

Supplementary Table 4, Related to Methods. Reagents and Resources.

REAGENT or RESOURCE	SOURCE	IDENTIFIER
Antibodies		
mouse anti-His tag	Cell Sciences	CSI20563B
rabbit anti-HVCN1	Aviva Systems Biology	OAPB01154
rabbit anti-HVCN1	Alomone Labs	AHC-001
rabbit anti-HVCN1	Invitrogen (Thermo Fisher Scientific)	PA5-24964
mouse anti- β -Actin	Cell Signaling Technology	8H10D10
mouse PE/Cy7 anti-human CD19	BioLegend	302215
mouse FITC anti-human CD3	BioLegend	300406
mouse Alexa Fluor® 700 anti-human CD14	BioLegend	325614
mouse PE anti-human CD4	BioLegend	317410
mouse APC anti-human CD8a	BioLegend	300912
mouse APC anti-human CD11b	BioLegend	301310
mouse Alexa Fluor® 700 anti-mouse/human CD11b	BioLegend	101222
PE/Cy7 Mouse IgG1, κ Isotype Ctrl Antibody	BioLegend	400126
FITC Mouse IgG1, κ Isotype Ctrl Antibody	BioLegend	400108
Alexa Fluor® 700 Mouse IgG1, κ Isotype Ctrl Antibody	BioLegend	400143
PE Mouse IgG1, κ Isotype Ctrl Antibody	BioLegend	400111
APC Mouse IgG1, κ Isotype Ctrl Antibody	BioLegend	400120
Goat anti-Mouse IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 680	Invitrogen	A-21057
Goat anti-Rabbit IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor 680	Invitrogen	A-21076
mouse anti-CC30 LukAB	This study, Envigo Inc.	N/A
Bacterial and Virus Strains		
<i>E. coli</i> Endura ElectroCompetent cells	Lucigen	60242
<i>E. coli</i> IM30B	1	VJT 48.100
<i>E. coli</i> T7 LysY/LacQ	NEB	C3013I
<i>E. coli</i> OverExpress C43(DE3) Chemically Competent Cells	Lucigen	60446-1
<i>S. aureus</i> 62300D1 (CC30)	2	VJT 48.91
<i>S. aureus</i> 62300D1 Δ lukAB	This study	VJT 61.87
<i>S. aureus</i> MUZ211 (CC30)	3	VJT 48.94
<i>S. aureus</i> RN4220	4	VJT 2.60
<i>S. aureus</i> Newman (CC8)	5	VJT 2.97
<i>S. aureus</i> Newman $\Delta\Delta\Delta$	6	VJT 31.58
<i>S. aureus</i> MW2 (CC1)	7	VJT 4.79
<i>S. aureus</i> Mu50 (CC5)	8	VJT 15.52
<i>S. aureus</i> Clinical isolate # 52 (CC8)	9	VJT 38.21
<i>S. aureus</i> MRSA252 (CC30)	10	VJT 21.18
<i>S. aureus</i> Clinical isolate # 33 (CC45)	9	VJT 38.08
<i>S. aureus</i> BVED 022 (CC398)	This study	VJT 46.40
<i>S. aureus</i> Newman $\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC1 LukAB	This study	VJT 46.29

<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC5 LukAB	This study	VJT 46.35
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC8 LukAB	¹¹	VJT 46.28
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC30 LukAB	This study	VJT 46.19
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC45 LukAB	This study	VJT 46.33
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC75 LukAB	This study	VJT 47.16
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-CC398 LukAB	This study	VJT 46.54
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis- <i>S. schweitzeri</i> LukAB	This study	VJT 48.11
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-LukE	⁶	VJT 37.02
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-LukD	⁶	VJT 37.31
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-HlgA	⁶	VJT 40.67
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-HlgB	⁶	VJT 37.37
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-LukS	⁶	VJT 37.05
<i>S. aureus</i> Newman $\Delta\Delta\Delta\Delta$ pOS1_PlukAB-lukAs.s.-6xHis-LukF	⁶	VJT 37.34
<i>S. aureus</i> USA300 LAC Δ lukAB	¹²	VJT 14.26
Biological Samples		
Human blood samples were obtained as buffy coats from healthy, anonymous, consenting adult donors	New York Blood Center	N/A
Chemicals, Peptides, and Recombinant Proteins		
GM-CSF (Leukine (250 mg GM-CSF))	NYU Langone Medical Center Pharmacy	N/A
Human IL-4 Carrier-Free Recombinant Protein, eBioscience	Invitrogen	34-8049-82
Purified recombinant LukED, HlgAB, and LukAB variants	This study	N/A
Blasticidin	Invivogen	ant-bl-05
Puromycin	Invivogen	ant-pr-1
Polybrene Infection/Transfection Reagent	Millipore	TR-1003-G
X-tremeGENE 9 DNA Transfection Reagent	Roche	XTG9-RO
Accumax Cell Dissociation Solution	Innovative Cell Technologies	AM105
eBioscience™ Fixable Viability Dye eFluor™ 450	Invitrogen	65-0863-14
HRP Streptavidin	BioLegend	405210
EZ-Link™ NHS-PEG4-Biotin, No-Weigh™ Format	Thermo Scientific	21329
Gateway™ BP Clonase™ II Enzyme mix	Invitrogen	11789020
Gateway™ LR Clonase™ II Enzyme mix	Invitrogen	11791020

Propidium Iodide Solution	G-biosciences	786-1272
NucBlue™ Live ReadyProbes™ Reagent (Hoechst 33342)	Thermo Fisher Scientific	R37605
Critical Commercial Assays		
CytoTox-ONE™ Homogeneous Membrane Integrity Assay	Promega	G7890
CellTiter 96® AQueous One Solution Cell Proliferation Assay (MTS)	Promega	G3580
EasySep™ Human CD4+ T Cell Isolation Kit	StemCell Technologies	17952
EasySep™ Human CD8+ T Cell Isolation Kit	StemCell Technologies	17953
EasySep™ Human B Cell Isolation Kit	StemCell Technologies	17954
CD14 MicroBeads	Miltenyi Biotec	130-050-201
Pierce™ BCA Protein Assay Kit	Thermo Scientific	23225
SYPRO™ Ruby Protein Gel Stain	Invitrogen (Thermo Fisher Scientific)	S12001
Deposited Data		
Experimental Models: Cell Lines		
THP1	ATCC	TIB-202
THP1 scramble shRNA	This study	N/A
THP1 <i>ITGAM</i> shRNA	This study	N/A
THP1 <i>ITGAM</i> shRNA, non-targeting sgRNA	This study	N/A
THP1 <i>ITGAM</i> shRNA, <i>HVCN1</i> sgRNA (1)	This study	N/A
THP1 <i>ITGAM</i> shRNA, <i>HVCN1</i> sgRNA (2)	This study	N/A
THP1 <i>ITGAM</i> shRNA, <i>OGT</i> sgRNA	This study	N/A
THP1 <i>ITGAM</i> shRNA, <i>ASGR1</i> sgRNA	This study	N/A
THP1 <i>ITGAM</i> shRNA, GECKO-libA	This study	N/A
THP1 <i>ITGAM</i> shRNA, GECKO-libB	This study	N/A
HL60	ATCC	CCL-240
HL60 scramble shRNA	¹³	N/A
HL60 <i>ITGAM</i> shRNA	¹³	N/A
HL60 <i>CD18</i> shRNA	¹³	N/A
CD18 CHO-K1	¹⁴	N/A
CD18 CHO-K1 Fluc	This study	N/A
CD18 CHO-K1 <i>HVCN1</i>	This study	N/A
CD18 CHO-K1 m <i>HVCN1</i>	This study	N/A
Lenti-X 293T	Takara Bio USA	632180
Experimental Models: Organisms/Strains		
Mouse: WT C57BL/6 mice	The Jackson Laboratory	
Mouse: h <i>HVCN1</i> C57BL/6 mice	This study	
Mouse: CD-1	Charles River Laboratories	

Oligonucleotides		
Primers used in this study, see Supplementary Table 5	see Supplementary Table 5	N/A
Recombinant DNA		
pIMAY	15	N/A
pIMAY-CC30-LukAB-Kan	This study	N/A
pLenti CMV Puro DEST (w118-1)	Was a gift from Eric Campeau & Paul Kaufman ¹⁶	Addgene plasmid #17452
pDONR221 (Gateway Donor vector used to generate pENTR clones)	Thermo Fisher Scientific	12536017
pENTR221 Fluc (Gateway-compatible plasmid encoding firefly luciferase (Fluc))	Gift from John Schoggins (UTSW) ¹⁷	N/A
pENTR221 human HVCN1 (Gateway-compatible plasmid encoding <i>HVCN1</i>)	Ultimate ORF Clones (Thermo Fisher Scientific)	N/A
pCMV-SPORT6 mHVCN1 (Used to amplify <i>Hvcn1</i> gene)	Dharmacon (Horizon Inspired Cell Technologies)	Clone ID: 4913027
pENTR211 mHVCN1 (Gateway-compatible plasmid encoding <i>Hvnc1</i>)	This study	N/A
pLenti CMV Puro Fluc (Used to generate stable cell lines expressing firefly luciferase (control gene))	This study	N/A
pLenti CMV Puro human HVCN1 (Used to generate stable cell lines expressing <i>HVCN1</i>)	This study	N/A
pLenti CMV Puro mHVCN1 (Used to generate stable cell lines expressing <i>Hvcn1</i>)	This study	N/A
pCMV6-AC-GFP-HVCN1-WT	OriGene	RG202323
pCMV6-AC-GFP-mHVCN1-WT	This study	N/A
pCMV6-AC-GFP-mHVCN1-hEC1 (amino acids 118-134 replaced with LDLKIIQPDKNYYAAMV)	This study	N/A
pCMV6-AC-GFP-mHVCN1-hEC2 (amino acids 187-193 replaced with QEHQFEA)	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis	18	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC1 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC5 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC8 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC30 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC45 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC75 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-CC398 LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis- <i>S. schweitzeri</i> LukAB	This study	N/A
pOS1_PlukAB-lukAs.s.-6xHis-LukE	6	N/A
pOS1_PlukAB-lukAs.s.-6xHis-LukD	6	N/A
pOS1_PlukAB-lukAs.s.-6xHis-HlgA	6	N/A
pOS1_PlukAB-lukAs.s.-6xHis-HlgB	6	N/A
pOS1_PlukAB-lukAs.s.-6xHis-LukS	6	N/A
pOS1_PlukAB-lukAs.s.-6xHis-LukF	6	N/A
pCMV-Gag-pol	Was a gift from Charles Rice	N/A

pCMV-VSVg	Was a gift from Charles Rice	N/A
pLKO.1-blast	Was a gift from Keith Mostov ¹⁹	Addgene plasmid #26655
pLKO.1-blast-SCRAMBLE	Was a gift from Keith Mostov ¹⁹	Addgene plasmid #26701
pLKO.1-blast-CD11b	This study	N/A
pLKO.1 puromycin SCRAMBLE	¹³	N/A
pLKO.1 puromycin CD11b	¹³	N/A
pLKO.1 puromycin CD18	¹³	N/A
pLentiCRISPRv2	Was a gift from Feng Zhang ²⁰	Addgene plasmid #52961
pLentiCRISPR_non targeting	This study	N/A
pLentiCRISPR_Hvcn1(1)	This study	N/A
pLentiCRISPR_Hvcn1(2)	This study	N/A
pLentiCRISPR_OGT	This study	N/A
pLentiCRISPR_ASGR1	This study	N/A
pLentiCRISPR_GeCKO-libA	Human GeCKOv2 CRISPR knockout pooled library was a gift from Feng Zhang ²⁰	Addgene #1000000048
pLentiCRISPR_GeCKO-libB	Human GeCKOv2 CRISPR knockout pooled library was a gift from Feng Zhang ²⁰	Addgene #1000000049
pET15b-6xHis-human CD11b I domain-Flag	¹³	N/A
pET-24a(+)	MilliporeSigma	69749-3
pET-24a(+)-HVCN1 Strep	This study	N/A
Software and Algorithms		
FlowJo (version 10.7.1)	BD Life Sciences	N/A
GraphPad Prism 8	GraphPad Software	N/A
HCS Studio software	Thermo Fisher Scientific	N/A
MegAlign	DNASar	N/A
ImageJ 1.51s	https://imagej.nih.gov/	N/A
Other		
CellInsight CX7 High-Content Screening (HCS) Platform	Thermo Fisher Scientific	N/A
autoMACS Pro Separator	Miltenyi Biotec	N/A
Octet RED96E System	Pall ForteBio	N/A
AKTA Pure FLPC	GE Healthcare	N/A

Supplementary Table 5, Related to Methods. Oligonucleotides used in this study.

Label	Description	Sequence
VJT1816	attB- <i>Hvcn1</i> -Forw	GGGGACAAGTTTGTACAAAAAAGCAGGCTT CACCATGACTTCCCATGACCCAAAG
VJT1817	attB- <i>Hvcn1</i> -Rev	GGGGACCACTTTGTACAAGAAAGCTGGGTC TAGTTCACGTCCCCGAGAAG
VJT1878	KpnI-upstream-MRSA252 <i>lukAB</i> -Forw	ATGCGGTACCTTTCAGTTTGTAGTTCAACAA TATCTG
VJT1879	upstream-MRSA252 <i>lukAB</i> - Rev	TACGCGCTTTTTATTTTTCATTG
VJT1880	downstream-MRSA252 <i>lukAB</i> -Forw	TAAGTTTTCGCAAGTTGCCTG
VJT1881	downstream-MRSA252 <i>lukAB</i> - <i>SacI</i> -Rev	ATGCGAGCTCTGCAGGTCATAATAGCACAT GG
VJT1882	upstream-MRSA252 <i>lukAB</i> overlap-aphA-3-Forw	CAATGAAAATAAAAAGCGCGTACTCGACGA TAAACCCAGCGAAC
VJT1883	downstream-MRSA252 <i>lukAB</i> overlap-aphA-3-Rev	CAGGCAACTTGCGAAAATTACTTTTTAGAC ATCTAAATCTAGGTAC
VJT544	<i>Bam</i> HI- <i>lukAB</i> -Forw	CCCGGATCCCATAAAGACTCTCAAGACCAA AAT
VJT543	<i>lukAB</i> - <i>Pst</i> I-Rev	CCCCTGCAGTTATTTCTTTTCATTATCATTAA GTAC
VJT1331	<i>Bam</i> HI-MRSA252 <i>lukAB</i> - Forw	CCCGGATCCAATAAAGACTCACAAGACCAA ACT
VJT628	MRSA252 <i>lukAB</i> - <i>Pst</i> I-Rev	CCCCTGCAGTTATTTCTGTTCTTTATCATTAA TTG
VJT1415	BVED 022 <i>lukAB</i> - <i>Pst</i> I-Rev	CCCCTGCAGTTATTTCTGTTCTTTATCATTAA GTA
VJT1399	clinical isolate # 33 <i>lukAB</i> - <i>Nhe</i> I-Rev	CCCGCTAGCTTATTTCTTTTCTTTATCATTAA ATG
VJT1759	Oligo1-HVCN1- HGLibB_22402	CACCGTGGGAGACGACTACCATGCC
VJT1760	Oligo2-HVCN1- HGLibB_22402	AAACGGCATGGTAGTCGTCTCCCAC
VJT1761	Oligo1-HVCN1- HGLibB_22403	CACCGCAGTTAAGACACGTTTCAGAA
VJT1762	Oligo2-HVCN1- HGLibB_22403	AAACTTCTGAACGTGTCTTAACTGC
VJT1769	Oligo1-OGT-HGLibA_33329	CACCGTGGCTTCTTCCAAGCGACCC
VJT1770	Oligo2-OGT-HGLibA_33329	AAACGGGTCGCTTGGAAGAAGCCAC
VJT1767	Oligo1-ASGR1- HGLibA_03287	CACCGGGGTGCTCAAGCCCTTGACC
VJT1768	Oligo2-ASGR1- HGLibA_03287	AAACGGTCAAGGGCTTGAGCACCCC
VJT1775	Oligo1-nt-HGLibA_64423	CACCGACATAGTCGACGGCTCGATT
VJT1776	Oligo2-nt-HGLibA_64423	AAACAATCGAGCCGTCGACTATGTC
VJT1627	v2Adaptor_F	AATGGACTATCATATGCTTACCGTAACTTGA AAGTATTTTCG

VJT1628	v2Adaptor_R	TCTACTATTCTTTCCCCTGCACTGTTGTGGG CGATGTGCGCTCTG
VJT1667	R_universal	CAAGCAGAAGACGGCATAACGAGATGTGACT GGAGTTCAGACGTGTGCTCTTCCGATCTTCT ACTATTCTTTCCCCTGCACTGT
VJT1663	F09	AATGATACGGCGACCACCGAGATCTACACT CTTTCCCTACACGACGCTCTTCCGATCTacga tcgatAGGTAAGGtcttgtggaaaggacgaaacaccg
VJT1664	F10	AATGATACGGCGACCACCGAGATCTACACT CTTTCCCTACACGACGCTCTTCCGATCTtAA CAATGGtcttgtggaaaggacgaaacaccg
VJT1665	F11	AATGATACGGCGACCACCGAGATCTACACT CTTTCCCTACACGACGCTCTTCCGATCTatAC TGTATCtcttgtggaaaggacgaaacaccg
VJT1666	F12	AATGATACGGCGACCACCGAGATCTACACT CTTTCCCTACACGACGCTCTTCCGATCTgatA GGTCGCAtcttgtggaaaggacgaaacaccg
VJT2065	HVCN1_F6	tatgtgtgtcgttcttactca
VJT2069	HVCN1_R6	caacatgaagaagaccaggatg
VJT2681	HVCN1_F12	TGTGTCACACCCTAGGACGA
VJT2683	HVCN1_R12	GCCGTGCCACACCTAAACAT
VJT2845	hHVCN1_F1	TCCGTGTGAATAGCACTGGC
VJT2846	hHVCN1_R1	GCTGGGCAAACACTCGTAGA
hHVCN1 template DNA	DNA template synthesized as GeneFragment by Gene Universal	ccccAATTCCTCCCCTCTCCAGGAGAACCC TGCCTTCTCCCCCTTTCCCCTGACTATGCAG GGTGGATGTGTCACACCCTAGGACGAGCTT AGCCCACTGGGCGAGAACACCGCCACCTCA CTCCCTGAGGACAGGCAGCCTTTGCAGGGA GGGGTATGTGTGTCGTCTTGTACTCAGAGT CCCAAGGCTGGGGTGTGTTGAATATCTTATT GAGCATCTGTTCTGCAGATGAACCACAGAG AGAGAAAAGGAGACTTAAACTCTATATGCC TTTTGAGAGTGGCATTGCTTTGAGAGCTGG TAATAAGAGAAACAGACTGGGTGGCTAGGG aACAGGGAGTGAGAGAGACTCCCCGAGCTC CCCACAGGGCACTGAGGGTTCCAGAGAAT GGAGGAGGCCCTGCCGTGCACTCAGAGCC TCTTGCTCCTCCCTCCAGGTCATCATATaT GCCTGGTGGTCCCTGGACGCCCTCCTCGTGC TTGCTGAACTCCTCCTGGATTTGAAGATCAT CcAGCCGGACaAGaAtaACTATGCGGcCaTGG TACGAACAGGGCACGCACACAGTGAATTGA GCTGCAGCTCCAGGCCAtcttttttttaagattatt atttattatatacagttacactgtagctgtcttcagacactccagga gatggagtcagatattgttacagatggtgtgagccaccatgtggt tgctgggaattgaactcaggaccttgaagagcagtcoggtgctc ttaaccactgagccattactccagccccCCAGGCCATCttt tttgtttgtttgtttttgagacagggtttctctgttagccctgctgtt ctggaactcactttgttagaccaggctggcctcaaactcagaaat ccacctgcctctgcctcccagtggtgggattaaggcgtgccc

		acctgtagcccaggaagtctggaatttgatcctcctgcctcagct tccgaagtgctgggatgatagCCAGGCCTGGCCAGA GATGTTTAGGTGTGGCACGGCCTGA
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