

Diversity of Neurotransmitter Producing Human Skin Commensals.

<i>E. durans</i>	-----MESLNDNLNALLSGTKLRATAKSI-KLVNRFGRPLGWRQNYMPQDM	47
<i>E. faecalis</i>	-----MKNELAKGEMNLNLFIDGKAENGQLYKDLLIDLVDHLGWRQNYMPQDM	51
<i>E. mundtii</i>	-----MESKVDNLNLFIDGKAENGQTYKALLNELVDHLGWRQNYMPQDM	48
<i>L. brevis</i>	MLNLQEVSDMEKSNRSLKDLNLFIDGKAENGQLYKDLLNKLVDHLGWRQNYIPSPD	60
<i>S. epidermidis</i>	-----MKRKDDINLHALFIDGKSENGELYKMDLINLVDHLGWRQNYMPQDK	47
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<i>E. durans</i>	PIITPEEKSSASFEHTVNRTKDVLSAISARMTHSVPHNAGRYWGHMNSLMPSLAY	107
<i>E. faecalis</i>	PVISSQERTSESYEKTVNHMKDVLNEISSRMTHSVPHNAGRYWGHMNSLMPSLAY	111
<i>E. mundtii</i>	PIITPEEKSSASFEHTVNRTKDVLSAISARMTHSVPHNAGRYWGHMNSLMPSLAY	108
<i>L. brevis</i>	NMIGPEDQNSPAFKKTVGHMKTVLDQLSERIRTESVPHNAGRYWGHMNSLMPALAY	120
<i>S. epidermidis</i>	PAISSHEKNSDYLNTIEHMKVMNEISSRMTHSVPHNAGRYWGHMNSLMPILAY	107
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<i>E. durans</i>	NFAMLWGNVAVYESSPATSQMEEVGLFAKLMSYKDGWGHIVADGSLANLEGLWYARN	167
<i>E. faecalis</i>	NFAMLWGNVAVYESSPATSQMEEVGLFAKLMSYKDGWGHIVADGSLANLEGLWYARN	171
<i>E. mundtii</i>	NFAMLWGNVAVYESSPATSQMEEVGLFAKLMSYKDGWGHIVADGSLANLEGLWYARN	168
<i>L. brevis</i>	NYAMLWGNVAVYESSPATSQMEEVGLFAKLMSYKDGWGHIVADGSLANLEGLWYARN	180
<i>S. epidermidis</i>	NFAMLWGNVAVYESSPATSQMEEVGLFAKLMSYKDGWGHIVADGSLANLEGLWYARN	167
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<i>E. durans</i>	IKSLPLAMQEVTPELVAGKSDWELNMSTKEIMDLDSVPDKIDDIKAHSARSQKLNQKL	227
<i>E. faecalis</i>	IKSLPFAMKEVPELVAGKSDWELNMPTKEIMDLLESADEIDEIKAHARSQKHLQAI	231
<i>E. mundtii</i>	IKSLPLAMKEVPELVAGKSDWELNMSTKEIMDLDSVPDKIDDIKAHSARSQKHLQKL	228
<i>L. brevis</i>	IKSLPFAMKEVPELVAGKSDWELNMPTKEIMDLLESADEIDEIKAHARSQKHLQKL	240
<i>S. epidermidis</i>	IKSLPLAMKCTPSLVENKTDWELNMSTKEIMDLLESADEIDEIKAHARSQKHLQKL	227
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<i>E. durans</i>	GKWLVPQTKHYSWLKAADIIGVGLDQVIVPVDHNYRMDINELEKIVRGAAEKTPIILGV	287
<i>E. faecalis</i>	GKWLVPQTKHYSWLKAADIIGVGLDQVIVPVDHNYRMDINELEKIVRGAAEKTPIILGV	291
<i>E. mundtii</i>	GKWLVPQTKHYSWLKAADIIGVGLDQVIVPVDHNYRMDINELEKIVRGAAEKTPIILGV	288
<i>L. brevis</i>	GKWLVPQTKHYSWLKAADIIGVGLDQVIVPVDHNYRMDINELEKIVRGAAEKTPIILGV	300
<i>S. epidermidis</i>	GKWLVPQTKHYSWLKAADIIGVGLDQVIVPVDHNYRMDINELEKIVRGAAEKTPIILGV	287
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<i>E. durans</i>	VGVGSTEEGAIDGIDKIVELRRVLEKDGIFYLHVDAAVGGYGRAIFLDEDNFIPFEE	347
<i>E. faecalis</i>	VGVGSTEEGAVDSIDKIIARDELMDKGIYFYLHVDAAVGGYGRAIFLDEDNFIPFEE	351
<i>E. mundtii</i>	VGVGSTEEGAIDGIDKIVELRRVLEKDGIFYLHVDAAVGGYGRAIFLDEDNFIPFEE	348
<i>L. brevis</i>	VGVGSTEEGAVDSIDKIVLRQLKQEGIFYLHVDAAVGGYGRAIFLDEDNFIPFEE	360
<i>S. epidermidis</i>	VGVGSTEEGAVDSIDKIVLRQLKQEGIFYLHVDAAVGGYGRAIFLDEDNFIPFEE	347
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<i>E. durans</i>	LKDVFHKNVFTENKNYILEEVHSAKAEIEEASVTIDPHKMGVVPYSAGGIVTDKDIRMR	407
<i>E. faecalis</i>	LQDVHEEVGFKEKKEHISREVYDAYKAEIEEASVTIDPHKMGVVPYSAGGIVTDKDIRMR	411
<i>E. mundtii</i>	LKEVHAKHVFTEKDYLLLEEVHSAKAEIEEASVTIDPHKMGVVPYSAGGIVTDKDIRMR	408
<i>L. brevis</i>	LQKVHAEHVFTEKDYLLLEEVHSAKAEIEEASVTIDPHKMGVVPYSAGGIVTDKDIRMR	420
<i>S. epidermidis</i>	LQKVHAEHVFTEKDYLLLEEVHSAKAEIEEASVTIDPHKMGVVPYSAGGIVTDKDIRMR	407
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<i>E. durans</i>	DVISYFATYVFEKGADIPALLGAYILEGSKAGATAASVWAAHVLPLNVTGYGKLMGASI	467
<i>E. faecalis</i>	DVISYFATYVFEKGADIPALLGAYILEGSKAGATAASVWAAHVLPLNVTGYGKLMGASI	471
<i>E. mundtii</i>	DVISYFATYVFEKGADIPALLGAYILEGSKAGATAASVWAAHVLPLNVTGYGKLMGASI	468
<i>L. brevis</i>	DTISYFATYVFEKGADIPALLGAYILEGSKAGATAASVWAAHVLPLNVTGYGKLMGASI	480
<i>S. epidermidis</i>	EVISYFATYVFEKNAEIPALLGAYILEGSKAGATAASVWAAHVLPLNVTGYGKLMGASI	467
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<i>E. durans</i>	EGAHRYFNFLNLSFKVGDKEIEVHPLTYPDFNMVDYVFEKGNDDLVAHNLNHDVYDY	527
<i>E. faecalis</i>	EGSHHFYFNFLNLSFKVGDKEIEVHPLTYPDFNMVDYVFEKGNDDLVAHNLNHDVYDY	531
<i>E. mundtii</i>	EGAHRYFNFLNLSFKVGDKEIEVHPLTYPDFNMVDYVFEKGNDDLVAHNLNHDVYDY	528
<i>L. brevis</i>	EGAHRYFNFLNLSFKVGDKEIEVHPLTYPDFNMVDYVFEKGNDDLVAHNLNHDVYDY	540
<i>S. epidermidis</i>	EGALRYFNFLNLSFKVGDKEIEVHPLTYPDFNMVDYVFEKGNDDLVAHNLNHDVYDY	527
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<i>E. durans</i>	SSYVKGSIYGNFELTSHDTFAIPDYGNSPLQFVNQLGFSDEEWNRAKGVTVLRASVMTPT	587
<i>E. faecalis</i>	ASYVKGSIYGNFELTSHDTFAIPDYGNSPLQFVNQLGFSDEEWNRAKGVTVLRASVMTPT	591
<i>E. mundtii</i>	SSYVKGSIYGNFELTSHDTFAIPDYGNSPLQFVNQLGFSDEEWNRAKGVTVLRASVMTPT	588
<i>L. brevis</i>	ASYVKGSIYGNFELTSHDTFAIPDYGNSPLQFVNQLGFSDEEWNRAKGVTVLRASVMTPT	600
<i>S. epidermidis</i>	ASYVKGSIYGNFELTSHDTFAIPDYGNSPLQFVNQLGFSDEEWNRAKGVTVLRASVMTPT	587
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<i>E. durans</i>	MNKEEFEEYAEKIKAAALQEKLEKIYADQLLASEAK	623
<i>E. faecalis</i>	MNDKEEFDDYAPKIQAAALQEKLEKIYADQLLASEAK	620
<i>E. mundtii</i>	MNKAEEFEEYAEKIKAAALQEKLEKIYADQLLASEAK	624
<i>L. brevis</i>	MNQRENFDYAPKIKAAALQEKLEKIYADQLLASEAK	635
<i>S. epidermidis</i>	MNDKDKFEETPKIKAAALQEKLEKIYADQLLASEAK	616
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Figure S1: Comparison of the amino acid sequence of tyrosine decarboxylase from *S. epidermidis* 102 with those of *Enterococcus durans* IPLA 655 (GenBank accession no. CAF33980), *E. faecalis* JH2-2 (GenBank accession no. AAM46082), *E. mundtii* QU 25 (GenBank accession no. BAO05941.1), and *Levilactobacillus brevis* IOEB (GenBank accession no. AAN77279) strains using Clustal Omega (1.2.4). The conserved HVDAAY motif and the PLP binding site are boxed. Conserved residues are marked with an asterisk (*).

SadA	MEMEFNENNIDLETIIRDEV--NKYLSRDIGDLPATQQAPLELREKYEKMEVPN-----K	53
TDC	--MK-RKDDINLHALFIGDKSENGELYKDM--LINLVDEHLGWRQNYMPQDKPAISSHEK	55
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SadA	GRDIY----EVLKDLNNEVLNYLYR---PNH-----PRSFSPFIP---GPASRLSWLG	95
TDC	NSDSYLNITIEHMKVMEISSRMRTHSVPHSAGRYWGHMNSETLLPSILAYNFAMLWNG	115
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SadA	DILTTANNIHASNANATLPINIERNLINLVGKIGYEIK-----PAGGVFVSGGSMAN	149
TDC	NNVAYESSPAT-----SQMEEVGYDLAKLMSYNNGWGHIVADGSLAN	158
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SadA	LTAIVAARDAQVE-----MEDIKK---	168
TDC	LEGLWYARNIKSLPLAMKKCTPSLVENKTDWELLNMSTQEIIDLMEKAEDRIDDLKQYSA	218
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SadA	-----ATVYLTSTQ-T-HHSVGKALHVAGFLKNNIRRIEYNDFTMNTDSLKAAIDKDI	219
TDC	RSQKNLQSLGKWLVPQTKHYSWLKAADIIGIGIDQIVSVPVDSYRMDIDELEKIIRTLV	278
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SadA	EEGYKAMVIATAGTTNTGSDVDFTTLGDI-----DHYNLWLHMDGAYGLSH---I---	268
TDC	NEGTPILGWVGWVGSTEEGAVDSIDQIVALREKLFSEGIYYIHMVDAAYGGYARSIFLDE	338
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SadA	-----LSDKAQHLFKGIERSDSASWDAHKLFLQTYSCAM	302
TDC	NNNFIPFDDLQKVHHEYGVFTENTYITKEVYEAFAKIELTESVTIDPHKMGYPYPSAGG	398
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SadA	VIVKEKNHLLQSFGEDAEYLDDIASDDVIDPEMLGIELT---RPARALKLWITLQVIG	358
TDC	IAIKDIRM-----REVISYFATYVFEKNAEIPALLGAYILEGSKAGATAVSVAAHVLPL	453
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SadA	EDEIIERIKYGEGLAEYAEYVSSLDNWRI-----ISHANLSIVNFRY	401
TDC	LN----ITGYGKLMGASIEG---ALRFYNFLNTQSFKIGDKEIELYTLTRPDFNMVDYVF	506
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SadA	ENSDLTEAQNQLNSMAAQK-----IADSGYAIAYTTVLNNQRVIRLCTTNPLTTH	452
TDC	K-----EKGNDLVSMNELNHSFYEQASYVSGNIYGNFITSHTD-FAIPDYGNSPLSFV	560
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SadA	DDIRET-----INRLDQYIGDYMKDA-----	474
TDC	KNLGFSGDEWDRAKVTILRAAVLTPYMNDKDKFEETPKIKSAIQDKLERIYKIK	616
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Figure S2: Comparison of the amino acid sequences of tyrosine decarboxylase from *S. epidermidis* 102 and SadA from *S. epidermidis* O47 (GenBank accession no. QKN61770.1) using Clustal Omega (1.2.4). Conserved residues are marked with an asterisk (*).

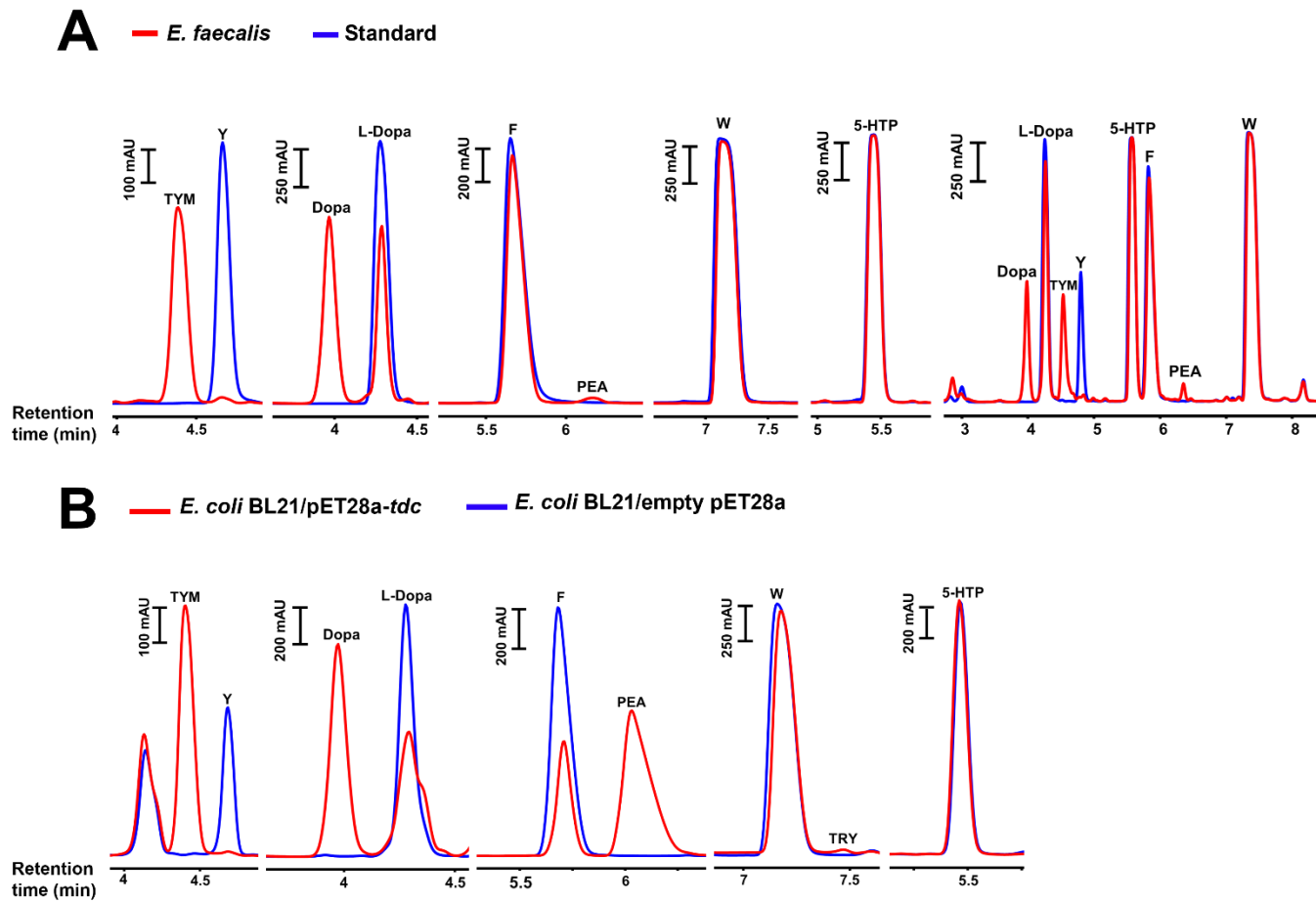


Figure S3: RP-HPLC chromatograms of neurotransmitter production by: **A)** *E. faecalis* ATCC 19433 after overnight incubation in 5xPBS buffer/10% glucose containing individual or a combination of substrates (1 mg/mL each). 5xPBS buffer/10% glucose supplemented with substrates (1 mg/mL each) was used as the standard; **B)** *E. coli* BL21 transformants harboring *tdc* gene from *E. faecalis* ATCC 19433 in the vector pET28a after overnight incubation in 5xPBS buffer/10% glucose containing individual substrates (1 mg/mL each) in comparison with transformants harboring empty plasmid. **5-HTP**, 5-hydroxytryptophan; **W**, tryptophan; **F**, phenylalanine; **Y**, tyrosine; **TRY**, tryptamine; **PEA**, phenethylamine; **Dopa**, dopamine; **TYM**, tyramine.

Table S1: Total bacterial count in the antecubital fossa area from 30 healthy subjects.

Volunteer	Age (years)	Gender	Total bacterial count (LogCFU/100 cm ²)
1	76	M	2.46
2	37	F	5.77
3	32	M	3.60
4	24	M	6.14
5	26	F	5.03
6	31	F	3.99
7	28	F	3.00
8	31	F	3.23
9	24	F	4.70
10	29	F	3.63
11	63	M	3.22
12	24	M	3.03
13	34	M	3.15
14	64	M	5.06
15	32	F	2.28
16	35	F	5.07
17	28	F	3.23
18	26	M	3.38
19	30	F	4.07
20	30	M	3.36
21	26	F	3.49
22	24	F	5.39
23	39	F	5.33
24	26	M	3.20
25	31	M	4.17
26	29	M	3.51
27	22	M	3.01
28	29	M	3.79
29	58	M	3.47
30	58	F	2.49

CFU, colony forming unit; F, female; M, male

Table S3: Primer sets for detection of sadA gene in *Staphylococcus* spp.

Primer set (5'→3')	Length (bp)	Species	Strain	NCBI accession number
F, CKGATAAGATATGTGAWAGTCC R, GTMTTGTATCTGGYGGTTCWA	394	<i>S. aureus</i>	MS4	CP009828.1
			M013	CP003166.2
			RIVM6519	CP015173.1
			SA957	CP003603.1
		<i>S. capitis</i>	Sc1516941	CP145206.1
		<i>S. caprae</i>	JMUB145	AP018585.1
		<i>S. carnosus</i>	LTH 3730	CP016760.1
			TM300	AM295250.1
		<i>S. condimenti</i>	StO 2014-01	CP018776.1
			DSM 11674	CP015114.1
		<i>S. epidermidis</i>	O47	CP040883.1
			SEI	CP009046.1
			PM221	HG813242.1
		<i>S. haemolyticus</i>	JCSC1435	AP006716.1
		<i>S. hominis</i>	S00278	NZ_JACHLT010000017
			SDD3	VJMX01000002.1
		<i>S. lugdunensis</i>	RMLUG4	CP084440.1
		<i>S. petrasii subsp. pragensis</i>	CCM 8529	SRPJ01000003.1
		<i>S. saprophyticus</i>	sap-wu-085	JARZPO010000009.1
F, GCGTTACGTTGATACAGAGA R, CCAGCACGATATGTATTTAGC	363	<i>S. coagulans</i>	M611545/16/1	JABTCP010000002.1
		<i>S. schleiferi</i>	TSCC54	AP014944.1
			1360-13	CP009470.1
			NCTC12218	LR962863.1
F, GGTGTTTTTGTTCAGGCGGTTC R, CCATAAGCGCCATCTGCATGGA	377	<i>S. lutrae</i>	ATCC 700373	CP020773.1

Table S7: Sequences of the oligonucleotides used in construction of *S. epidermidis* 102 mutant lacking *tdc* gene (102 Δ *tdc*) and expression vectors.

Primers	Sequence 5'→3'
KOS1F	CGCGCAGATCTGTCGACGATAATTAAAAACCCCTTTCTCTTTTTTC
KOS1R	GAGATGGATTTTTACCTCCAAAAGGTACAAACACTACTGAGC
KOS2F	CAGTAGTGTGTGTACCTTTTGGAGGTAAAAATCCATCTC
KOS2R	TGCAGGCATGCAAGCTTGATCTAAAATTAATTGTTGTTTTAATGAGG
KOS3F	GCGTTACGGGTATTAGCTTT
KOS3R	GGGGTGTTCAATTCCTTAT
32S	GGTGGTGGTGCTCGAGTGCTTATTTTACGTCGTAAATTTGTTT
33S	CGCGGCAGCCATATGGCTAGCATGAAAAACGAAAAATTAGCAAAAG
42S	GCAGGAATATCGGCACCTTT
44S	GACACATCGTTGCTGATGGT
78S	GGTGGTGGTGCTCGAGTGCTTATTTAATTTTATAAATTCTTTCTAATTTATCTTG
79S	CGCGGCAGCCATATGGCTAGCATGAAAAGAAAAGACGATATCAATTTG
81S	GAAACAGCTGTAGCACCAGC
82S	GCATTATTCTTGGTTAAAAGC