

1 **Supplemental Materials**

2 **Moulds and *Staphylococcus aureus* enterotoxins are relevant allergens to affect**
3 **type2-inflammation in CRS patients**

4 Yoshihiro Kanemitsu, MD, PhD^a, Kensuke Fukumitsu, MD, PhD^a, Ryota Kurokawa,
5 MD^a, Norihisa Takeda, MD, PhD^a, Yoshiyuki Ozawa MD, PhD^b, Ayako Masaki, MD,
6 PhD^c, Junya Ono, BS, PhD^d, Kenji Izuhara, MD, PhD^e, Jennifer Maries Yap, MS^a,
7 Hirono Nishiyama, MD^a, Satoshi Fukuda, MD, PhD^a, Takehiro Uemura, MD, PhD^a,
8 Tomoko Tajiri, MD, PhD^a, Hirotosugu Ohkubo, MD, PhD^a, Ken Maeno, MD, PhD^a,
9 Yutaka Ito, MD, PhD^a, Tetsuya Oguri, MD, PhD^a, Masaya Takemura, MD, PhD^a,
10 Motohiko Suzuki, MD, PhD^f, and Akio Niimi, MD, PhD^a.

11

12 **Affiliation**

13 a) Department of Respiratory Medicine, Allergy and Clinical Immunology, Nagoya
14 City University School of Medical Sciences, Aichi, Japan.

15 b) Department of Radiology, Nagoya City University School of Medical Sciences,
16 Aichi, Japan.

17 c) Department of Pathology and Molecular Diagnostics, Nagoya City University
18 School of Medical Sciences, Aichi, Japan.

19 d) Shino-Test Corporation, Sagamihara, Japan

20 e) Division of Medical Biochemistry, Department of Biomolecular Sciences, Saga
21 Medical School, Saga, Japan

22 f) Department of Otorhinolaryngology, Nagoya City University School of Medical
23 Sciences, Aichi, Japan.

24 **Corresponding author:** Yoshihiro Kanemitsu, MD, PhD

25 **Contact address:** 1, Kawasumi, Mizuho-cho, Mizuho-ku, Nagoya, Aichi, Japan

26 **Tell:** +81-52-853-8216

27 **Fax:** +81-52-852-0849

28 **Email:** kaney32@med.nagoya-cu.ac.jp

29 **Table E1. The influence of interaction between moulds and SEs sensitization for clinical**
 30 **outcomes in CRS patients**

	F value	p value
The prevalence of asthma	6.39	0.01
Systemic biomarkers		
Blood eosinophils count, / μ L	0.20	0.66
Serum total IgE, IU/mL	1.71	0.20
Serum periostin, ng/mL	4.24	0.04
Upper airways biomarkers		
Sinus eosinophils, /HPF	0.06	0.81
Nasal polyp, presence	7.50	0.006
Nasal polyps, eosinophils, HPF [†]	0.65	0.43
Eosinophilic CRS, presence	4.02	0.045
Lund-Mackay scores, points	2.27	0.14
SNOT-22, points	0.47	0.49
Open essence scores, points	0.98	0.32
Lower airways biomarkers		
AQLQ, points [*]	0.81	0.38
Sputum eosinophils, % [†]	4.95	0.03
periostin, ng/mL [†]	0.60	0.44
FeNO, ppb	0.11	0.74

31 Eosinophilic CRS: defined when eosinophils in sinus or NP tissue show ≥ 70 HPF, ^{*}n = 20, [†]n =
 32 45, AQLQ: Asthma Quality of Life Questionnaire, FeNO: Fractional nitric oxide (One patient
 33 without moulds/SEs sensitization could not measure FeNO because of apparatus failure

34 **Table E2. The impact of sensitization to moulds/SEs (≥ 0.35 UA/mL) on clinical outcomes**

	All participants (n = 84)	moulds/SEs+ (n = 11)	moulds/SEs- (n = 45)	Healthy subjects (n = 28)	p value *	p value ** Alt/SEs+ vs Alt/SEs-	p value ** Alt/SEs+ vs H	p value ** Alt/SEs- vs H
Systemic biomarkers								
Blood eosinophils count, / μL^\dagger	246 (143, 526)	419 (167, 653)	228 (135, 478)	-	-	0.22	-	-
Serum total IgE, IU/mL [†]	137 (26, 431)	569 (389, 1580)	116 (27, 212)	44 (11, 357)	0.0003	0.0005	0.002	0.67
Serum periostin, ng/mL [†]	86 (74, 108)	93 (78, 138)	84 (73, 116)	84 (74, 101)	0.45	0.75	0.42	0.73
Upper airways markers								
Sinus eosinophils, /HPF [‡]	66 (20, 168)	82 (16, 335)	64 (20, 156)	-	-	0.57	-	-
Nasal polyps, presence (%) [†]	38 (68)	8 (73)	30 (67)	-	-	>0.99	-	-
, eosinophils, HPF [§]	85 (6, 145)	135 (77, 291)	77 (4, 126)	-	-	0.03	-	-
Eosinophilic CRS, presence (%) [†]	33 (59)	7 (64)	26 (58)	-	-	>0.99	-	-
Lund-Mackay scores, points [†]	12 (7, 16)	14 (7, 16)	11 (7, 17)	-	-	0.80	-	-
SNOT-22, points	15 (3, 35)	46 (29, 68)	23 (12, 36)	2 (0, 4)	<0.0001	0.052	<0.0001	<0.0001
Open essence scores, points	7 (3, 9)	4 (0, 9)	5 (0, 8)	9 (7, 10)	<0.0001	0.96	0.04	<0.0001
Lower airways markers								
AQLQ, points [¶]	5.8 (5.5, 6.7)	6.2 (4.5, 6.8)	5.6 (5.5, 6.3)	-	-	0.55	-	-
Sputum eosinophils, % ^{††}	0 (0, 3.2)	2.3 (0.5, 35.2)	0.3 (0, 7.0)	0 (0, 0.4)	0.02	0.67	0.02	0.06
periostin, ng/mL ^{††}	7.1 (1.5, 16.3)	19.3 (9.8, 39.0)	11.7 (3.7, 21.0)	1.6 (0.5, 3.4)	<0.0001	0.24	0.0002	0.0001
FeNO, ppb ^{‡‡}	25.8 (17.7, 38.7)	39.4 (24.7, 57.4)	29.0 (21.6, 50.6)	20.6 (16.1, 26.2)	0.004	0.64	0.01	0.01

35 * Analysed by Kruskal-Wallis test, ** Analysed by Steel-Dwass analysis, Wilcoxon rank sum test or Fischer's exact test, [†]n = 56, [‡]n = 76 (CRS/H:

36 56/20) n= 54 (moulds/SEs+/-: 10/44), [§]n = 38(moulds/SEs+/-: 8/30), [¶]n = 20 (moulds/SEs +/-: 7/13), ^{††}n = 65 (moulds/SEs +/-: 8/37, H: 20), ^{‡‡}n = 83,

37 ^{§§}n = 45. moulds: Alternaria and Aspergillus, SEs, Staphylococcus enterotoxins A and B, H: healthy subjects, Eosinophilic CRS: defined when

- 38 eosinophils in sinus or NP tissue show ≥ 70 HPF, AQLQ: Asthma Quality of Life Questionnaire, FeNO: Fractional nitric oxide (One patient without
- 39 moulds/SEs sensitization could not measure FeNO because of apparatus failure)