

Table 1. TLR-expressions in CRS found by different authors

Receptor type	CRSsNP group	CRSwNP group	Tissue or cell type	Regulation	References
TLR1	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Detected (mRNA); same as control	Lane AP, 2006 [9]
TLR2	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Upregulated mRNA	↑ Lane AP, 2006 [9]
	30 patients	Not given	Nasal epithelial cells (in smears)	Upregulated mRNA	↑ Dong Z, 2005 [10]
	Not known	Not known	Primary culture of polyp epithelial cells	Detected (protein)	Wang J, 2007 [11]
	12 patients	40 patients	Polyp tissue	Down-regulated mRNA in patients with microbial colonization	↓ Pitzurra L, 2004 [12]
	30 patients with and without nasal polyp		Nasal biopsies	No difference in mRNA	Claeys S, 2003 [13]
	40 patients	38 patients	Sinonasal mucosa or polyp tissue	Upregulated mRNA in patients in CRSwNP	↑ Zhang QI, 2013 [14]
	Not given	8 patients	Primary culture of polyp epithelial cells	Upregulated mRNA after airborne fungi activation	↑ Shin SH, 2010 [15]
	20 patients	16 patients	Ethmoid mucosa	Down-regulation mRNA in CRS	↓ Detwiller KY, 2014 [16]
	31 patients	Not given	Sinus tissue	mRNA and protein level elevated in biofilm-positive compared to biofilm negative CRS	↑ Sun Y, 2012 [17]
	TLR3	12 patients	Not known	Primary culture of polyp epithelial cells	Upregulated protein expression
Not given		8 patients	Primary culture of polyp epithelial cells	Upregulated mRNA after airborne fungi activation	↑ Shin SH, 2010 [15]
TLR4	30 patients with and without nasal polyp		Nasal biopsies	No difference in mRNA	Claeys S, 2003 [13]
	12 patients	40 patients	Polyp tissue	Down-regulated mRNA in patients with microbial colonization	↓ Pitzurra L, 2004 [12]
	30 patients	Not given	Nasal epithelial cells (in smears)	Upregulated mRNA	↑ Dong Z, 2005 [10]
	Not known	Not known	Primary culture of polyp epithelial cells	Detected protein	Wang J, 2007 [11]
	40 patients	38 patients	Sinonasal mucosa or polyp tissue	Increased expression (mRNA and protein) in CRSwNP Decreased expression in CRSsNP group	↑ ↓ Zhang QI, 2013 [14]
	31 patients	Not given	Sinus tissue	Increased expression in CRSsNP (mRNA and protein)	↑ Sun Y, 2012 [17]
TLR5, TLR6	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Detected (mRNA); same as control	Lane AP, 2006 [9]
TLR7	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Detected (mRNA); same as control	Lane AP, 2006 [9]
	40 patients	38 patients	Sinonasal mucosa or polyp tissue	Increased expression (mRNA and protein) in CRSwNP Decreased expression in CRSsNP group	↑ ↓ Zhang QI, 2013 [14]
TLR8	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Detected (mRNA); same as control	Lane AP, 2006 [9]
TLR9	10 patients	20 patients	Ethmoid mucosa (not polypoid)	Detected (mRNA); same as control; Down-regulated in patients with early recurrence	↓ Lane AP, 2006 [9]
	Not given	10(mRNA)+20(protein) patients	Pooled NP tissue	Upregulated (mRNA and protein)	↑ Zhao CY, 2011 [18]
	20 patients	16 patients	Ethmoid mucosa	No difference in mRNA	Detwiller KY, 2014 [16]
	18 patients with CF	Not given	Sinonasal epithelial cells from middle meatus	Upregulated	↑ Melvin TA, 2013 [19]
	Not given	10 patients	Primary culture of polyp epithelial cells	Down-regulated (protein)	↓ Ramanathan, 2007 [20]

Table 2. Demographic data of the subjects

Characteristics	CRSsNP n=19	CRSwNP ASA(-) n=17	CRSwNP ASA(+) n=7	Controls n=12	Total
Age (year)	43 (25-75)	43 (25-75)	57 (55-64)	33 (26-59)	
Male	11	11	2	6	30
Female	8	6	5	6	25
Allergic rhinitis	5	4	1	0	10
Other atopic disease	2	3	2	0	7
Asthma	4	4	5* ‡	0	13
Smoking	0	1	0	0	1
Systemic steroid < 3 months	0	0	0	0	0
Topical steroid	19	17	7	0	43
Inhalative steroid	4	4	5	0	13
Prior ESS (mean)	0.19±0.1	1.59±0.4 +	3.2±1.2 ++	0	

CRSsNP: CRS without nasal polyps; CRSwNP: CRS with nasal polyps; ASA(-): aspirin- tolerant; ASA(+): aspirin-sensitive; ESS: Endoscopic Sinus Surgery; \*ASA(+) vs CRSsNP p=0.004; ‡ASA(+) vs ASA(-) p=0.004; +CRSsNP vs ASA(-) p=0.005; ++CRSsNP vs ASA(+) p=0.001.

Table 3A. Relative expression of genes compared to controls and comparison of expressions between CRS subgroups

Genes	CRSsNP/Control		CRSwNP/Control		CRSwNP/CRSsNP	
	Relative expression	p-value	Relative expression	p-value	Relative expression	p-value
TLR1	1.703	1.000	1.487	0.626	0.873	0.583
TLR2	5.472	0.025*	6.594	0.005*	1.199	1.000
TLR3	1.724	1.000	3.528	0.167	2.066	1.000
TLR4	1.234	1.000	1.408	0.571	1.141	0.536
TLR5	1.763	0.327	2.057	0.004*	1.193	0.532
TLR6	3.342	0.084	2.902	0.038*	0.868	1.000
TLR7	1.829	0.789	5.219	0.000*	2.853	0.027*
TLR8	1.580	1.000	3.345	0.000*	2.117	0.008*
TLR9	1.417	1.000	2.112	0.008*	1.490	0.008*
TLR10	2.615	0.077	1.922	0.226	0.734	1.000
CAMP	17.540	0.209	18.415	0.036*	1.049	1.000
FOXP3	1.609	0.405	2.041	0.001*	1.268	0.149
LYZ	1.231	1.000	1.568	0.106	1.122	0.483
LTF	1.644	0.044*	2.128	0.005*	1.294	1.000
DEFB1	0.954	0.991	2.254	0.001*	2.362	0.036*
DEFB3	1.580	1.000	1.189	0.443	0.752	1.000
DEFB104A	1.852	0.608	3.248	0.009*	1.753	0.414
DEFB102	3.885	1.000	1.249	1.000	0.321	1.000
TBX21	4.893	0.005*	6.346	0.000*	1.296	1.000
GATA-3	3.770	0.368	4.696	0.557	1.245	1.000

CRSsNP: CRS without nasal polyps; CRSwNP: CRS with nasal polyps;  $p \leq 0.05$  was considered as significant (\*).

Table 3B. Expression of proteins compared to controls and comparison of expressions between CRS subgroups

<b>Proteins</b>	<b>CRSsNP/Control</b>	<b>CRSwNP/Control</b>	<b>CRSwNP/CRSsNP</b>
	p-value	p-value	p-value
TLR2	0.009*	0.033*	0.000*
TLR3	0.000*	0.027*	0.145
TLR4	0.446	0.002*	0.001*
TLR5	0.032*	0.449	0.001*
CAMP	0.029*	0.146	0.094
LYZ	0.149	0.035*	0.344
LTF	0.422	0.012*	0.008*
HBD2	0.258	0.024*	0.020*
T-bet	0.084	0.082	0.380
GATA3	0.079	0.038*	0.190

CRSsNP: CRS without nasal polyps; CRSwNP: CRS with nasal polyps; ASA(-): aspirin-tolerant; ASA(+): aspirin-intolerant;  $p \leq 0.05$  was considered as significant (\*).

Table 4A. Relative expression of genes compared between aspirin tolerant and intolerant subgroups of patients and controls

Genes	ASA(+)/ASA(-)CRSwNP		ASA(+) CRSwNP/Control		ASA(-) CRSwNP/Control	
	Relative expression	p-value	Relative expression	p-value	Relative expression	p-value
TLR1	1.315	1.000	1.779	0.976	1.352	1.000
TLR2	0.932	1.000	6.199	0.145	6.651	0.018*
TLR3	3.425	1.000	6.871	0.522	2.006	0.570
TLR4	0.791	1.000	1.186	1.000	1.499	1.000
TLR5	0.933	1.000	1.960	0.440	2.100	0.008*
TLR6	1.271	1.000	3.419	0.582	2.689	0.103
TLR7	2.001	1.000	8.004	0.005*	4.000	0.005*
TLR8	0.739	1.000	2.676	0.120	3.620	0.001*
TLR9	0.725	1.000	1.665	1.000	2.295	0.006*
TLR10	1.327	1.000	2.329	0.450	1.755	0.877
CAMP	0.066	1.000	1.536	1.000	23.237	0.039*
FOXP3	0.846	1.000	1.809	0.500	2.137	0.001*
LYZ	0.872	0.542	1.403	1.000	1.932	0.068
LTF	1.873	1.000	3.177	0.074	1.696	0.026*
DEFB1	0.438	1.000	1.183	0.795	2.695	0.001*
DEFB3	0.711	1.000	0.924	1.000	1.298	0.622
DEFB104A	1.051	1.000	3.364	0.707	3.200	0.016*
DEFB102	0.769	1.000	1.023	1.000	1.329	1.000
TBX21	1.722	1.000	9.030	0.113	5.241	0.001*
GATA-3	1.821	1.000	6.792	1.000	3.728	1.000

CRSsNP: CRS without nasal polyps; CRSwNP: CRS with nasal polyps;  $p \leq 0.05$  was considered as significant (\*).

Table 4B. Expression of proteins compared between aspirin tolerant and intolerant subgroups of patients and controls

	<b>ASA(+)/ASA(-)CRSwNP</b>	<b>ASA(+) CRSwNP/Co</b>	<b>ASA(-) CRSwNP/Co</b>
Proteins	p-value	p-value	p-value
TLR2	0.204	0.204	0.052
TLR3	1.000	1.000	0.013*
TLR4	0.125	0.125	0.000*
TLR5	0.184	0.184	0.364
CAMP	0.441	0.441	0.097
LYZ	0.091	0.091	0.032*
LTF	0.029	0.029*	0.018*
HBD2	0.044	0.044*	0.024*
T-bet	0.039	0.039*	0.141
GATA3	0.011	0.011*	0.054

CRSsNP: CRS without nasal polyps; CRSwNP: CRS with nasal polyps; ASA(-): aspirin-tolerant; ASA(+): aspirin-intolerant;  $p \leq 0.05$  was considered as significant (\*).

## Legends to Figures

Figure 1. **TLR-2 expression in macrophages.** TLR-2 positive macrophages (arrows) in (a) CRSwNP(ASA-) and in (b) CRSwNP(ASA+) samples. TLR-2 5x(a); 20x(b).

Figure 2. **Lysozyme expression in CRS tissue.** Intraepithelial and subepithelial lysozyme positive macrophages (arrows) in CRSwNP(ASA-) /a/ and in CRSwNP(ASA+) tissue /b/. Lysozyme. 20x.

Figure 3. **Significantly up-regulated genes in CRSsNP and CRSwNP compared to controls.** \*Significant expression in CRSwNP versus CRSsNP (TLR7: 2.853, p=0.027; TLR8: 2.117, p=0.008; TLR9: 1.490, p=0.008; DEFB1: 2.362, p=0.036)