

Supplementary Materials

Table S1. Quantification of S100⁺ and CD56⁺ cells in VS primary cultures.

Primary culture number	S100 [%]	CD56 [%]
1	82.20	76.24
2	94.95	88.08
3	92.22	86.42
4	90.07	79.20
5	89.63	94.47
6	86.69	71.28

Table S2. Antibodies used for immunofluorescence.

Antibody	Source / Isotype	Dilution	Manufacturer
S100	Mouse IgG	1:400	Cell signaling
CD56	Mouse IgG	1:400	Protein Simple
Anti-mouse-antibody	Goat Fab fragments	1:1000	Cell signaling

Table S3. Homo sapiens specific primers used for quantitative Real-Time PCR.

Gene symbol	Primer sequence 5' to 3' (Forward, Reverse)	Annealing temperature (°C)	Product length	Reference sequence
<i>CD68</i>	CGCAGCACAGTGGACATTCT, GGATCAGGCCGATGATGAGAG	60	236	NM_001251.3
<i>CD163</i>	AAAAAGCCACAACAGGTCGC, ATGGCCTCCTTTTCCATTCCA	60	322	NM_004244.5
<i>MKI67</i>	GATCGTCCCAGTGGAAAGAGTT, ATTGCCTCCTGCTCATGGATT	60	276	NM_002417.5
<i>CCL20</i>	CGAATCAGAAGCAGCAAGCAAC, TTGCGCACACAGACAACCTTTT	61	161	NM_004591.3
<i>CCL22</i>	GCCGTGATTACGTCCGTTAC, GAGAATCATCTTCACCCAGGGC	61	155	NM_002990.5
<i>IL10</i>	AACCTGCCTAACATGCTTCGAG, GGTCTTGGTTCTCAGCTTGGG	61	202	NM_000572.3
<i>IRF4</i>	CCCAGCAGGTTCACTACTACA, TCGGCAGACCTTATGCTTGG	60	241	NM_002460.4
<i>TGFB1</i>	CAAGTGGACATCAACGGGTTC, GCAGAAGTTGGCATGGTAGC	60	270	NM_000660.7
<i>GDF15</i>	GGAGGTGCAAGTGACCATGT, ACCATGGGATTGTAGCTGGC	60	150	NM_004864.4
<i>GAPDH</i>	TCGTGGAAGGACTCATGACC, TTCCCGTTCAGCTCAGGGAT	60	172	NM_002046.7

Table S4. Assessment of the correlations.

Spearman's r	Assessment
0.000 – 0.199	Very weak correlation
0.200 – 0.399	Weak correlation
0.400 – 0.599	Moderate correlation
0.600 – 0.799	Strong correlation
0.800 – 1.000	Very strong correlation

Table S5. Baseline data for correlation analysis of investigated cytokines in 144 patients with sporadic VS.

Variable	Total (n=144)	Percentage of all patients (n=175)
Male	61	34.7
Female	83	47.2
Mean age (years) and standard deviation (SD)	51 ± 12.55 (18-77)	
Median age (years) and interquartile range (IQR)	52 (15.25)	
Koos grade		
I	4	2.3
II	47	26.7
III	51	29.0
IV	42	23.9
AAO-HNS ¹ (hearing class)		
A	44	25
B	43	24.4
C	30	17.0
D	16	9.1
DS ²	10	5.7
Without preoperative hearing class	1	0.06
Mean tumor volume (cm ³) and SD	4.0 ± 5.43 (0.1-37.0)	
Median tumor volume (cm ³) and IQR	2.3 (4.51)	
Mean growth rate (cm ³ /year) and SD	0.7 ± 0.76 (0.04-2.7)	
Median growth rate (cm ³ /year) and IQR	0.3 (0.83)	
Mean relative growth rate (%/year) and SD	2.9 ± 3.37(0.6-17.8)	
Median relative growth rate (%/year) and IQR	1.8 (1.71)	

¹ AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery

² DS: surditas for deafness

Table S6. Spearman's r and p-values for correlation analysis of investigated cytokines and clinical parameters in 144 patients with sporadic VS.

Row	Column	Spearman's r	p-value
Age at surgery	Koos	0.046	0.732
Age at surgery	Hearing class	0.386	<0.001
Koos	Hearing class	0.196	0.049
Age at surgery	Tumor volume	0.120	0.326
Koos	Tumor volume	0.891	<0.001
Hearing class	Tumor volume	0.220	0.039
Age at surgery	Relative growth rate	-0.125	0.679
Koos	Relative growth rate	0.124	0.679
Hearing class	Relative growth rate	-0.076	0.806
Tumor volume	Relative growth rate	0.224	0.403
Age at surgery	Growth rate	0.288	0.214
Koos	Growth rate	0.755	<0.001

Hearing class	Growth rate	0.234	0.350
Tumor volume	Growth rate	0.888	<0.001
Relative growth rate	Growth rate	0.364	0.098
Age at surgery	<i>CCL2</i>	-0.021	0.880
Koos	<i>CCL2</i>	-0.005	0.966
Hearing class	<i>CCL2</i>	-0.135	0.208
Tumor volume	<i>CCL2</i>	-0.115	0.350
Relative growth rate	<i>CCL2</i>	-0.192	0.467
Growth rate	<i>CCL2</i>	-0.331	0.147
Age at surgery	<i>CCL5</i>	0.087	0.467
Koos	<i>CCL5</i>	0.275	0.003
Hearing class	<i>CCL5</i>	0.078	0.526
Tumor volume	<i>CCL5</i>	0.267	0.009
<i>CCL2</i>	<i>CCL5</i>	0.369	<0.001
Relative growth rate	<i>CCL5</i>	-0.111	0.717
Growth rate	<i>CCL5</i>	0.049	0.880
Age at surgery	<i>CCL18</i>	0.020	0.884
Koos	<i>CCL18</i>	0.349	<0.001
Hearing class	<i>CCL18</i>	0.135	0.210
Tumor volume	<i>CCL18</i>	0.314	0.002
Relative growth rate	<i>CCL18</i>	0.120	0.696
Growth rate	<i>CCL18</i>	0.302	0.210
<i>CCL2</i>	<i>CCL18</i>	0.093	0.448
<i>CCL5</i>	<i>CCL18</i>	0.408	<0.001
Age at surgery	<i>CCL20</i>	-0.271	0.004
Koos	<i>CCL20</i>	-0.067	0.617
Hearing class	<i>CCL20</i>	-0.113	0.324
Tumor volume	<i>CCL20</i>	-0.049	0.732
Relative growth rate	<i>CCL20</i>	-0.029	0.933
Growth rate	<i>CCL20</i>	-0.251	0.324
<i>CCL2</i>	<i>CCL20</i>	0.412	<0.001
<i>CCL5</i>	<i>CCL20</i>	0.379	<0.001
<i>CCL18</i>	<i>CCL20</i>	0.067	0.617
Age at surgery	<i>CCL22</i>	-0.082	0.498
Koos	<i>CCL22</i>	0.194	0.054
Hearing class	<i>CCL22</i>	0.077	0.526
Tumor volume	<i>CCL22</i>	0.153	0.192
Relative growth rate	<i>CCL22</i>	0.188	0.493
Growth rate	<i>CCL22</i>	0.099	0.734
<i>CCL2</i>	<i>CCL22</i>	0.139	0.199
<i>CCL5</i>	<i>CCL22</i>	0.481	<0.001
<i>CCL18</i>	<i>CCL22</i>	0.216	0.031
<i>CCL20</i>	<i>CCL22</i>	0.427	<0.001
Age at surgery	<i>IL10</i>	-0.064	0.629
Koos	<i>IL10</i>	-0.045	0.732
Hearing class	<i>IL10</i>	0.022	0.880
Tumor volume	<i>IL10</i>	-0.108	0.399
Relative growth rate	<i>IL10</i>	0.010	0.966
Growth rate	<i>IL10</i>	-0.196	0.467

<i>CCL2</i>	<i>IL10</i>	0.579	<0.001
<i>CCL5</i>	<i>IL10</i>	0.380	<0.001
<i>CCL18</i>	<i>IL10</i>	0.146	0.179
<i>CCL20</i>	<i>IL10</i>	0.572	<0.001
<i>CCL22</i>	<i>IL10</i>	0.393	<0.001
Age at surgery	<i>TGFB1</i>	0.010	0.942
Koos	<i>TGFB1</i>	0.126	0.243
Hearing class	<i>TGFB1</i>	0.077	0.526
Tumor volume	<i>TGFB1</i>	0.148	0.199
Relative growth rate	<i>TGFB1</i>	-0.092	0.743
Growth rate	<i>TGFB1</i>	0.018	0.948
<i>CCL2</i>	<i>TGFB1</i>	0.174	0.085
<i>CCL5</i>	<i>TGFB1</i>	0.534	<0.001
<i>CCL18</i>	<i>TGFB1</i>	0.197	0.052
<i>CCL20</i>	<i>TGFB1</i>	0.357	<0.001
<i>CCL22</i>	<i>TGFB1</i>	0.588	<0.001
<i>IL10</i>	<i>TGFB1</i>	0.243	0.011
Age at surgery	<i>GDF15</i>	-0.047	0.734
Koos	<i>GDF15</i>	0.239	0.023
Hearing class	<i>GDF15</i>	-0.060	0.682
Tumor volume	<i>GDF15</i>	0.260	0.020
Relative growth rate	<i>GDF15</i>	-0.102	0.734
Growth rate	<i>GDF15</i>	0.005	0.980
<i>CCL2</i>	<i>GDF15</i>	0.324	0.001
<i>CCL5</i>	<i>GDF15</i>	0.192	0.079
<i>CCL18</i>	<i>GDF15</i>	-0.024	0.880
<i>CCL20</i>	<i>GDF15</i>	0.009	0.948
<i>CCL22</i>	<i>GDF15</i>	0.144	0.210
<i>IL10</i>	<i>GDF15</i>	0.089	0.493
<i>TGFB1</i>	<i>GDF15</i>	-0.008	0.951
Age at surgery	<i>IRF4</i>	-0.053	0.606
Koos	<i>IRF4</i>	0.285	0.002
Hearing class	<i>IRF4</i>	0.061	0.647
Tumor volume	<i>IRF4</i>	0.321	0.001
Relative growth rate	<i>IRF4</i>	-0.046	0.880
Growth rate	<i>IRF4</i>	-0.026	0.937
<i>CCL2</i>	<i>IRF4</i>	0.164	0.111
<i>CCL5</i>	<i>IRF4</i>	0.640	<0.001
<i>CCL18</i>	<i>IRF4</i>	0.278	0.003
<i>CCL20</i>	<i>IRF4</i>	0.351	<0.001
<i>CCL22</i>	<i>IRF4</i>	0.519	<0.001
<i>IL10</i>	<i>IRF4</i>	0.257	0.007
<i>TGFB1</i>	<i>IRF4</i>	0.540	<0.001
<i>GDF15</i>	<i>IRF4</i>	0.159	0.168
Age at surgery	<i>MKI67</i>	0.056	0.793
Koos	<i>MKI67</i>	-0.378	<0.001
Hearing class	<i>MKI67</i>	0.010	0.942
Tumor volume	<i>MKI67</i>	-0.313	0.002
Relative growth rate	<i>MKI67</i>	0.212	0.427

Growth rate	MKI67	-0.047	0.880
CCL2	MKI67	-0.244	0.010
CCL5	MKI67	-0.089	0.460
CCL18	MKI67	-0.087	0.475
CCL20	MKI67	-0.046	0.732
CCL22	MKI67	0.028	0.863
IL10	MKI67	-0.045	0.732
TGFB1	MKI67	0.222	0.022
GDF15	MKI67	-0.404	<0.001
IRF4	MKI67	0.026	0.877
Age at surgery	CD163	0.031	0.833
Koos	CD163	0.189	0.060
Hearing class	CD163	0.181	0.074
Tumor volume	CD163	0.200	0.068
Relative growth rate	CD163	0.039	0.901
Growth rate	CD163	0.142	0.629
CCL2	CD163	0.162	0.116
CCL5	CD163	0.348	<0.001
CCL18	CD163	0.208	0.039
CCL20	CD163	0.347	<0.001
CCL22	CD163	0.377	<0.001
IL10	CD163	0.281	0.003
TGFB1	CD163	0.453	<0.001
GDF15	CD163	0.016	0.918
IRF4	CD163	0.202	0.042
MKI67	CD163	0.181	0.073
Age at surgery	CD68	-0.048	0.729
Koos	CD68	0.368	<0.001
Hearing class	CD68	0.108	0.347
Tumor volume	CD68	0.344	<0.001
Relative growth rate	CD68	-0.051	0.880
Growth rate	CD68	0.312	0.191
CCL2	CD68	0.168	0.098
CCL5	CD68	0.462	<0.001
CCL18	CD68	0.398	<0.001
CCL20	CD68	0.246	0.010
CCL22	CD68	0.429	<0.001
IL10	CD68	0.235	0.015
TGFB1	CD68	0.502	<0.001
GDF15	CD68	0.100	0.442
IRF4	CD68	0.317	<0.001
MKI67	CD68	-0.052	0.696
CD163	CD68	0.666	<0.001

Significant p-values are written in bold ($p \leq 0.05$).

Table S7. Regression analysis of markers correlating significantly with tumor volume in correlation analysis of investigated cytokines in 144 patients with sporadic VS.

Coefficients	Estimate	Standard error	t-value	p-value
Growth rate	2.940	0.434	6.764	<0.001
CCL5	0.067	0.121	0.552	0.589

<i>CCL18</i>	-0.002	0.001	-2.049	0.058
<i>GDF15</i>	0.084	0.172	0.491	0.630
<i>IRF4</i>	1.063	0.358	2.966	0.010
<i>MKI67</i>	-0.228	0.392	-0.582	0.569
<i>CD68</i>	0.545	0.208	2.624	0.019
Multiple R-squared: 0.930; Adjusted R-squared: 0.898				
F-statistic: 28.65 on 7 and 15 DF, p-value: <0.001				

Table S8. Baseline data for examining differential expression of studied markers in large and small VS.

Variable	Small VS (n=20)	Percentage of all patients (n=175)	Large VS (n=20)	Percentage of all patients (n=175)	p- value
Male	8	4.5	10	5.7	0.75
Female	12	6.8	10	5.7	
Mean age (years) and SD	49 ± 9.87 (18-61)		49 ± 13.46 (25-75)		0.94
Median age (years) and IQR	51 (16)		49 (20.25)		
Koos grade					<0.001
I	3	1.7	0	0	
II	17	9.7	0	0	
III	0	0	0	0	
IV	0	0	20	11.4	
AAO-HNS ¹ (hearing class)					0.02
A	8	4.5	3	1.7	
B	8	4.5	5	2.8	
C	2	1.1	5	2.8	
D	1	0.06	3	1.7	
DS ²	1	0.06	4	2.3	
Mean tumor volume (cm ³) and SD	0.3 ± 0.16 (0.1-0.4)		13.8 ± 6.97 (7.5-37.0)		<0.001
Median tumor volume (cm ³) and IQR	0.3 (0.17)		12.5 (7.59)		

¹ AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery

² DS: surditas for deafness

Table S9. P-values for differential expression of studied markers in large and small VS.

	Median small tumors and IQR	Median large tumors and IQR	p-value
<i>CCL2</i> mRNA level	1.54 (1.28)	0.98 (1.37)	0.056
<i>CCL5</i> mRNA level	1.71 (1.17)	3.25 (4.40)	0.16
<i>CCL18</i> mRNA level	0.69 (3.08)	5.26 (68.61)	0.017
<i>CCL20</i> mRNA level	0.65 (0.52)	0.44 (0.47)	0.53
<i>CCL22</i> mRNA level	2.01 (1.56)	2.50 (2.46)	0.25
<i>IL10</i> mRNA level	1.41 (1.43)	0.51 (0.86)	0.13
<i>IRF4</i> mRNA level	0.61 (0.74)	1.56 (1.44)	0.013
<i>TGFB1</i> mRNA level	0.83 (0.54)	0.90 (0.79)	0.76
<i>GDF15</i> mRNA level	0.55 (0.92)	1.19 (1.42)	0.1

Table S10. Medians and 75th percentiles of RNA transcription data of 10 tumors and corresponding nerves.

Gene	Tumor median [TPM]	Tumor 75 th percentile [TPM]	Nerve median [TPM]	Nerve 75 th percentile [TPM]	p-value
<i>CCL2</i>	30.33	48.74	451.84	619.04	0.02
<i>CCL5</i>	7.48	9.66	8.31	13.09	0.42
<i>CCL18</i>	0.00	0.06	0.00	0.00	0.12
<i>CCL20</i>	0.80	1.09	1.72	3.47	0.13
<i>CCL22</i>	0.23	0.41	0.22	0.37	0.60
<i>IL10</i>	0.48	1.07	1.32	2.80	0.05
<i>GDF15</i>	13.57	29.22	18.36	37.59	0.30
<i>TGFB1</i>	76.38	124.72	49.62	53.57	0.006
<i>TGFB2</i>	2.04	2.55	4.49	10.54	0.04
<i>IRF4</i>	0.20	0.31	0.46	0.8	0.15
<i>MKI67</i>	0.58	1.24	0.08	0.22	0.02
<i>S100B</i>	4355.96	4920.55	440.60	504.20	0.007
<i>CCR2</i>	1.09	1.60	0.29	0.85	0.03
<i>CCR5</i>	1.68	4.01	2.50	3.03	0.68
<i>IL10RB</i>	36.29	39.68	18.55	22.50	<0.001
<i>TGFBR1</i>	8.83	11.22	4.05	5.73	0.002
<i>TGFR2</i>	75.37	162.89	31.82	44.15	0.005

Table S11. Baseline data for cytokine concentrations in CCS of 45 VS primary cultures and correlation analysis of primary cultures from 45 patients with sporadic VS.

Variable	Total (n=45)	Percentage of all patients (n=175)
Male	18	10.2
Female	27	15.3
Mean age (years) and SD	48 ± 12.69 (18-71)	
Median age (years) and IQR	48 (18)	
Koos grade		
I	0	0
II	16	9.1
III	13	7.4
IV	16	9.1
AAO-HNS ¹ (hearing class)		
A	15	8.5
B	12	6.8
C	2	1.1
D	7	4.0
DS ²	7	4.0
Without preoperative hearing class	2	1.1
Mean tumor volume (cm ³) and SD	3.6 ± 4.13 (0.1-18.0)	
Median tumor volume (cm ³) and IQR	2.47 (3.44)	

¹ AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery

² DS: surditas for deafness

Table S12. CCS cytokine concentrations of investigated cytokines in 45 VS primary cultures.

Cytokine	Median CCS concentration and IQR
CCL2	13199 (15899)
CCL5	12.90 (16.86)
CCL18	1.36 (3.99)
TGFB1	2092 (1705)
GDF15	378 (562)

Table S13. Spearman's r and p-values of investigated cytokines and clinical parameters in 45 VS primary cultures.

Row	Column	Spearman's r	p-value
Age at surgery	Hearing class	0.542	0.002
Age at surgery	Koos	-0.050	0.849
Hearing class	Koos	-0.016	0.993
Age at surgery	Tumor volume	0.097	0.803
Hearing class	Tumor volume	0.095	0.820
Koos	Tumor volume	0.912	<0.001
Age at surgery	CCL2 qPCR	0.248	0.288
Hearing class	CCL2 qPCR	0.012	0.993
Koos	CCL2 qPCR	0.047	0.885
Tumor volume	CCL2 qPCR	0.062	0.885
Age at surgery	CCL5 qPCR	0.002	0.993
Hearing class	CCL5 qPCR	-0.140	0.631
Koos	CCL5 qPCR	0.065	0.885
Tumor volume	CCL5 qPCR	0.001	0.993
CCL2 qPCR	CCL5 qPCR	0.420	0.025
Age at surgery	CCL18 qPCR	0.142	0.622
Hearing class	CCL18 qPCR	0.195	0.470
Koos	CCL18 qPCR	0.198	0.453
Tumor volume	CCL18 qPCR	0.208	0.454
CCL2 qPCR	CCL18 qPCR	0.668	<0.001
CCL5 qPCR	CCL18 qPCR	0.410	0.029
Age at surgery	TGFB1 qPCR	-0.047	0.885
Hearing class	TGFB1 qPCR	-0.185	0.499
Koos	TGFB1 qPCR	0.301	0.157
Tumor volume	TGFB1 qPCR	0.217	0.436
CCL2 qPCR	TGFB1 qPCR	0.100	0.769
CCL5 qPCR	TGFB1 qPCR	0.349	0.079
CCL18 qPCR	TGFB1 qPCR	-0.053	0.885
Age at surgery	GDF15 qPCR	0.143	0.621
Hearing class	GDF15 qPCR	-0.076	0.884
Koos	GDF15 qPCR	0.455	0.015
Tumor volume	GDF15 qPCR	0.436	0.029
CCL2 qPCR	GDF15 qPCR	0.243	0.295
CCL5 qPCR	GDF15 qPCR	0.150	0.600

<i>CCL18</i> qPCR	<i>GDF15</i> qPCR	0.133	0.631
<i>TGFB1</i> qPCR	<i>GDF15</i> qPCR	0.548	0.002
Age at surgery	CCL2 ELISA	0.147	0.600
Hearing class	CCL2 ELISA	-0.044	0.885
Koos	CCL2 ELISA	-0.049	0.885
Tumor volume	CCL2 ELISA	-0.048	0.885
<i>CCL2</i> qPCR	CCL2 ELISA	0.626	<0.001
<i>CCL5</i> qPCR	CCL2 ELISA	0.343	0.085
<i>CCL18</i> qPCR	CCL2 ELISA	0.399	0.033
<i>TGFB1</i> qPCR	CCL2 ELISA	0.154	0.600
<i>GDF15</i> qPCR	CCL2 ELISA	0.055	0.885
Age at surgery	CCL5 ELISA	0.100	0.767
Hearing class	CCL5 ELISA	-0.214	0.402
Koos	CCL5 ELISA	0.065	0.885
Tumor volume	CCL5 ELISA	0.029	0.958
<i>CCL2</i> qPCR	CCL5 ELISA	0.184	0.489
<i>CCL5</i> qPCR	CCL5 ELISA	0.534	0.002
<i>CCL18</i> qPCR	CCL5 ELISA	0.003	0.993
<i>TGFB1</i> qPCR	CCL5 ELISA	0.403	0.032
<i>GDF15</i> qPCR	CCL5 ELISA	0.372	0.053
CCL2 ELISA	CCL5 ELISA	0.411	0.025
Age at surgery	CCL18 ELISA	0.122	0.669
Hearing class	CCL18 ELISA	0.060	0.885
Koos	CCL18 ELISA	0.112	0.718
Tumor volume	CCL18 ELISA	0.058	0.885
<i>CCL2</i> qPCR	CCL18 ELISA	0.487	0.007
<i>CCL5</i> qPCR	CCL18 ELISA	0.247	0.288
<i>CCL18</i> qPCR	CCL18 ELISA	0.681	<0.001
<i>TGFB1</i> qPCR	CCL18 ELISA	0.039	0.906
<i>GDF15</i> qPCR	CCL18 ELISA	0.059	0.885
CCL2 ELISA	CCL18 ELISA	0.663	<0.001
CCL5 ELISA	CCL18 ELISA	0.286	0.167
Age at surgery	TGFB1 ELISA	0.044	0.885
Hearing class	TGFB1 ELISA	0.001	0.993
Koos	TGFB1 ELISA	0.333	0.086
Tumor volume	TGFB1 ELISA	0.341	0.109
<i>CCL2</i> qPCR	TGFB1 ELISA	-0.203	0.436
<i>CCL5</i> qPCR	TGFB1 ELISA	0.002	0.993
<i>CCL18</i> qPCR	TGFB1 ELISA	-0.265	0.244
<i>TGFB1</i> qPCR	TGFB1 ELISA	0.547	0.002
<i>GDF15</i> qPCR	TGFB1 ELISA	0.253	0.278
CCL2 ELISA	TGFB1 ELISA	0.214	0.387
CCL5 ELISA	TGFB1 ELISA	0.423	0.022
CCL18 ELISA	TGFB1 ELISA	0.133	0.631
Age at surgery	GDF15 ELISA	-0.010	0.993
Hearing class	GDF15 ELISA	-0.014	0.993
Koos	GDF15 ELISA	0.532	0.002
Tumor volume	GDF15 ELISA	0.473	0.015
<i>CCL2</i> qPCR	GDF15 ELISA	-0.158	0.591

<i>CCL5</i> qPCR	GDF15 ELISA	-0.133	0.631
<i>CCL18</i> qPCR	GDF15 ELISA	-0.159	0.591
<i>TGFB1</i> qPCR	GDF15 ELISA	0.373	0.053
<i>GDF15</i> qPCR	GDF15 ELISA	0.431	0.022
<i>CCL2</i> ELISA	GDF15 ELISA	0.170	0.520
<i>CCL5</i> ELISA	GDF15 ELISA	0.287	0.167
<i>CCL18</i> ELISA	GDF15 ELISA	0.108	0.730
<i>TGFB1</i> ELISA	GDF15 ELISA	0.734	<0.001

Significant p-values are written in bold (p≤0.05).

Table S14. Regressions of investigated cytokines with tumor volume in 45 VS primary cultures.

Coefficients	Estimate	Standard error	t-value	p-value
<i>GDF15</i> qPCR	1.637	0.282	5.806	<0.001
Multiple R-squared: 0.484, Adjusted R-squared: 0.4692 F-statistic: 33.71 on 1 and 36 DF, p value: <0.001				
GDF15 ELISA	2.909	2.808	1.036	0.307
Multiple R-squared: 0.028; Adjusted R-squared: 0.001919 F-statistic: 1.073 on 1 and 37 DF, p-value: 0.307				

Table S15. Baseline data for correlation analysis of CSF samples from 52 patients with sporadic VS.

Variable	Patients (n=52)	Percentage of all patients (n=175)	Small VS (n=20)	Percentage of all patients (n=175)	Large VS (n=20)	Percentage of all patients (n=175)	p-value large vs. small VS
Male	24	13.6	8	4.5	9	5.1	>0.999
Female	28	15.9	12	6.8	11	6.3	
Mean age (years) and IQR	49 ± 11.84 (18-71)		48 ± 7.8 (34-63)		53 ± 12.12 (30-71)		0.16
Median age (years) and SD	50 (14.25)		48 (12.25)		55 (16.5)		
Koos grade							<0.001
I	0	0	0	0	0	0	
II	13	7.4	11	6.3	0	0	
III	16	9.1	9	5.1	2	1.1	
IV	23	13.1	0	0	18	10.2	
AAO-HNS ¹ (hearing class)							0.93
A	17	9.7	6	3.4	4	2.3	
B	14	8.0	4	2.3	6	3.4	
C	3	1.7	1	0.06	2	1.1	
D	9	5.1	5	2.8	3	1.7	
DS ²	6	3.4	3	1.7	3	1.7	
Without preoperative hearing class	3	1.7	1	0.06	2	1.1	

Mean tumor volume (cm ³) and SD	4.3 ± 4.50 (0.1-20.1)	1.0 ± 0.65 (0.1-2.3)	8.2 ± 4.67 (3.1-20.1)	<0.001
Median tumor volume (cm ³) and IQR	2.8 (4.55)	0.8 (1.09)	7.3 (4.03)	
Mean growth rate (cm ³ /year) and SD	0.9 ± 1.01 (0.03-3.7)	n. i. ³	n. i.	
Median growth rate (cm ³ /year) and IQR	0.6 (1.19)	n. i.	n. i.	
Mean relative growth rate (%/year) and SD	3.8 ± 4.58 (0.9-16.9)	n. i.	n. i.	
Median relative growth rate (%/year) and IQR	2.2 (2.35)	n. i.	n. i.	

¹ AAO-HNS: American Academy of Otolaryngology-Head and Neck Surgery;

² DS: surditas for deafness; ³ n.i.: not investigated due to the small sample number

Table S16. Baseline data of CSF control group.

Variable	Total (n=14)	Percentage of all control samples (n=14)
Male	5	35.7
Female	9	64.3
Mean age (years) and SD	54 (20-84)	
Median age (years) and IQR	50.5 (33.5)	

Table S17. Median concentrations of investigated cytokines in CSF of 52 patients and 14 healthy controls.

	Controls	Patients	Large VS	Small VS
Median CCL2 CSF concentration [pg/ml] and IQR	460.50 (177.50)	207.00 (126.00)	225.00 (176.25)	174.50 (73.75)
Median CCL5 CSF concentration [pg/ml] and IQR	1.17 (2.52)	91.45 (434.07)	7.99 (166.65)	334.50 (365.50)
Median CCL18 CSF concentration [pg/ml] and IQR	84.85 (67.47)	248.00 (263.75)	342.00 (309.50)	211.50 (156.00)

Median GDF15 CSF concentration [pg/ml] and IQR	227.00 (296.25)	181.00 (164.25)	230.00 (275.25)	169.00 (106.25)
Median TGFB1 CSF concentration [pg/ml] and IQR	173.00 (82.50)	342.50 (594.25)	233.50 (382.52)	620.00 (483.00)

Table S18. Correlations and p-values of investigated cytokines in CSF of 52 VS patients.

Row	Column	Spearman's r	p-value
Age at surgery	Hearing class	0.490	0.002
Age at surgery	Koos	0.111	0.715
Hearing class	Koos	0.025	0.935
Age at surgery	Tumor volume	0.227	0.430
Hearing class	Tumor volume	0.092	0.715
Koos	Tumor volume	0.880	<0.001
Age at surgery	Growth rate	0.802	0.009
Hearing class	Growth rate	0.263	0.715
Koos	Growth rate	0.887	<0.001
Tumor volume	Growth rate	0.958	<0.001
Age at surgery	Relative growth rate	0.294	0.715
Hearing class	Relative growth rate	-0.234	0.715
Koos	Relative growth rate	0.209	0.715
Tumor volume	Relative growth rate	0.343	0.656
Growth rate	Relative growth rate	0.531	0.319
Age at surgery	CCL2 CSF	-0.085	0.715
Hearing class	CCL2 CSF	-0.163	0.656
Koos	CCL2 CSF	-0.094	0.715
Tumor volume	CCL2 CSF	-0.093	0.715
Growth rate	CCL2 CSF	0.203	0.715
Relative growth rate	CCL2 CSF	0.154	0.758
Age at surgery	CCL5 CSF	-0.169	0.637
Hearing class	CCL5 CSF	-0.021	0.936
Koos	CCL5 CSF	-0.528	<0.001
Tumor volume	CCL5 CSF	-0.487	0.002
Growth rate	CCL5 CSF	-0.336	0.656
Relative growth rate	CCL5 CSF	-0.182	0.715
CCL2 CSF	CCL5 CSF	-0.101	0.715
Age at surgery	CCL18 CSF	0.172	0.637
Hearing class	CCL18 CSF	0.330	0.095
Koos	CCL18 CSF	0.042	0.899
Tumor volume	CCL18 CSF	0.159	0.657
Growth rate	CCL18 CSF	0.217	0.715
Relative growth rate	CCL18 CSF	0.441	0.522
CCL2 CSF	CCL18 CSF	0.106	0.715
CCL5 CSF	CCL18 CSF	-0.002	0.990
Age at surgery	TGFB1 CSF	-0.081	0.715
Hearing class	TGFB1 CSF	-0.002	0.990
Koos	TGFB1 CSF	-0.647	<0.001
Tumor volume	TGFB1 CSF	-0.645	<0.001

Growth rate	TGFB1 CSF	-0.322	0.677
Relative growth rate	TGFB1 CSF	-0.210	0.715
CCL2 CSF	TGFB1 CSF	-0.115	0.715
CCL5 CSF	TGFB1 CSF	0.881	<0.001
CCL18 CSF	TGFB1 CSF	0.028	0.926
Age at surgery	GDF15 CSF	0.346	0.061
Hearing class	GDF15 CSF	0.180	0.637
Koos	GDF15 CSF	0.038	0.902
Tumor volume	GDF15 CSF	-0.003	0.990
Growth rate	GDF15 CSF	-0.067	0.926
Relative growth rate	GDF15 CSF	-0.378	0.637
CCL2 CSF	GDF15 CSF	-0.068	0.758
CCL5 CSF	GDF15 CSF	-0.221	0.630
CCL18 CSF	GDF15 CSF	0.114	0.715
TGFB1 CSF	GDF15 CSF	-0.131	0.715

Significant p-values are written in bold (p≤0.05).

Table S19. Regression of investigated cytokines with tumor volume in CSF of 52 VS patients.

Coefficients	Estimate	Standard error	t-value	p-value
Growth rate	1.986	0.166	11.934	<0.001
CCL5 CSF	0.001	0.001	1.250	0.247
TGFB1 CSF	-0.015	0.014	-1.088	0.308
Multiple R-squared: 0.956; Adjusted R-squared: 0.9395 F-statistic: 57.9 on 3 and 8 DF, p-value: <0.001				
CCL5 CSF	0.003	0.004	0.839	0.406
TGFB1 CSF	-0.149	0.059	-2.505	0.016
Multiple R-squared: 0.244; Adjusted R-squared: 0.2111 F-statistic: 7.422 on 2 and 46 DF, p-value: 0.002				