

Additional File 1 – Supplementary Tables

Supplementary Table S1. Patient characteristics. Abbreviations: HLA, human leukocyte antigen; TBI, total body irradiation; CY, Cyclophosphamide; VP16, Etoposide; BU, Busulfan; MEL, Melphalan; GvHD, graft-versus-host disease.

Characteristics		Number of patients	Percentage of all patients (%)
Transplant recipients		29	100
Average recipient age in years		9.5 (Range: 2.5-16.4)	NA
Gut microbiota characterized	At ≤ 6 timepoints	9	31
	At 7-8 timepoints	13	44.8
	At 9-10 timepoints	7	24.1
Oral microbiota characterized	At ≤ 6 timepoints	3	10.3
	At 7-8 timepoints	11	37.9
	At 9-10 timepoints	15	51.7
Nasal microbiota characterized	At ≤ 6 timepoints	3	10.3
	At 7-8 timepoints	9	31
	At 9-10 timepoints	17	58.6
Patient sex	Female	13	44.8
	Male	16	55.2
Disease at transplantation	Malignant hematologic diseases	20	69
	Severe aplastic anemia	1	3.4
	Other benign disorders including immunodeficiencies	8	27.6
Donor type	HLA-matched sibling	14	48.3
	HLA-matched unrelated donor (9/10 or 10/10 match)	12	41.4
	Haplo-identical related donor (5/10 match)	3	10.3
Stem cell source	Bone marrow	23	79.3
	Umbilical cord blood	2	6.9
	Peripheral blood	4	13.8
Conditioning regimen	TBI + CY / TBI + VP16	6	20.7
	Combinations of BU, CY, VP16 and MEL	6	20.7
	Fludarabine-thiotepa combinations	12	41.4

	Other combinations with fludarabine	5	17.2
Anti-thymocyte globulin treatment		16	55.2
Antibiotics pre- and post-HSCT		29	100
Sex mismatch (female donor to male recipient)		7	24.1
Acute GvHD	Grade 0-I	20	69
	Grade II-IV	9	31
Infections	At least one registered bacterial infection	25	86.2
	At least one registered viral infection	29	100
	At least one registered fungal infection	14	48.3
Overall Survival*	Alive	26	89.7
	Dead	3	10.3
Relapse of primary disease*		2	6.9
Non-relapse mortality		2	6.9
Re-transplantation		1	3.4

*Mean follow-up time after HSCT: 21.4 months (range: 10.1 – 32.7 months)

Supplementary Table S2. Taxonomy of a subset of LDA clade members and corresponding LDA-coefficients in the gut, oral cavity, and nasal cavity.

ASV number	Body site	Phylum	Family	Genus/Species/Description	LDA coefficient (beta)	Number of patients with presence of this ASV at ≥ 1 time point
	Gut					
ASV_1	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.082	29
ASV_30	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	26
ASV_158	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	13
ASV_178	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	12
ASV_344	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	8
ASV_395	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.012	14
ASV_424	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.012	9
ASV_543	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	7
ASV_552	gut	Firmicutes	Enterococcaceae	<i>Enterococcus avium</i>	0.006	7
ASV_720	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.078	15
ASV_730	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	12
ASV_784	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	8
ASV_951	gut	Firmicutes	Enterococcaceae	<i>Enterococcus</i> sp.	0.006	12
ASV_1186	gut	Firmicutes	Enterococcaceae	<i>Melissococcus</i> sp.	0.006	9
ASV_3	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	0.011	26
ASV_31	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	0.006	11
ASV_67	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus sakei</i>	0.006	15
ASV_74	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	0.006	16
ASV_144	gut	Firmicutes	Lactobacillaceae	<i>Pediococcus</i> sp.	0.006	10
ASV_151	gut	Firmicutes	Lactobacillaceae	<i>Pediococcus pentosaceus</i>	0.006	12
ASV_189	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	0.006	10
ASV_222	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus rhamnosus</i>	0.006	8
ASV_586	gut	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	0.006	9
ASV_78	gut	Firmicutes	Lachnospiraceae	<i>Blautia</i> sp.	-0.039	26
ASV_237	gut	Firmicutes	Lachnospiraceae	<i>Blautia faecis</i>	-0.026	23
ASV_265	gut	Firmicutes	Lachnospiraceae	<i>Blautia</i> sp.	-0.026	24
ASV_271	gut	Firmicutes	Lachnospiraceae	<i>Blautia obeum</i>	-0.026	12
ASV_375	gut	Firmicutes	Lachnospiraceae	<i>Blautia</i> sp.	-0.026	15
ASV_554	gut	Firmicutes	Lachnospiraceae	<i>Blautia</i> sp.	-0.026	16
ASV_1291	gut	Firmicutes	Lachnospiraceae	<i>Blautia</i> sp.	-0.026	9
ASV_132	gut	Firmicutes	Ruminococcaceae	<i>Ruminococcus bromii</i>	-0.007	16
ASV_192	gut	Firmicutes	Ruminococcaceae	<i>Ruminococcus bromii</i>	-0.007	24
ASV_206	gut	Firmicutes	Ruminococcaceae	DTU089	-0.024	23
ASV_306	gut	Firmicutes	Ruminococcaceae	<i>Ruminococcus</i> sp.	-0.007	13

ASV_348	gut	Firmicutes	Ruminococcaceae	<i>Ruminococcus</i> sp.	-0.007	11
ASV_556	gut	Firmicutes	Ruminococcaceae	<i>Caproiciproducens</i> sp.	-0.024	9
ASV_566	gut	Firmicutes	Ruminococcaceae	<i>Ruminoclostridium</i> sp.	-0.024	13
ASV_583	gut	Firmicutes	Ruminococcaceae	<i>Ruminoclostridium</i> sp.	-0.024	23
ASV_682	gut	Firmicutes	Ruminococcaceae	<i>Caproiciproducens</i> sp.	-0.024	9
ASV_750	gut	Firmicutes	Ruminococcaceae	<i>Caproiciproducens</i> sp.	-0.024	13
ASV_792	gut	Firmicutes	Ruminococcaceae	<i>Ruminoclostridium</i> sp.	-0.024	15
	<u>Oral</u>					
ASV_18	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.021	27
ASV_66	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	26
ASV_117	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces naeslundii</i>	0.016	27
ASV_126	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces naeslundii</i>	0.016	19
ASV_138	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	22
ASV_155	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces odontolyticus</i>	0.003	20
ASV_227	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.016	7
ASV_235	oral	Actinobacteria	Actinomycetaceae	F0332	0.003	18
ASV_262	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	18
ASV_345	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.016	9
ASV_389	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces odontolyticus</i>	0.003	7
ASV_403	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	15
ASV_407	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.016	7
ASV_2693	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.021	5
ASV_422	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces odontolyticus</i>	0.003	15
ASV_431	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.016	12
ASV_2697	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces naeslundii</i>	0.016	9
ASV_461	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	11
ASV_475	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces gerencseriae</i>	0.003	6
ASV_484	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	4
ASV_501	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces odontolyticus</i>	0.003	13
ASV_516	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces odontolyticus</i>	0.003	12
ASV_2700	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces gerencseriae</i>	0.003	14
ASV_568	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	12
ASV_600	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	7
ASV_642	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	7
ASV_798	oral	Actinobacteria	Actinomycetaceae	F0332	0.003	10
ASV_871	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces massiliensis</i>	0.003	13
ASV_2729	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces graevenitzii</i>	0.003	9
ASV_1055	oral	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	0.003	6

ASV_1172	oral	<i>Actinobacteria</i>	<i>Actinomycetaceae</i>	<i>Actinomyces</i> sp.	0.003	7
ASV_2751	oral	<i>Actinobacteria</i>	<i>Actinomycetaceae</i>	<i>Actinomyces</i> sp.	0.016	8
ASV_2664	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	29
ASV_10	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	29
ASV_16	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	29
ASV_27	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	29
ASV_28	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.040	28
ASV_37	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	19
ASV_48	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	27
ASV_173	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus salivarius</i>	0.010	15
ASV_183	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	19
ASV_188	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	14
ASV_2674	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	14
ASV_230	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	8
ASV_269	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus cristatus</i>	0.010	29
ASV_282	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus parasanguinis</i>	0.010	13
ASV_2683	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus mitis</i>	0.010	11
ASV_480	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	18
ASV_481	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus peroris</i>	0.010	12
ASV_802	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	24
ASV_1531	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	11
ASV_1599	oral	<i>Firmicutes</i>	<i>Streptococcaceae</i>	<i>Streptococcus</i> sp.	0.010	13
ASV_42	oral	<i>Bacteroidetes</i>	<i>Prevotellaceae</i>	<i>Prevotella melaninogenica</i>	0.028	27
ASV_226	oral	<i>Bacteroidetes</i>	<i>Prevotellaceae</i>	<i>Prevotella melaninogenica</i>	0.028	15
ASV_800	oral	<i>Bacteroidetes</i>	<i>Prevotellaceae</i>	<i>Prevotella</i> sp.	0.028	6
ASV_2665	oral	<i>Firmicutes</i>	Family XI	<i>Gemella</i> sp.	0.009	29
ASV_208	oral	<i>Firmicutes</i>	Family XI	<i>Gemella sanguinis</i>	0.009	28
ASV_2701	oral	<i>Firmicutes</i>	Family XI	<i>Gemella</i> sp.	0.009	5
Nasal						
ASV_14	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Corynebacterium</i> sp.	0.117	24
ASV_354	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Corynebacterium durum</i>	0.054	15
ASV_360	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Corynebacterium</i> sp.	0.054	17
ASV_2704	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Corynebacterium</i> sp.	0.022	12
ASV_2707	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Corynebacterium durum</i>	0.054	14
ASV_1206	nasal	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Lawsonella</i> sp.	0.007	16

Supplementary Table S3. Taxonomy of aGvHD predictors within the fecal, oral, and nasal microbiota. ASVs that were significantly predicting aGvHD severity according to the conditional inference tree regression model are highlighted in bold. Of the 50 most important gut ASVs identified by the svmLinear model, 17 were confirmed by Boruta feature selection and are listed here. In the oral and nasal cavities, 26 and 12 ASVs were confirmed by Boruta selection, respectively. Listed in bold are those ASVs with a significant predictive effect on aGvHD severity, tested in a regression framework with CTREE (see Methods).

ASV number	Phylum	Family	Genus/Species/Description	Body Site	Importance in svmLinear model	Mean Importance in Boruta
	Gut					
ASV_3	Firmicutes	Lactobacillaceae	<i>Lactobacillus</i> sp.	gut	0.74	8.85
ASV_7	Bacteroidetes	Tannerellaceae	<i>Parabacteroides merdae</i>	gut	0.63	4.62
ASV_8	Proteobacteria	Enterobacteriaceae	<i>Escherichia/Shigella</i> sp.	gut	0.70	4.16
ASV_12	Firmicutes	Ruminococcaceae	UBA1819 sp.	gut	0.68	5.52
ASV_35	Bacteroidetes	Bacteroidaceae	<i>Bacteroides uniformis</i>	gut	0.68	4.66
ASV_50	Firmicutes	Ruminococcaceae	<i>Subdoligranulum</i> sp.	gut	0.60	3.78
ASV_128	Bacteroidetes	Tannerellaceae	<i>Parabacteroides distasonis</i>	gut	0.68	7.42
ASV_131	Bacteroidetes	Tannerellaceae	<i>Parabacteroides distasonis</i>	gut	0.66	6.49
ASV_166	Fusobacteria	Fusobacteriaceae	<i>Fusobacterium</i> sp.	gut	0.60	4.08
ASV_268	Firmicutes	Lachnospiraceae	<i>Lachnospiraceae</i> _NK4A136_group sp.	gut	0.61	5.02
ASV_361	Bacteroidetes	Tannerellaceae	<i>Parabacteroides</i> sp.	gut	0.61	4.40
ASV_477	Firmicutes	Lachnospiraceae	<i>Eisenbergiella tayi</i>	gut	0.62	3.64
ASV_507	Firmicutes	Lachnospiraceae	<i>Lachnospira pectinoschiza</i>	gut	0.60	3.91
ASV_563	Firmicutes	Erysipelotrichaceae	<i>Coprobacillus cateniformis</i>	gut	0.63	5.38
ASV_567	Firmicutes	Ruminococcaceae	<i>Flavonifractor</i> sp.	gut	0.60	2.81
ASV_585	Bacteroidetes	Tannerellaceae	<i>Parabacteroides</i> sp.	gut	0.62	4.53
ASV_687	Firmicutes	Lachnospiraceae	NA	gut	0.59	3.83
	Oral					
ASV_15	Firmicutes	Streptococcaceae	<i>Lactococcus</i> sp.	oral	0.61	7.31
ASV_34	Proteobacteria	Neisseriaceae	<i>Neisseria</i> sp.	oral	0.62	5.08
ASV_66	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	oral	0.65	4.84
ASV_72	Actinobacteria	Micrococcaceae	<i>Rothia</i> sp.	oral	0.63	4.49
ASV_92	Bacteroidetes	Bacteroidaceae	<i>Bacteroides</i> sp.	oral	0.65	5.36
ASV_98	Actinobacteria	Micrococcaceae	<i>Rothia mucilaginosa</i>	oral	0.58	5.87
ASV_135	Firmicutes	Streptococcaceae	<i>Streptococcus mutans</i>	oral	0.60	4.24

ASV_205	Firmicutes	Ruminococcaceae	<i>Ruminococcacea e_UCG-002</i> sp.	oral	0.63	4.38
ASV_226	Bacteroidetes	Prevotellaceae	<i>Prevotella_7 melaninogenica</i>	oral	0.63	8.19
ASV_247	Firmicutes	Ruminococcaceae	<i>Ruminococcacea e_UCG-013</i> sp.	oral	0.66	4.80
ASV_270	Firmicutes	Veillonellaceae	<i>Veillonella</i> sp.	oral	0.59	3.47
ASV_338	Bacteroidetes	Prevotellaceae	<i>Alloprevotella</i> sp.	oral	0.61	4.26
ASV_360	Actinobacteria	Corynebacteriaceae	<i>Corynebacterium</i> sp.	oral	0.64	6.50
ASV_374	Fusobacteria	Leptotrichiaceae	<i>Leptotrichia wadei</i>	oral	0.60	4.39
ASV_378	Firmicutes	Lachnospiraceae	<i>Oribacterium sinus</i>	oral	0.65	7.17
ASV_500	Actinobacteria	Propionibacteriaceae	<i>Pseudopropionibacterium propionicum</i>	oral	0.67	8.51
ASV_518	Bacteroidetes	Bacteroidaceae	<i>Bacteroides</i> sp.	oral	0.64	4.67
ASV_568	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	oral	0.71	8.79
ASV_640	Bacteroidetes	Tannerellaceae	<i>Parabacteroides</i> sp.	oral	0.62	2.81
ASV_871	Actinobacteria	Actinomycetaceae	<i>Actinomyces massiliensis</i>	oral	0.61	4.65
ASV_894	Firmicutes	Ruminococcaceae	<i>Ruminococcacea e_UCG-014</i> sp.	oral	0.62	2.74
ASV_140_3	Firmicutes	Veillonellaceae	<i>Selenomonas_3</i> sp.	oral	0.59	2.82
ASV_266_4	Firmicutes	Streptococcaceae	<i>Streptococcus</i> sp.	oral	0.68	6.11
ASV_266_6	Actinobacteria	Micrococcaceae	<i>Rothia dentocariosa</i>	oral	0.61	4.47
ASV_267_6	Firmicutes	Aerococcaceae	<i>Abiotrophia defectiva</i>	oral	0.61	5.74
ASV_269_2	Actinobacteria	Micrococcaceae	<i>Rothia</i> sp.	oral	0.62	6.30
	Nasal					
ASV_266_4	Firmicutes	Streptococcaceae	<i>Streptococcus</i> sp.	nasal	0.61	11.49
ASV_266_6	Actinobacteria	Micrococcaceae	<i>Rothia dentocariosa</i>	nasal	0.56	5.80
ASV_47	Actinobacteria	Micrococcaceae	<i>Rothia</i> sp.	nasal	0.59	6.41
ASV_51	Proteobacteria	Pasteurellaceae	<i>Haemophilus</i> sp.	nasal	0.64	5.67
ASV_52	Actinobacteria	Micrococcaceae	<i>Rothia mucilaginosa</i>	nasal	0.61	8.58
ASV_66	Actinobacteria	Actinomycetaceae	<i>Actinomyces</i> sp.	nasal	0.67	9.05
ASV_267_0	Proteobacteria	Neisseriaceae	NA	nasal	0.61	6.69
ASV_117	Actinobacteria	Actinomycetaceae	<i>Actinomyces naeslundii</i>	nasal	0.58	4.73
ASV_125	Actinobacteria	Corynebacteriaceae	<i>Corynebacterium 1 accolens</i>	nasal	0.57	5.43
ASV_252	Firmicutes	Veillonellaceae	<i>Veillonella rogosae</i>	nasal	0.58	5.54
ASV_270	Firmicutes	Veillonellaceae	<i>Veillonella</i> sp.	nasal	0.57	5.41

ASV_269 4	<i>Actinobacteria</i>	<i>Corynebacteriaceae</i>	<i>Lawsonella</i> sp.	nasal	0.65	8.42
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