

Supplementary Table 1. Primer sequences used in this study

Gene	Forward 5'-3'	Reverse 5'-3'
IL17a	CAGACTACCTCAACCGTTCCAC	TCCAGCTTTCCTCCGCATTGA
Cxcl2	CATCCAGAGCTTGAGTGTGACG	GGCTTCAGGGTCAAGGCAAAC
Cxcr2	CTCTATTCTGCCAGATGCTGTCC	ACAAGGCTCAGCAGAGTCACCA
IL10	CGGGAAGACAATAACTGCACCC	CGGTTAGCAGTATGTTGTCCAGC
β -actin	CATTGCTGACAGGATGCAGAAGG	TGCTGGAAGGTGGACAGTGAGG
<i>E. lenta</i> ¹	CTTGCTCCGGACAACCTTGGA	CTTCTTCTGCAGGTACCGTCAATT
16S	ACTCCTACGGGAGGCAGCAGT	ATTACCGCGGCTGCTGGC

Supplementary Table 2. Detail information of the dysregulated genes of Cancer Pathway in AOM model (AOM+Smoking vs AOM)

Gene	Full name	P value	FDR	Fold Change
Tbx2	T-box transcription factor 2	0.02	0.14	3.58
Pgf	Placental growth factor	0.11	0.19	3.50
Flt1	FMS-like tyrosine kinase 1	0.13	0.20	3.12
Mki67	Marker of proliferation Ki-67	0.07	0.18	2.90
Stmn1	Stathmin 1	0.05	0.18	2.88
Cdc20	Cell division cycle 20	0.09	0.18	2.84
Skp2	S-phase kinase-associated protein 2	0.08	0.18	2.77
Angpt2	Angiopoietin 2	0.08	0.18	2.63
Aurka	Aurora kinase A	0.07	0.18	2.61
Acly	ATP citrate lyase	0.06	0.18	2.57
Igfbp3	Insulin-like growth factor binding protein 3	0.08	0.18	2.53
Tnks	Tankyrase	0.01	0.09	2.49
Ccl2	Chemokine (C-C motif) ligand 2	0.29	0.35	2.34
Cdh2	Cadherin 2	0.48	0.55	2.22
Ercc5	Excision repair cross-complementation group 5	0.08	0.18	2.17
Xrcc4	X-ray repair cross-complementing 4	0.02	0.14	2.15
Dkc1	Dyskeratosis congenita 1	0.12	0.20	2.09
Mcm2	Minichromosome maintenance deficient 2	0.12	0.20	2.09
Snai1	Snail family zinc finger 1	0.47	0.54	2.01
Atrx	Alpha thalassemia/mental retardation syndrome X-linked homolog	0.09	0.18	0.47
Snai3	Snail family zinc finger 3	0.30	0.36	0.44
Tek	Tyrosine kinase	0.15	0.23	0.41
Apaf1	Apoptotic peptidase activating factor 1	0.17	0.24	0.41
Tinf2	Terf1 (TRF1)-interacting nuclear factor 2	0.07	0.18	0.41
Terf2ip	Telomeric repeat binding factor 2	0.13	0.20	0.40
Gadd45g	Growth arrest and DNA-damage-inducible 45γ	0.07	0.18	0.28

Supplementary Table 3. Detail information of the dysregulated genes of Inflammatory Response and Autoimmunity in AOM model (AOM+Smoking vs AOM)

Gene	Full name	P value	FDR	Fold Change
Cxcl5	Chemokine (C-X-C motif) ligand 5	0.03	0.26	14.61
Ifng	Interferon gamma	0.01	0.24	5.40
Cxcl1	Chemokine (C-X-C motif) ligand 1	0.21	0.45	4.09
Ccl19	Chemokine (C-C motif) ligand 19	0.28	0.51	3.81
Tnfsf14	Tumor necrosis factor (ligand) superfamily, member 14	0.11	0.34	3.79
Cxcr1	Chemokine (C-X-C motif) receptor 1	0.05	0.27	3.69
Sele	Selectin, endothelial cell	0.07	0.27	3.65
Il6ra	Interleukin 6 receptor, alpha	0.07	0.27	3.62
Il17a	Interleukin 17A	0.07	0.27	3.58
Il6	Interleukin 6	0.12	0.34	3.45
Cxcr4	Chemokine (C-X-C motif) receptor 4	0.92	0.96	3.21
Ccl3	Chemokine (C-C motif) ligand 3	0.08	0.27	3.19
Cxcl2	Chemokine (C-X-C motif) ligand 2	0.09	0.29	2.98
Cd40lg	CD40 ligand	0.21	0.45	2.80
Tlr9	Toll-like receptor 9	0.88	0.96	2.70
Ccl7	Chemokine (C-C motif) ligand 7	0.04	0.27	2.67
Ltb	Lymphotoxin B	0.96	0.98	2.66
Il1b	Interleukin 1 beta	0.03	0.26	2.63
Il22	Interleukin 22	0.27	0.51	2.62
Il23a	Interleukin-23 subunit alpha	0.08	0.27	2.62
Cxcl9	Chemokine (C-X-C motif) ligand 9	0.30	0.51	2.39
Ccr3	Chemokine (C-C motif) receptor 3	0.05	0.27	2.38
Ccr4	Chemokine (C-C motif) receptor 4	0.20	0.45	2.33
Lta	Lymphotoxin A	0.89	0.96	2.32
Ccl2	Chemokine (C-C motif) ligand 2	0.03	0.26	2.09
Itgb2	Integrin beta 2	0.30	0.51	2.06
Il5	Interleukin 5	0.28	0.51	2.00
Ccr2	Chemokine (C-C motif) receptor 2	0.24	0.49	0.40
Ccr7	Chemokine (C-C motif) receptor 7	0.39	0.57	0.36
Il10	Interleukin 10	0.12	0.34	0.29
Ccl22	Chemokine (C-C motif) ligand 22	0.12	0.34	0.26
Ccl24	Chemokine (C-C motif) ligand 24	0.00	0.24	0.20

Supplementary Table 4. Detail information of the dysregulated genes of Cancer Pathway in germ-free model (GF-AOMS vs GF-AOM)

Gene	Full name	<i>P</i> value	<i>FDR</i>	Fold Change
Map2k1	Mitogen-activated protein kinase kinase 1	0.40	0.90	2.10
Casp2	Caspase 2	0.57	0.90	1.90
Mki67	Marker of proliferation Ki-67	0.66	0.90	1.89
Pgf	Placental growth factor	0.96	0.98	1.70
Gsc	Goosecoid	0.52	0.90	1.69
Igfbp5	Insulin-like growth factor binding protein 5	0.12	0.90	1.68
Fasl	Fas ligand (TNF superfamily, member 6)	0.47	0.90	1.57
Car9	Carbonic anhydrase 9	0.64	0.90	1.56
Angpt2	Angiopoietin 2	0.72	0.90	1.53
Cpt2	Carnitine palmitoyltransferase 2	0.10	0.90	0.53
Apaf1	Apoptotic peptidase activating factor 1	0.39	0.90	0.48
Gadd45g	Growth arrest and DNA-damage-inducible 45γ	0.49	0.90	0.37

Supplementary Table 5. Detail information of the dysregulated genes of Inflammatory Response and Autoimmunity in germ-free model (GF-AOMS vs GF-AOM)

Gene	Full name	<i>P</i> value	<i>FDR</i>	Fold Change
Cxcl2	Chemokine (C-X-C motif) ligand 2	0.01	0.43	6.20
Nos2	Nitric oxide synthase 2	0.22	0.81	4.92
Cxcl3	Chemokine (C-X-C motif) ligand 3	0.10	0.81	4.66
Cxcr2	Chemokine (C-X-C motif) receptor 2	0.29	0.81	4.05
Cd40lg	CD40 ligand	0.13	0.81	3.71
Il17a	Interleukin 17A	0.20	0.81	3.57
Sele	Selectin, endothelial cell	0.33	0.81	3.46
Ccl5	Chemokine (C-C motif) ligand 5	0.16	0.81	3.24
Ifng	Interferon gamma	0.38	0.81	2.80
Ccr4	Chemokine (C-C motif) receptor 4	0.22	0.81	2.74
Cxcl11	Chemokine (C-X-C motif) ligand 11	0.43	0.81	2.63
Crp	C-reactive protein	0.23	0.81	2.59
Cd14	CD14 molecule	0.01	0.43	2.38
C3	Complement component 3	0.32	0.81	2.31
Ccl19	Chemokine (C-C motif) ligand 19	0.03	0.74	2.26
C4b	Complement component 4B	0.25	0.81	2.00

Reference

1. Kageyama A, Benno Y, Nakase T. Phylogenetic evidence for the transfer of *Eubacterium lentum* to the genus *Eggerthella* as *Eggerthella lenta* gen. nov., comb. nov. *Int J Syst Bacteriol* 1999;49 Pt 4:1725-32. doi: 10.1099/00207713-49-4-1725 [published Online First: 1999/11/11]