to viral reverse transcription *Blood* 1997 Aug 1;90(3):1141-9
- Meckelein B, Nikiforov T, Clemen A, Appelhans H. The location of inhibitory specificities in human mucus proteinase inhibitor (MPI): separate expression of the COOH-terminal domain yields an active inhibitor of three different proteinases *Protein Eng* 1990 Jan;3(3):215-20
- Menckeberg CL, Hol J, Simons-Oosterhuis Y, Raatgeep HR, de Ruiter LF, Lindenbergh-Kortleve DJ, Korteland-van Male AM, El Aidi S, van Lierop PP, Kleerebezem M, Groeneweg M, Kraal G, Elink-Schuurman BE, de Jongste JC, Nieuwenhuis EE, Samsom JN. Human buccal epithelium acquires microbial hyporesponsiveness at birth, a role for secretory leukocyte protease inhibitor *Gut* 2015 Jun;64(6):884-93
- Mihaila A, Tremblay GM. Human alveolar macrophages express elafin and secretory leukocyte protease inhibitor *Z Naturforsch C* 2001 Mar-Apr;56(3-4):291-7
- Moriyama A, Shimoya K, Ogata I, Kimura T, Nakamura T, Wada H, Ohashi K, Azuma C, Saji F, Murata Y. Secretory leukocyte protease inhibitor (SLPI) concentrations in cervical mucus of women with normal menstrual cycle *Mol Hum Reprod* 1999 Jul;5(7):656-61
- Mueller AM, Pedré X, Stempf I, Kleiter I, Couillard-Despres S, Aigner L, Giegerich G, Steinbrecher A. Novel role for SLPI in MOG-induced EAE revealed by spinal cord expression analysis *J Neuroinflammation* 2008 May 26;5:20
- Nagashunmugam T, Malamud D, Davis C, Abrams WR, Friedman HM. Human submandibular saliva inhibits human immunodeficiency virus type 1 infection by displacing envelope glycoprotein gp120 from the virus *J Infect Dis* 1998 Dec;178(6):1635-41
- Naif HM, Li S, Alali M, Sloane A, Wu L, Kelly M, Lynch G, Lloyd A, Cunningham AL. CCR5 expression correlates with susceptibility of maturing monocytes to human immunodeficiency virus type 1 infection *J Virol* 1998 Jan;72(1):830-6
- Nakamura K, Takamoto N, Hongo A, Kodama J, Abzua F, Nasu Y, Kumon H, Hiramatsu Y. Secretory leukoprotease inhibitor inhibits cell growth through apoptotic pathway on ovarian cancer *Oncol Rep* 2008 May;19(5):1085-91
- Nishimura J, Saiga H, Sato S, Okuyama M, Kayama H, Kuwata H, Matsumoto S, Nishida T, Sawa Y, Akira S, Yoshikai Y, Yamamoto M, Takeda K. Potent antimycobacterial activity of mouse secretory leukocyte protease inhibitor *J Immunol* 2008 Mar 15;180(6):4032-9
- Nittayananta W, Kemapunmanus M, Yangngam S, Talungchit S, Sriplung H. Expression of oral secretory leukocyte protease inhibitor in HIV-infected subjects with long-term use of antiretroviral therapy *J Oral Pathol Med* 2013 Mar;42(3):208-15
- Nyström M, Bergenfeldt M, Ljungcrantz I, Lindeheim A, Ohlsson K. Production of secretory leukocyte protease inhibitor (SLPI) in human pancreatic beta-cells *Mediators Inflamm* 1999;8(3):147-51
- Odaka C, Mizuochi T, Yang J, Ding A. Murine macrophages produce secretory leukocyte protease inhibitor during clearance of apoptotic cells: implications for resolution of the inflammatory response *J Immunol* 2003 Aug 1;171(3):1507-14
- Ohlsson K, Bjartell A, Lilja H. Secretory leukocyte protease inhibitor in the male genital tract: PSA-induced proteolytic processing in human semen and tissue localization *J Androl* 1995 Jan-Feb;16(1):64-74
- Ohlsson K, Tegner H. Inhibition of elastase from granulocytes by the low molecular weight bronchial protease inhibitor *Scand J Clin Lab Invest* 1976 Sep;36(5):437-45
- Ohlsson S, Ljungcrantz I, Ohlsson K, Segelmark M, Wieslander J. Novel distribution of the secretory leukocyte protease inhibitor in kidney *Mediators Inflamm* 2001 Dec;10(6):347-50
- Py B, Basmaciogullari S, Bouchet J, Zarka M, Moura IC, Benhamou M, Monteiro RC, Hocini H, Madrid R, Benichou S. The phospholipid scramblases 1 and 4 are cellular receptors for the secretory leukocyte protease inhibitor and interact with CD4 at the plasma membrane *PLoS One* 2009;4(3):e5006
- Ramadas RA, Wu L, LeVine AM. Surfactant protein A enhances production of secretory leukoprotease inhibitor and protects it from cleavage by matrix metalloproteinases *J Immunol* 2009 Feb 1;182(3):1560-7
- Reid PT, Marsden ME, Cunningham GA, Haslett C, Sallenave JM. Human neutrophil elastase regulates the expression and secretion of elafin (elastase-specific inhibitor) in type II alveolar epithelial cells *FEBS Lett* 1999 Aug 20;457(1):33-7
- Rein DT, Breidenbach M, Nettelbeck DM, Kawakami Y, Siegal GP, Huh WK, Wang M, Hemminki A, Bauerschmitz GJ, Yamamoto M, Adachi Y, Takayama K, Dall P, Curiel DT. Evaluation of tissue-specific promoters in carcinomas of the cervix uteri *J Gene Med* 2004 Nov;6(11):1281-9
- Rosso M, Lapyckyj L, Amiano N, Besso MJ, Sánchez M, Chuluyan E, Vazquez-Levin MH. Secretory Leukocyte Protease Inhibitor (SLPI) expression downregulates E-cadherin, induces -catenin re-localisation and triggers apoptosis-related events in breast cancer cells *Biol Cell* 2014 Sep;106(9):308-22
- Sallenave JM. Antimicrobial activity of antiproteinases *Biochem Soc Trans* 2002 Apr;30(2):111-5
- Samsom JN, van der Marel AP, van Berkel LA, van Helvoort JM, Simons-Oosterhuis Y, Jansen W, Greuter M, Nelissen RL, Meeuwisse CM, Nieuwenhuis EE, Mebius RE, Kraal G. Secretory leukoprotease inhibitor in mucosal lymph node dendritic cells regulates the threshold for mucosal tolerance *J Immunol* 2007 Nov 15;179(10):6588-95
- Schneeberger S, Hautz T, Wahl SM, Brandacher G, Sucher R, Steinmassl O, Steinmassl P, Wright CD, Obrist P, Werner ER, Mark W, Troppmair J, Margreiter R, Amberger A. The effect of secretory leukocyte protease inhibitor (SLPI) on ischemia/reperfusion injury in cardiac transplantation *Am J Transplant* 2008 Apr;8(4):773-82
- Seemüller U, Arnhold M, Fritz H, Wiedenmann K, Machleidt W, Heinzel R, Appelhans H, Gassen HG, Lottspeich F. The acid-stable proteinase inhibitor of human mucous secretions (HUSI-I, antileukoprotease) Complete amino acid sequence as revealed by protein and cDNA



- sequencing and structural homology to whey proteins and Red Sea turtle proteinase inhibitor FEBS Lett
- Shugars DC, Watkins CA, Cowen HJ. Salivary concentration of secretory leukocyte protease inhibitor, an antimicrobial protein, is decreased with advanced age Gerontology 2001 Sep-Oct;47(5):246-53
- Si-Tahar M, Merlin D, Sitaraman S, Madara JL. Constitutive and regulated secretion of secretory leukocyte proteinase inhibitor by human intestinal epithelial cells Gastroenterology 2000 Jun;118(6):1061-71
- Simpkins FA, Devoogdt NM, Rasool N, Tchabo NE, Alejandro EU, Kamrava MM, Kohn EC. The alarm anti-protease, secretory leukocyte protease inhibitor, is a proliferation and survival factor for ovarian cancer cells Carcinogenesis 2008 Mar;29(3):466-72
- Skott P, Lucht E, Ehnlund M, Björling E. Inhibitory function of secretory leukocyte proteinase inhibitor (SLPI) in human saliva is HIV-1 specific and varies with virus tropism Oral Dis 2002 May;8(3):160-7
- Skrzeczynska-Moncznik J, Wlodarczyk A, Banas M, Kwitniewski M, Zabieglo K, Kapinska-Mrowiecka M, Dubin A, Cichy J. DNA structures decorated with cathepsin G/secretory leukocyte proteinase inhibitor stimulate IFN $\gamma$  production by plasmacytoid dendritic cells Am J Clin Exp Immunol 2013 Jun 15;2(2):186-94
- Song Xy, Zeng L, Jin W, Thompson J, Mizel DE, Lei K, Billingham RC, Poole AR, Wahl SM. Secretory leukocyte protease inhibitor suppresses the inflammation and joint damage of bacterial cell wall-induced arthritis J Exp Med 1999 Aug 16;190(4):535-42
- Sriuranpong V, Mutirangura A, Gillespie JW, Patel V, Amornphimoltham P, Molinolo AA, Kerekhanjanarong V, Supanakorn S, Supiyaphun P, Rangaeng S, Voravud N, Gutkind JS. Global gene expression profile of nasopharyngeal carcinoma by laser capture microdissection and complementary DNA microarrays Clin Cancer Res 2004 Aug 1;10(15):4944-58
- Stetler G, Brewer MT, Thompson RC. Isolation and sequence of a human gene encoding a potent inhibitor of leukocyte proteases Nucleic Acids Res 1986 Oct 24;14(20):7883-96
- Stoff-Khalili MA, Stoff A, Rivera AA, Banerjee NS, Everts M, Young S, Siegal GP, Richter DF, Wang M, Dall P, Mathis JM, Zhu ZB, Curiel DT. Preclinical evaluation of transcriptional targeting strategies for carcinoma of the breast in a tissue slice model system Breast Cancer Res 2005;7(6):R1141-52
- Suter S. The imbalance between granulocyte neutral proteases and antiproteases in bronchial secretions from patients with cystic fibrosis Antibiot Chemother (1971) 1989;42:158-68
- Taggart CC, Cryan SA, Weldon S, Gibbons A, Greene CM, Kelly E, Low TB, O'Neill SJ, McElvaney NG. Secretory leukoprotease inhibitor binds to NF-kappaB binding sites in monocytes and inhibits p65 binding J Exp Med 2005 Dec 19;202(12):1659-68
- Tateosian NL, Pasquinelli V, Hernández Del Pino RE, Ambrosi N, Guerrieri D, Pedraza-Sánchez S, Santucci N, D'Attilio L, Pellegrini J, Araujo-Solis MA, Musella RM, Palmero DJ, Hernandez-Pando R, Garcia VE, Chuluyan HE. The impact of IFN- $\gamma$  receptor on SLPI expression in active tuberculosis: association with disease severity Am J Pathol 2014 May;184(5):1268-73
- Thompson RC, Ohlsson K. Isolation, properties, and complete amino acid sequence of human secretory leukocyte protease inhibitor, a potent inhibitor of leukocyte elastase Proc Natl Acad Sci U S A 1986 Sep;83(18):6692-6
- Tomee JF, Hiemstra PS, Heinzel-Wieland R, Kauffman HF. Antileukoprotease: an endogenous protein in the innate mucosal defense against fungi J Infect Dis 1997 Sep;176(3):740-7
- Tomova S, Cutruzzola F, Barra D, Amiconi G, Ascenzi P, Djinojvic M, Carugo K, Menegatti E, Sarti P, Schnebli HP, Bolognesi M. Selective oxidation of methionyl residues in the human recombinant secretory leukocyte proteinase inhibitor Effect on the inhibitor binding properties J Mol Recognit
- Velarde MC, Parisek SI, Eason RR, Simmen FA, Simmen RC. The secretory leukocyte protease inhibitor gene is a target of epidermal growth factor receptor action in endometrial epithelial cells J Endocrinol 2005 Jan;184(1):141-51
- Verma C, Seebah S, Low SM, Zhou L, Liu SP, Li J, Beuerman RW. Defensins: antimicrobial peptides for therapeutic development Biotechnol J 2007 Nov;2(11):1353-9
- Vogelmeier C, Gillissen A, Buhl R. Use of secretory leukoprotease inhibitor to augment lung antineutrophil elastase activity Chest 1996 Dec;110(6 Suppl):261S-266S
- Wang N, Thuraingam T, Fallavollita L, Ding A, Radzioch D, Brodt P. The secretory leukocyte protease inhibitor is a type 1 insulin-like growth factor receptor-regulated protein that protects against liver metastasis by attenuating the host proinflammatory response Cancer Res 2006 Mar 15;66(6):3062-70
- Wang X, Li X, Xu L, Zhan Y, Yaish-Ohad S, Erhardt JA, Barone FC, Feuerstein GZ. Up-regulation of secretory leukocyte protease inhibitor (SLPI) in the brain after ischemic stroke: adenoviral expression of SLPI protects brain from ischemic injury Mol Pharmacol 2003 Oct;64(4):833-40
- Weldon S, McNally P, McElvaney NG, Elborn JS, McAuley DF, Wartelle J, Belaouaj A, Levine RL, Taggart CC. Decreased levels of secretory leukoprotease inhibitor in the Pseudomonas-infected cystic fibrosis lung are due to neutrophil elastase degradation J Immunol 2009 Dec 15;183(12):8148-56
- Wen J, Nikitakis NG, Chaisuparat R, Greenwell-Wild T, Gliozi M, Jin W, Adli A, Moutsopoulos N, Wu T, Warburton G, Wahl SM. Secretory leukocyte protease inhibitor (SLPI) expression and tumor invasion in oral squamous cell carcinoma Am J Pathol 2011 Jun;178(6):2866-78
- Wiedow O, Harder J, Bartels J, Streit V, Christophers E. Antileukoprotease in human skin: an antibiotic peptide constitutively produced by keratinocytes Biochem Biophys Res Commun 1998 Jul 30;248(3):904-9
- Wifflingseder J, Sunzenauer J, Toronyi E, Heinzel A, Kainz A, Mayer B, Perco P, Telkes G, Langer RM, Oberbauer R. Molecular pathogenesis of post-transplant acute kidney injury: assessment of whole-genome mRNA and miRNA profiles PLoS One 2014 Aug 5;9(8):e104164
- Williams SE, Brown TI, Roghanian A, Sallenave JM. SLPI and elafin: one glove, many fingers Clin Sci (Lond) 2006 Jan;110(1):21-35
- Wingens M, van Bergen BH, Hiemstra PS, Meis JF, van Vlijmen-Willems IM, Zeeuwen PL, Mulder J, Kramps HA, van Ruissen F, Schalkwijk J. Induction of SLPI (ALP/HUSI-

l) in epidermal keratinocytes J Invest Dermatol 1998 Dec;111(6):996-1002

Yang J, Zhu J, Sun D, Ding A. Suppression of macrophage responses to bacterial lipopolysaccharide (LPS) by secretory leukocyte protease inhibitor (SLPI) is independent of its anti-protease function Biochim Biophys Acta 2005 Sep 30;1745(3):310-7

Zabieglo K, Majewski P, Majchrzak-Gorecka M, Wlodarczyk A, Grygier B, Zegar A, Kapinska-Mrowiecka

M, Naskalska A, Pyrc K, Dubin A, Wahl SM, Cichy J. The inhibitory effect of secretory leukocyte protease inhibitor (SLPI) on formation of neutrophil extracellular traps J Leukoc Biol 2015 Jul;98(1):99-106

Zelvyte I, Wallmark A, Piitulainen E, Westin U, Janciauskiene S. Increased plasma levels of serine proteinase inhibitors in lung cancer patients Anticancer Res 2004 Jan-Feb;24(1):241-7

Zhang D, Simmen RC, Michel FJ, Zhao G, Vale-Cruz D, Simmen FA. Secretory leukocyte protease inhibitor mediates proliferation of human endometrial epithelial cells by positive and negative regulation of growth-associated genes J Biol Chem 2002 Aug 16;277(33):29999-30009

van Wetering S, van der Linden AC, van Sterkenburg MA, de Boer WI, Kuijpers AL, Schalkwijk J, Hiemstra PS. Regulation of SLPI and elafin release from bronchial epithelial cells by neutrophil defensins Am J Physiol Lung Cell Mol Physiol 2000 Jan;278(1):L51-8

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