**Supplementary Table 1: Demographic table in all MSKCC patients, cGVHD cases, and controls**

| | All patients | cGVHD cases | controls |
|---|---|---|---|
| n | 1081[1] | 54 | 171 |
| sex = M (%) | 652 (60.3) | 28 (51.9) | 119 (69.6) |
| age (mean (SD)) | 53.63 (+/-12.86) | 54.5 (+/-11.03) | 57.2 (+/-13.68) |
| **Disease (%)** | | | |
| Leukemia | 550 (50.9) | 26 (48.1) | 72 (42.1) |
| Non-Hodgkin's Lymphoma | 187 (17.3) | 17 (31.5) | 44 (25.7) |
| Myelodysplastic Syndrome | 162 (15.0) | 7 (13.0) | 23 (13.5) |
| Myeloproliferative Disorder | 40 (3.7) | 2 (3.7) | 12 (7.0) |
| Multiple Myeloma | 100 (9.3) | 2 (3.7) | 6 (3.5) |
| Aplastic Anemia | 5 (0.5) | 0 (0.0) | 2 (1.2) |
| Hodgkin's Disease | 26 (2.4) | 0 (0.0) | 10 (5.8) |
| Non-Malignant Disorders | 11 (1.0) | - | 2 (1.2) |
| **CIBMTR Disease Risk (%)** | | | |
| High | 254 (23.5) | 12 (22.2) | 38 (22.2) |
| Intermediate | 250 (23.1) | 18 (33.3) | 51 (29.8) |
| Low | 498 (46.1) | 20 (37.0) | 60 (35.1) |
| Not Applicable | 79 (7.3) | 4 (7.4) | 22 (12.9) |
| **Conditioning Intensity (%)** | | | |
| Myeloablative | 602 (55.7) | 23 (42.6) | 67 (39.2) |
| Non-myeloablative | 112 (10.4) | 7 (13.0) | 25 (14.6) |
| Reduced intensity | 367 (34.0) | 24 (44.5) | 79 (46.2) |
| **Donor (%)** | | | |
| Related | 375 (34.6) | 18 (33.3) | 72 (42.1) |
| Unrelated | 706 (65.4) | 36 (66.7) | 99 (57.9) |
| **HLA matching (%)** | | | |
| Related Haploidentical | 34 (3.1) | 2 (3.7) | 18(10.5) |
| Related Identical Non-Sibling | 2 (0.2) | - | 1 (0.6) |
| Related Identical Sibling | 291 (26.9) | 16 (29.6) | 49 (28.7) |
| Related Non-Identical | 7 (0.6) | - | 4 (2.3) |
| Unrelated Identical | 450 (41.6) | 32 (59.3) | 82 (48.0) |
| Unrelated Non-identical[2] | 297 (27.5) | 4 (7.4) | 17 (9.9) |
| **Graft type (%)** | | | |
| CD34-selected | 438 (40.5) | 6 (11.1) | 20 (11.7) |
| Unmodified PBSC | 375 (34.7) | 39 (72.2) | 117 (68.4) |
| Unmodified marrow | 92 (8.6) | 9 (16.7) | 33 (19.3) |
| Cord blood | 176 (16.3) | - | - |

[1] Two patients with available stool samples did not have any samples which reached appropriate threshold for inclusion in the alpha-diversity plot in Figure 1A (due to low counts) thus only 1079 patients are shown in 1A.
[2] Includes umbilical cord blood as graft source

**Supplementary Table 2: Acute GVHD subtyping**

| | ***cGVHD cases (n = 54)*** | ***Controls (n = 171)*** |
|---|---|---|
| Prior acute GVHD Grade | | |
| 0 | 31 (57%) | 86 (50.2%) |
| 1 | 4 (7.4%) | 14 (8.2%) |
| 2 | 15 (27%) | 51 (29.8%) |
| 3 | 2 (3.7%) | 16 (9.4%) |
| 4 | 2 (3.7%) | 0 (0%) |
| | | |
| Prior acute lower GI GVHD (Stage) | | |
| 0 | 47 (87%) | 143 (83.6%) |
| 1 | 3 (5.5%) | 11 (6.4%) |
| 2 | 2 (3.7%) | 8 (4.6%) |
| 3 | 0 | 5 (2.9%) |
| 4 | 2 (3.7%) | 4 (2.3%) |

Neither grade 3-4 GVHD, or severe (stage 3-4) lower GI GVHD were different among cases and controls (Fishers exact text, p = 0.78 for Grade 3-4, p >0.99 for stage 3-4 GI only).

**Supplementary Table 3: Antibiotic exposure**

Early and peri-engraftment exposure to broad spectrum antibiotics (d-7 to 21)

| | ***cGVHD cohort n = 54 patients*** | ***Control cohort N=171 patients*** |
|---|---|---|
| Piperacillin/tazobactam | 27 (50%) | 94 (54%) |
| Cefepime | 9 (16.6%) | 37 (21.6%) |
| Meropenem | 11 (20.3) | 20 (11.6%) |
| None | 21 (38.8%) | 54 (31.5%) |

**Supplementary Table 4: Alpha-diversity comparison between cGVHD cases and controls in each time window**

| | ***cGVHD*** | ***Control*** | |
|---|---|---|---|
| | ***Median alpha-div (n)*** | ***Median alpha-div (n)*** | ***P value*** |
| Pre-transplant (single sample d-30 to d0) | 13.09 (n = 43) | 15.54 (n = 168) | 0.62 |
| Peri-engraftment (single sample closest to d14, in the d7-21 window) | 3.71 (n= 42) | 3.45 (n = 144) | 0.90 |
| Peri-d100 (d70-130) | 6.39 (n = 9) | 7.4 (n = 37) | 0.6 |

**Supplementary Table 5: ADONIS test of beta-diversity between cases and controls in each time window**

| | *Samples available for analysis (n)* | | |
|---|---|---|---|
| | ***cGVHD*** | ***Control*** | ***P (ADONIS)*** |
| Pre-transplant (single first sample d-30 to 0) | 43 | 168 | 0.160 |
| Peri-engraftment (single sample closest to d14, in the d9-19 window) | 42 | 144 | 0.738 |
| Peri-d100 (d70-130) | 9 | 36 | 0.958 |

**Supplementary Table 6: Duke and Regensburg patient demographics**

| | Duke cross-section | Regensburg cross-section |
|---|---|---|
| Patients (n) | 37 | 89 |
| **sex = M (%)** | 25 (67.6) | 56 (62.9) |
| **age (mean (SD))** | 53.7 (+/- 11.87) | 54.0 (+/- 11.55) |
| **Disease (%)** | | |
| Leukemia | 17 (45.9) | 53 (59.6) |
| Non-Hodgkin's Lymphoma | 4 (10.8) | 12 (13.5) |
| Myelodysplastic Syndrome | 11 (29.7) | 11 (12.3) |
| Myeloproliferative Disorder | 1 (2.7) | 6 (6.7) |
| Multiple Myeloma | 3 (8.1) | 1 (1.1) |
| Aplastic Anemia | - | 4 (4.5) |
| Hodgkin's Disease | 1 (2.7) | - |
| Non-Malignant Disorders | - | 2 (2.2) |
| **Conditioning Intensity (%)** | | |
| Myeloablative | 31 (83.8) | 12 (13.4) |
| Non-myeloablative | 5 (13.5) | 1 (1.1) |
| Reduced intensity | 1 (2.7) | 76 (85.3) |
| **Donor (%)** | | |
| Related | 12 (32.4) | 34 (38.2) |
| Unrelated* | 25 (67.6) | 55 (61.8) |
| **HLA matching (%)** | | |
| Related Identical | 12 (32.4) | 31 (34.8) |
| Unrelated Identical | 20 (54.1) | 31 (34.8) |
| Unrelated Non-identical | 5 (13.5) | 24 (26.9) |
| Related Haploidentical | - | 3 (3.3) |
| **Graft type (%)** | | |
| Unmodified PBSC | 28 (75.7) | 71 (79.8) |
| Unmodified marrow | 4 (10.8) | 18 (20.2) |
| Cord blood | 5 (13.5) | - |

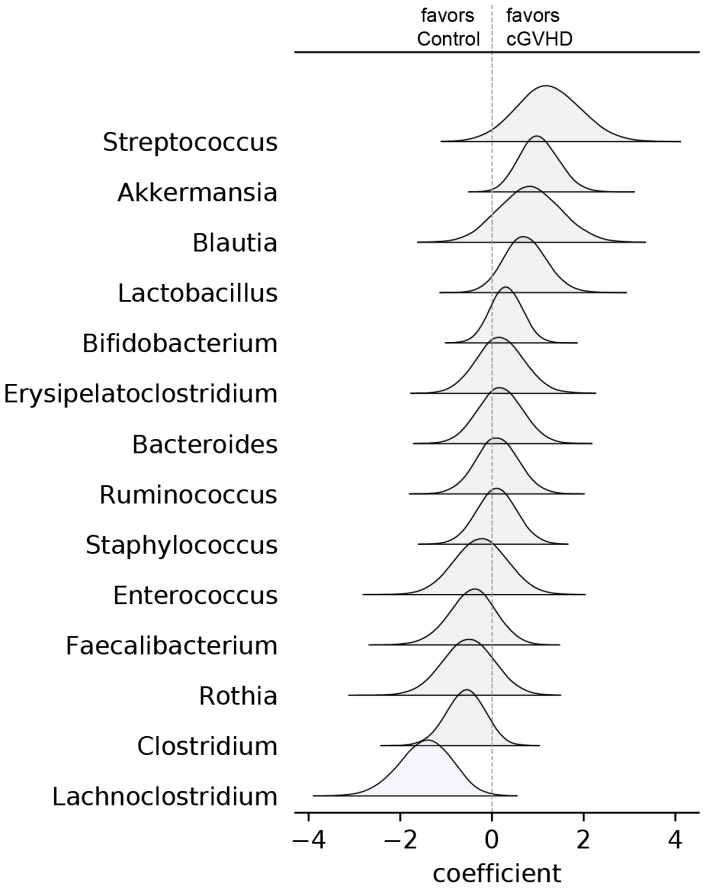
**Supplementary Figure 1 and additional methods:**

Legend and additional methods: All patients included in this analysis received unmodified grafts (9 cases, 36 control). We ran four independent MCMC chains to convergence (shown in Fig S2) using 10,000 No-U-turn sampling steps (plus 2,000 burn-in steps). We assigned mildly regularizing priors for coefficients ($\beta$) of all predictors and restricted the intercept term to the interval close to the true case:control ratio. This resulted in our model of the probability of cGVHD given the log family (*Taxon*) relative abundances:

$$Intercept \sim Uniform([inverse\_logistic(0.19),\ inverse\_logistic(0.21)])$$
$$\beta\ Akkermansia \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Bacteroides \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Bifidobacterium \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Blautia \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Clostridium \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Enterococcus \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Erysipelatoclostridium \sim \mathcal{N}(\mu = 0, \sigma = 1.0)$$
$$\beta\ Faecalibacterium \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Lachnoclostridium \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Lactobacillus \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Rothia \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Ruminococcus \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Staphylococcus \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$\beta\ Streptococcus \sim \mathcal{N}(\mu = 0, \sigma = 10)$$
$$p = invlogit(Intercept + \sum_{X}^{Taxa} \beta_x\ Taxon\ )$$
$$cGVHD \sim Binomial(\ p)$$

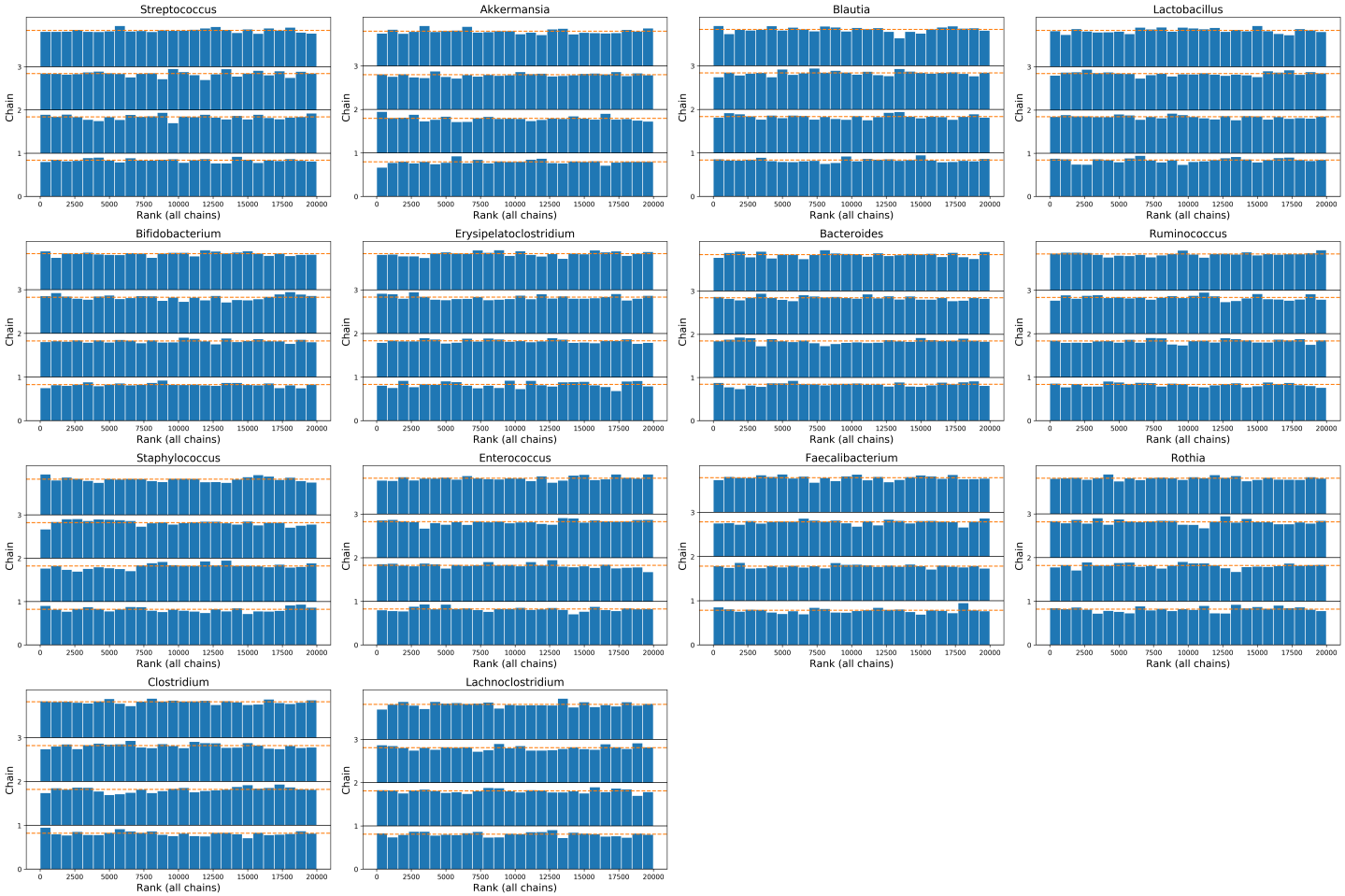
Posteriors were used to jointly sample 10,000 coefficient sets for the 14 genera and the intercept term to make predictions of the likelihood of cGVHD for different gut microbiota compositions. As our case-control design fixes the intercept, we converted[1] the inferred intercept term, $I_0^*$, as so: $I = I_0^* - \ln[\ (1-\tau)/\ \tau\ *(\ddot{y}/(1-\ddot{y}))\ ]$ using 0.4 as the known population rate, $\tau$, of cGVHD among our cohort [2] and $\ddot{y}$=0.2, i.e. the sampled probability of cGVHD. For each set of coefficients, we sampled 1,000 randomly assembled communities of microbes, fixing the focal taxon at the specified relative abundance.

**Fig S1.** Full posterior distributions of coefficients from a logistic regression

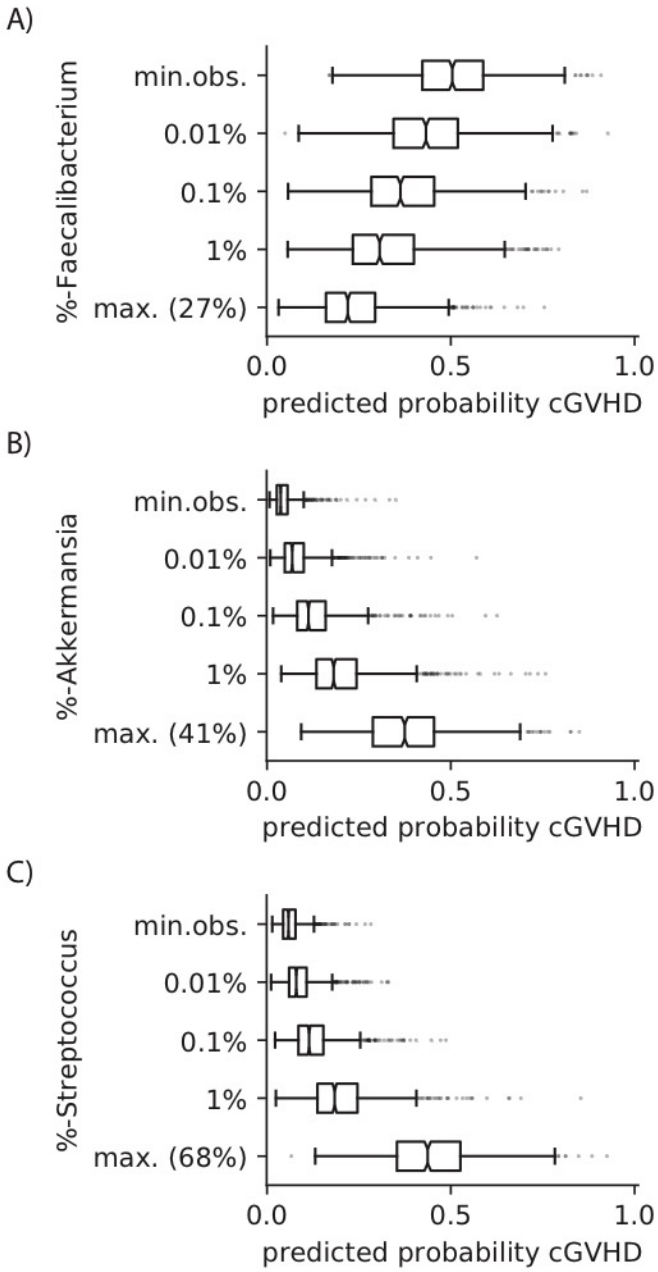


**Supplementary Figure 2:**

Rank plot [3] coefficient value ranks across 4 independent Markov chain Monte Carlo (MCMC) chains with 10,000 No-U-turn sampling steps each. Similar rank distributions across the 4 chains indicate convergence.



**Supplementary Figure 3:**



**Supplementary Figure 4:**

Figure S4A: Duke University, bar plot demonstrating composition of stool samples

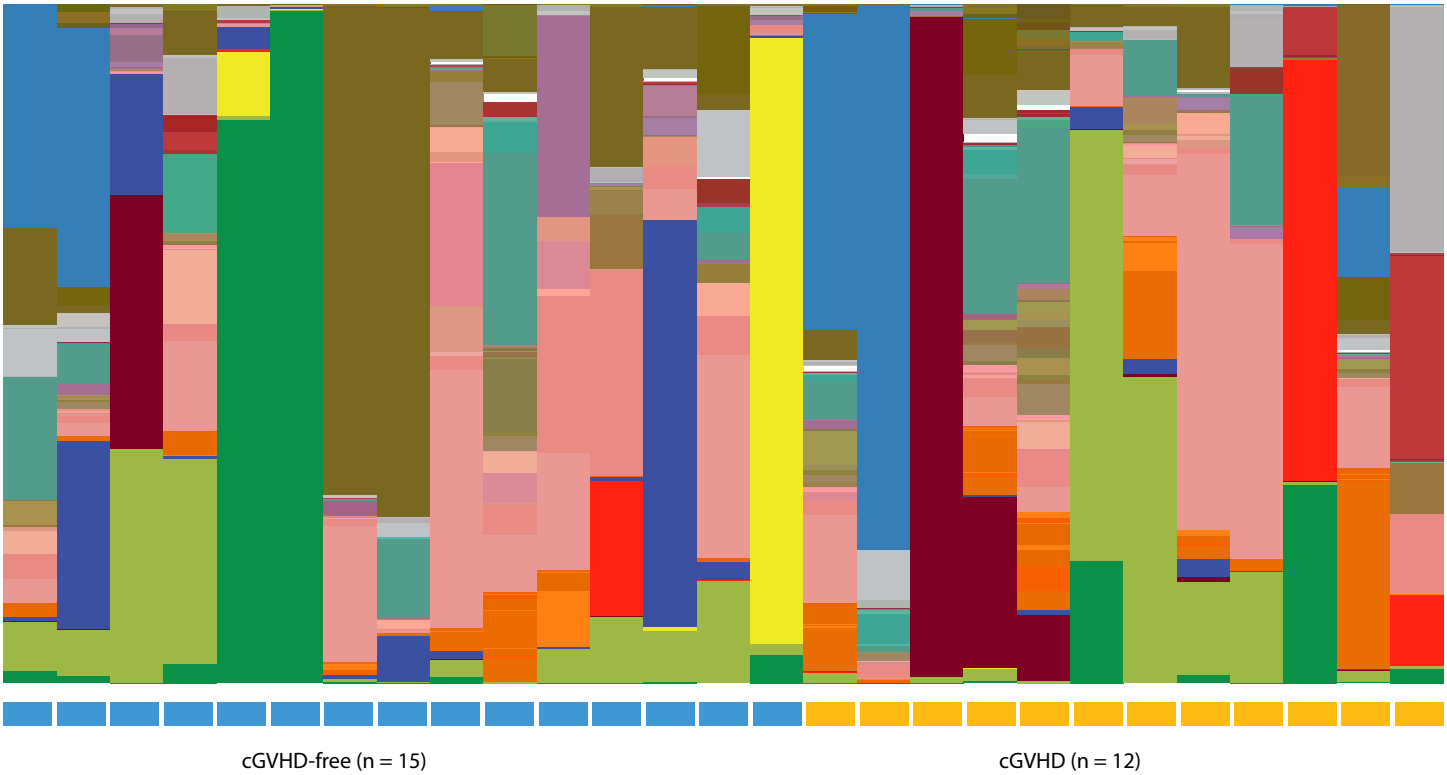
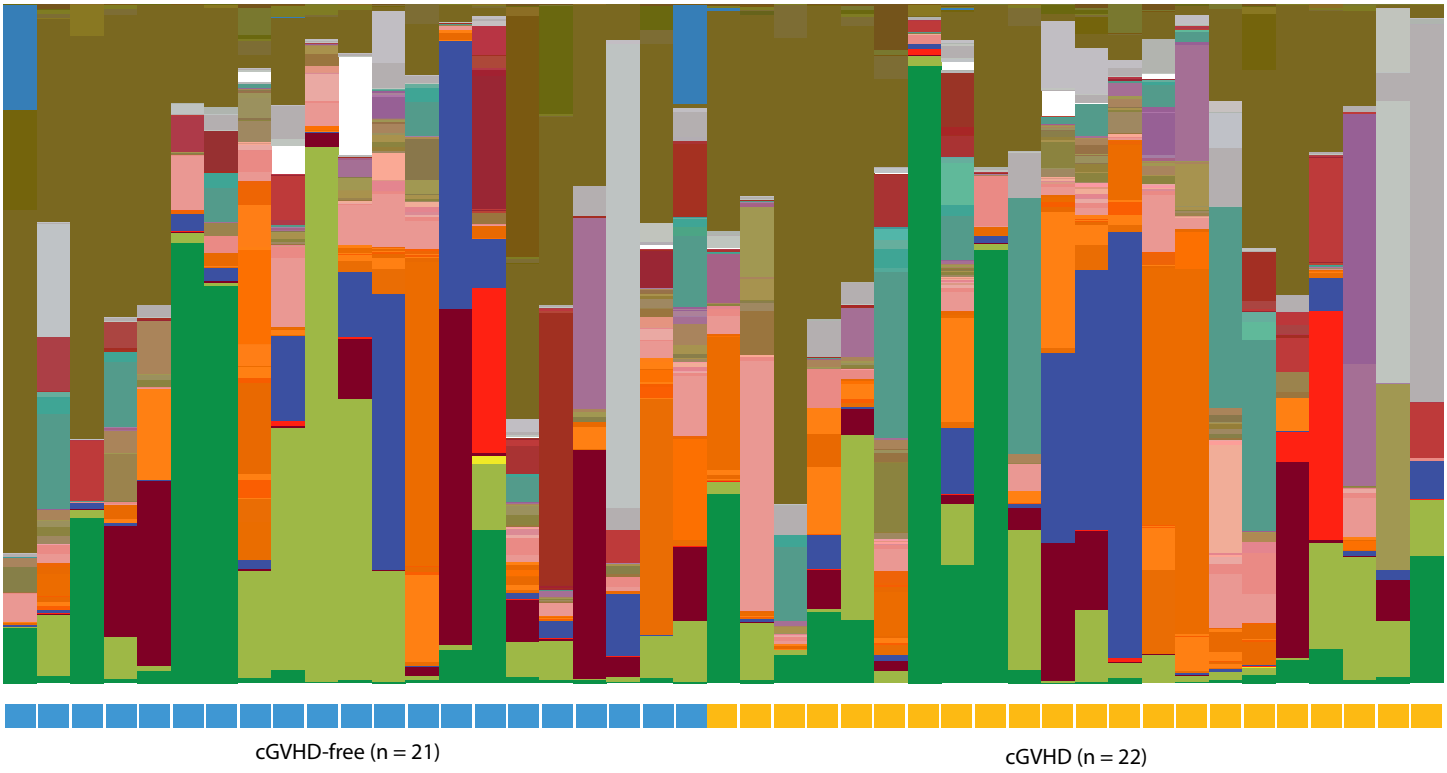
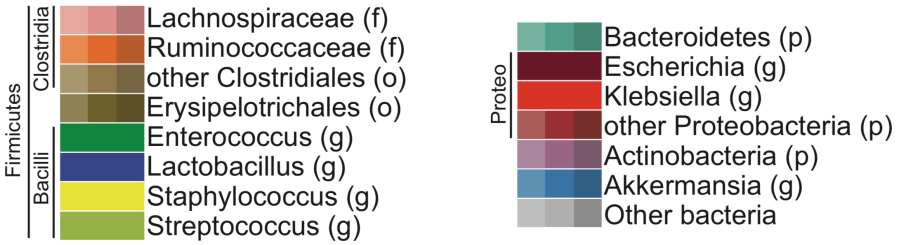



Figure S4B: Regensburg University Medical Center, bar plot demonstrating composition of stool samples



Legend for Figure S4A and S4B:



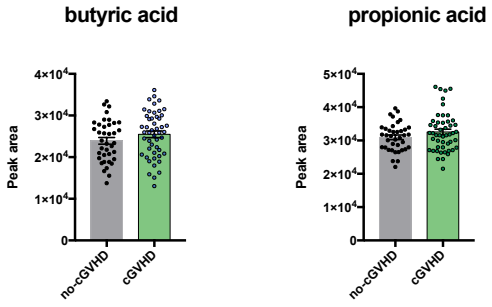

Summary table: Alpha diversity in the additional cross-sectional cohorts

| | ***cGVHD*** | ***No-cGVHD*** | |
|---|---|---|---|
| | ***Median alpha-div (n)*** | ***Median alpha-div (n)*** | ***P value*** |
| Duke peri d100 samples | 5.56 (n = 12) | 6.64 (n = 15) | 0.76 |
| Regensburg peri d100 samples | 6.48 (n=31) | 5.92 (n =25) | 0.52 |

Summary table: Beta diversity in the additional cross-sectional cohorts

| | ***Samples available for analysis (n)*** | | |
|---|---|---|---|
| | ***cGVHD*** | ***No-cGVHD*** | ***P (ADONIS)*** |
| Duke peri d100 samples | 12 | 15 | 0.344 |
| Regensburg peri d100 samples | 23 | 21 | 0.078 |

**Supplementary Figure 5: Regensburg Serum SCFA data**




Regensburg University serum samples from cross-sectional cohort (as serum was the available banked sample type, rather than plasma as in the other centers). N = 50 patients who developed cGVHD, 38 patients who did not.

**References**


1. King, G. and L. Zeng, *Inference in Case-control studies*, in *Encyclopedia of Biopharmaceutical Statistics*, S.-C. Chow, Editor. 2004, Marcel Dekker: New York.
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3. Aki Vehtari, et al., *Rank-normalization, folding, and localization: An improved R for assessing convergence of MCMC.* arXiv.org, 2019. **arXiv:1903.08008**.