
Supplementary information

Bacteriophage targeting of gut bacterium attenuates alcoholic liver disease

In the format provided by the
authors and unedited

Yi Duan, Cristina Llorente, Sonja Lang, Katharina Brandl, Huikuan Chu, Lu Jiang, Richard C. White, Thomas H. Clarke, Kevin Nguyen, Manolito Torralba, Yan Shao, Jinyuan Liu, Adriana Hernandez-Morales, Lauren Lessor, Imran R. Rahman, Yukiko Miyamoto, Melissa Ly, Bei Gao, Weizhong Sun, Roman Kiesel, Felix Hutmacher, Suhan Lee, Meritxell Ventura-Cots, Francisco Bosques-Padilla, Elizabeth C. Verna, Juan G. Abraldes, Robert S. Brown Jr, Victor Vargas, Jose Altamirano, Juan Caballería, Debbie L. Shawcross, Samuel B. Ho, Alexandre Louvet, Michael R. Lucey, Philippe Mathurin, Guadalupe Garcia-Tsao, Ramon Bataller, Xin M. Tu, Lars Eckmann, Wilfred A. van der Donk, Ry Young, Trevor D. Lawley, Peter Stärkel, David Pride, Derrick E. Fouts & Bernd Schnabl

Supplementary Table 1: Demographic and laboratory results of controls and patients with alcohol use disorder or alcoholic hepatitis

Variables	Controls (n=26)	Alcohol use disorder (n=44)	Alcoholic hepatitis (n=88)
Sex (% male), n (%), n=158	16 (61.5)	37 (84.1)	60 (68.2)
Age (years), n=158	48.5 (27.0-74.0)	44.0 (27.0-67.0)	50.0 (30.0-75.0)
BMI (kg/m ²), n=132	26.0 (18.8-35.6)	24.3 (17.9-37.0)	27.2 (16.3-48.3)
Creatinine (mg/dL), n=128		0.8 (0.5-1.3)	0.8 (0.3-8.1)
Bilirubin (mg/dL), n=130		0.5 (0.2-6.4)	15.6 (2.5-38.6)
AST (IU/L), n=132		47.5 (15.0-283.0)	132.0 (38.0-456.0)
ALT (IU/L), n=132		37.5 (9.0-184.0)	45.0 (15.0-216.0)
Albumin (g/dL), n=124		4.4 (2.2-5.2)	2.4 (1.3-4.1)
INR, n=128		1.0 (0.8-2.0)	1.8 (1.0-4.4)
GGT (IU/L), n=83		111.5 (16.0-1131.0)	196.0 (33.0-3632.0)
Platelet count (10 ⁹ /L), n=122		221.0 (21.0-434.0)	127.0 (13.0-447.0)
MELD, n=87			24.0 (12.0-46.0)
FIB-4, n=122		1.6 (0.4-21.4)	7.8 (0.7-73.4)
FIB-4 > 3.25 (F3-F4), n (%)		8 (21.1)	75 (89.3)
Prior length of alcohol abuse, n=111			
1-5 years, n (%)		4 (12.9)	16 (20.0)
5-10 years, n (%)		13 (41.9)	16 (20.0)
>10 years, n (%)		14 (45.2)	48 (60.0)

Values are presented as median with range in brackets for continuous variables or number and percentage in brackets for categorical variables. Percentages are calculated based on the actual number of patients in each group where the respective data was available. The number of subjects for which the respective data was available is indicated in the first column.

BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; GGT, gamma-glutamyl transferase; MELD, model for end-stage liver disease; FIB-4, fibrosis-4 index

Supplementary Table 2: Characteristics of patients with alcoholic hepatitis patients (n=82) for cytolytic analysis

Treatment at admission	
Steroids, n (%), n=80	30 (37.5)
Pentoxifylline, n (%), n=70	7 (10.0)
Antibiotics, n (%), n=80	40 (50.0)
Proton pump inhibitors, n (%), n=42	2 (4.7)
Clinical characteristics	
Infections, n (%), n=66	16 (24.2)
Abstinent at day 30, n=46	
Abstinent, n (%)	39 (84.8)
Reduced alcohol consumption, n (%)	4 (8.7)
Continued alcohol abuse, n (%)	3 (6.5)
Abstinent at day 90, n=30	
Abstinent, n (%)	27 (90.0)
Reduced alcohol consumption, n (%)	2 (6.7)
Continued alcohol abuse, n (%)	1 (3.3)
Liver biopsy available, n (%), n=82	49 (59.8)
Stage of Fibrosis, n (%), n=48	0 / 1 / 2 / 3 / 4
	2 (4.1) / 0 (0.0) / 8 (16.7) / 8 (16.7) / 30 (62.5)
Clinical scores and outcome	
MELD, median (range), n=81	24.0 (12.0–46.0)
MELD > 21, n (%)	61 (75.3)
Child-Pugh stage, n (%), n=80	A / B / C
	1 (1.3) / 24 (30.0) / 55 (68.8)
Maddrey's DF, median (range), n=66	68.0 (3.0–246.0)
Maddrey's DF > 32, n (%)	60 (90.9)
ABIC, median (range), n=82	6.7 (4.0–9.5)
30 day mortality rate, n (%), n=76	8 (10.5)
90 day mortality rate, n (%), n=57	14 (24.6)
Causes of death within 180 days	
Liver failure*	12
Gastrointestinal bleeding	3
Septic shock	2
Unknown	3

*One patient underwent liver transplantation.

Antibiotics include prophylactic antibiotics. Four patients with infections were not treated with antibiotics at the time of enrollment. Values are presented as median (range) for continuous variables or number (percentage) for categorical variables. Percentages are calculated based on the actual number of patients in each group where the respective data was available. The number of subjects for which the respective data was available is indicated in the first column.

MELD, model for end-stage liver disease; DF, discriminant function; ABIC, Age, serum bilirubin, INR, and serum creatinine score

Supplementary Table 3: Univariate logistic regression analysis of laboratory and clinical parameters associated with cytolyisin, and Cox regression analysis assessing the association between cytolyisin and survival in alcoholic hepatitis patients

Univariate logistic regression*	OR	95% CI	P value[†]
Steroids	2.42	0.92-6.50	0.074
PTX	3.09	0.62-16.97	0.165
Antibiotics	1.80	0.70-4.81	0.230
Infections	1.90	0.55-6.29	0.295
Cirrhosis	2.33	0.65-9.79	0.212
Abstinence day 30 follow-up	1.55	0.22-31.43	0.704
Creatinine	2.17	1.28-4.78	0.019
GGT	0.99	0.98-1.00	0.058
INR	2.35	1.07-5.66	0.040
Platelet count	0.99	0.98-1.00	0.012
MELD	1.18	1.08-1.31	6.51e-04
MELDNa	1.20	1.09-1.35	9.21e-04
Maddrey's DF > 32	50.52	0.23-134999.59	1.000
Maddrey's DF	1.01	1.00-1.02	0.090
ABIC	1.68	1.13-2.62	0.014

Univariate Cox regression*	HR	95% CI	P value[†]
30 day mortality	7.46	1.50-36.99	0.014
90 day mortality	16.72	3.73-74.85	2.31e-04
180 day mortality	22.24	5.14-96.30	3.35e-05

Multivariate Cox regression[‡]	HR	95% CI	P value[†]
Cytolyisin	14.07	2.83-69.85	0.001
MELD	1.09	1.01-1.16	0.022

*For Univariate logistic and Cox regression, n=82.

[†]Significance is indicated in bold.

[‡]Hazard ratio (HR) for 180-day mortality (n=79 for cytolyisin; n=78 for MELD), based on multivariate Cox regression analysis, adjusted for geographic region of patient enrollment; treatment with antibiotics; and platelet count. HR for cytolyisin was additionally adjusted for creatinine, bilirubin and INR as components of the MELD score.

Antibiotics include prophylactic antibiotics. In the Cox regression, patients were censored at the time point they were last seen alive. *P* values were determined by two-sided Wald test.

OR, odds ratio; HR, hazard ratio; CI, confidence interval; PTX, pentoxifylline; GGT, gamma-glutamyl transferase; INR, international normalized ratio; MELD, model for end-stage liver disease; MELDNa, sodium MELD; DF, discriminant function; ABIC, Age, serum bilirubin, INR, and serum creatinine score

Supplementary Table 4: Univariate logistic regression of virulence genes and antimicrobial resistance genes of *E. faecalis* and clinical outcomes in alcoholic hepatitis patients (n=25)

Gelatinase (<i>gelE</i>)	OR	95% CI	P value*
Infections	2.83	0.76-14.57	0.133
90 day mortality rate	1.22	0.24-4.75	0.771
ALT	0.99	0.97-1.02	0.545
AST	1.00	0.98-1.01	0.558
Platelet count	1.00	0.99-1.02	0.484
INR	3.02	0.33-39.85	0.347
Bilirubin	1.00	0.91-1.13	0.982
MELD	1.09	0.93-1.34	0.325
ABIC	0.65	0.26-1.41	0.291
Maddrey's DF	0.97	0.94-0.99	0.041
Serine protease (<i>sprE</i>)			
Infections	1.41	0.28-5.44	0.617
90 day mortality rate	1.83	0.33-10.22	0.440
ALT	0.99	0.96-1.01	0.277
AST	0.99	0.98-1.00	0.232
Platelet count	1.00	0.99-1.02	0.782
INR	4.25	0.37-82.85	0.275
Bilirubin	0.99	0.89-1.12	0.794
MELD	1.09	0.91-1.36	0.367
ABIC	0.55	0.19-1.32	0.212
Maddrey's DF	0.99	0.97-1.00	0.108
Hyaluronidase (<i>EF0818</i>)			
Infections	1.17	0.23-4.34	0.814
90 day mortality rate	3.67	1.05-19.45	0.062
ALT	0.99	0.97-1.01	0.400
AST	0.99	0.98-1.00	0.248
Platelet count	1.00	0.99-1.00	0.323
INR	3.38	0.49-33.05	0.240
Bilirubin	1.03	0.94-1.14	0.592
MELD	1.11	0.96-1.33	0.200
ABIC	0.57	0.25-1.14	0.137
Maddrey's DF	1.00	0.98-1.01	0.659
Hyaluronidase (<i>EF3023</i>)			
Infections	2.00	0.56-9.97	0.301
90 day mortality rate	1.10	0.33-3.65	0.876
ALT	1.00	0.98-1.02	0.945
AST	1.00	0.99-1.01	0.467
Platelet count	1.00	0.99-1.01	0.637
INR	2.59	0.43-20.22	0.319
Bilirubin	1.06	0.97-1.19	0.224
MELD	1.08	0.94-1.26	0.299
ABIC	0.76	0.38-1.43	0.402
Maddrey's DF	1.00	0.98-1.01	0.775

Quorum sensing system regulator (<i>fsrA</i>)			
Infections	2.00	0.56-9.97	0.301
90 day mortality rate	1.10	0.33-3.65	0.876
ALT	1.00	0.98-1.02	0.945
AST	1.00	0.99-1.01	0.467
Platelet count	1.00	0.99-1.01	0.637
INR	2.59	0.43-20.22	0.319
Bilirubin	1.06	0.97-1.19	0.224
MELD	1.08	0.94-1.26	0.299
ABIC	0.76	0.38-1.43	0.402
Maddrey's DF	1.00	0.98-1.01	0.775
Quorum sensing system regulator (<i>fsrB</i>)			
Infections	2.35	0.65-11.82	0.209
90 day mortality rate	2.83	0.84-14.26	0.120
ALT	1.00	0.97-1.02	0.645
AST	1.00	0.99-1.01	0.497
Platelet count	1.00	0.99-1.01	0.554
INR	2.95	0.46-25.79	0.277
Bilirubin	1.04	0.95-1.15	0.462
MELD	1.12	0.97-1.34	0.171
ABIC	0.61	0.28-1.19	0.171
Maddrey's DF	0.99	0.97-1.00	0.183
Quorum sensing system regulator (<i>fsrC</i>)			
Infections	2.35	0.65-11.82	0.209
90 day mortality rate	2.83	0.84-14.2	0.120
ALT	1.00	0.97-1.02	0.645
AST	1.00	0.99-1.01	0.497
Platelet count	1.00	0.99-1.01	0.554
INR	2.95	0.46-25.79	0.277
Bilirubin	1.04	0.95-1.15	0.462
MELD	1.12	0.97-1.34	0.171
ABIC	0.61	0.28-1.19	0.171
Maddrey's DF	0.99	0.97-1.00	0.183
Adhesin (<i>ace</i>)			
Infections	1.32	0.37-6.53	0.674
90 day mortality rate	0.76	0.22-2.52	0.635
ALT	1.01	0.99-1.03	0.596
AST	1.00	0.99-1.01	0.670
Platelet count	0.99	0.98-1.00	0.180
INR	2.35	0.39-17.78	0.365
Bilirubin	1.01	0.92-1.10	0.841
MELD	1.04	0.91-1.20	0.585
ABIC	0.73	0.36-1.39	0.355
Maddrey's DF	0.99	0.97-1.01	0.255

Aggregation substance (EF0485)			
Infections	1.32	0.37-6.53	0.674
90 day mortality rate	0.76	0.22-2.52	0.635
ALT	1.01	0.99-1.03	0.596
AST	1.00	0.99-1.01	0.670
Platelet count	0.99	0.98-1.00	0.180
INR	2.35	0.39-17.78	0.365
Bilirubin	1.01	0.92-1.10	0.841
MELD	1.04	0.91-1.20	0.585
ABIC	0.73	0.36-1.39	0.355
Maddrey's DF	0.99	0.97-1.01	0.255
Aggregation substance (prgBlasc10)			
Infections	0.01	2.53e-06-2.16e+01	0.308
90 day mortality rate	42.29	1.98e-04-1.43e+05	1.000
ALT	0.99	0.96-1.01	0.602
AST	1.00	0.98-1.01	0.539
Platelet count	1.00	0.98-1.01	0.425
INR	14.99	1.47-357.43	0.046
Bilirubin	0.96	0.85-1.06	0.443
MELD	1.03	0.89-1.19	0.692
ABIC	1.28	0.64-2.71	0.490
Maddrey's DF	1.00	0.99-1.02	0.570
Erythromycin resistance (ermB)			
Infections	0.55	0.13-2.90	0.413
90 day mortality rate	0.76	0.22-2.52	0.635
ALT	0.99	0.95-1.01	0.477
AST	1.00	0.98-1.01	0.430
Platelet count	1.00	0.99-1.01	0.365
INR	0.64	0.07-5.08	0.673
Bilirubin	1.02	0.93-1.13	0.617
MELD	1.08	0.93-1.28	0.309
ABIC	1.02	0.48-2.13	0.963
Maddrey's DF	1.00	0.98-1.02	0.834
Tetracycline resistance (tetM)			
Infections	1.00	0.28-4.96	1.000
90 day mortality rate	33.79	1.12e-04-1.14e+05	1.000
ALT	0.99	0.95-1.01	0.306
AST	1.00	0.99-1.01	0.918
Platelet count	1.00	0.99-1.01	0.883
INR	1.31	0.21-8.66	0.770
Bilirubin	1.07	0.98-1.18	0.177
MELD	1.18	1.01-1.46	0.065
ABIC	1.35	0.71-2.75	0.368
Maddrey's DF	1.00	0.98-1.01	0.876

*Significance is indicated in bold.

P values from Univariate logistic regression were determined by two-sided Wald test.

OR, odds ratio; CI, confidence interval; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; MELD, model for end-stage liver disease; ABIC, Age, serum bilirubin, INR, and serum creatinine score; DF, discriminant function

Supplementary Table 5: Univariate linear regression analysis of laboratory and clinical parameters associated with the total amount of fecal *E. faecalis*, and Cox regression analysis assessing the association between total amount of *E. faecalis* and survival in alcoholic hepatitis patients (n=82)

Univariate linear regression	Coefficient	SE	R²	P value*
Steroids	-0.222	0.769	0.001	0.770
PTX	-0.785	1.332	0.005	0.560
Antibiotics	0.022	0.745	0.000	0.980
Infections	0.002	1.002	0.000	1.000
Cirrhosis	0.031	0.967	0.000	0.974
Abstinence day 30 follow-up	0.936	1.325	0.011	0.483
Creatinine	-0.364	0.298	0.018	0.230
GGT	-0.000	0.001	0.010	0.532
INR	-0.122	0.614	0.000	0.843
Platelet count	-0.003	0.004	0.006	0.500
MELD	-0.035	0.057	0.005	0.547
MELDNa	-0.051	0.066	0.008	0.442
Maddrey's DF > 32	-1.610	1.290	0.024	0.219
Maddrey's DF	0.004	0.008	0.004	0.602
ABIC	-0.250	0.286	0.009	0.386

Univariate Cox regression	HR	95% CI	P value*
30 day mortality	0.95	0.76-1.18	0.648
90 day mortality	0.91	0.76-1.09	0.296
180 day mortality	1.03	0.91-1.17	0.618

*Significance is indicated in bold.

Antibiotics include prophylactic antibiotics. The total amount of fecal *E. faecalis* was log-transformed. In the univariate Cox regression, patients were censored at the time point they were last seen alive. *P* values were determined by two-sided Wald test.

Coefficient = non-standardized regression coefficient; SE, standard error; R² = coefficient of determination; HR, hazard ratio; CI, confidence interval; PTX, pentoxifylline; GGT, gamma-glutamyl transferase; INR, international normalized ratio; MELD, model for end-stage liver disease; MELDNa, sodium MELD; DF, discriminant function; ABIC, Age, serum bilirubin, INR, and serum creatinine score

Supplementary Table 6: Univariate logistic regression analysis of laboratory and clinical parameters associated with *E. faecalis* positivity, and Cox regression analysis assessing the association between *E. faecalis* positivity and survival in alcoholic hepatitis patients (n=82)

Univariate logistic regression	OR	95% CI	P value*
Steroids	1.25	0.39-4.40	0.712
PTX	1.41	0.21-27.97	0.760
Antibiotics	3.41	1.05-13.36	0.053
Infections	0.95	0.24-4.76	0.946
Cirrhosis	2.50	0.63-10.34	0.191
Abstinence day 30 follow-up	3.43	0.57-19.33	0.157
Creatinine	1.07	0.70-2.15	0.790
GGT	1.00	1.00-1.00	0.011
INR	7.20	1.66-45.63	0.019
Platelet count	0.99	0.99-1.00	0.050
MELD	1.09	0.98-1.22	0.129
MELDNa	1.12	1.00-1.29	0.066
Maddrey's DF > 32	2.50	0.32-14.77	0.326
Maddrey's DF	1.00	0.99-1.02	0.525
ABIC	1.16	0.75-1.82	0.517

Univariate Cox regression	HR	95% CI	P value*
30 day mortality	1.59	0.20-12.96	0.663
90 day mortality	3.10	0.40-23.68	0.276
180 day mortality	5.96	0.79-44.88	0.083

*Significance is indicated in bold.

Antibiotics include prophylactic antibiotics. In the univariate Cox regression, patients were censored at the time point they were last seen alive. *P* values were determined by two-sided Wald test.

OR, odds ratio; HR, hazard ratio; CI, confidence interval; PTX, pentoxifylline; GGT, gamma-glutamyl transferase; INR, international normalized ratio; MELD, model for end-stage liver disease; MELDNa, sodium MELD; DF, discriminant function; ABIC, Age, serum bilirubin, INR, and serum creatinine score

Supplementary Table 7: Region/center specific clinical characteristics of patients with alcoholic hepatitis (n=88)

Variables	France (n=17)	Mexico (n=6)	Spain (n=7)	UK (n=11)	USA East (n=17)	USA Midwest (n=14)	USA West (n=16)	<i>P</i> value*
Sex (% male), n=88	13 (76.5)	5 (83.3)	6 (85.7)	5 (45.5)	7 (41.2)	8 (57.1)	16 (100.0)	0.002
Age (years), n=88	55.0 (30.0- 75.0)	37.0 (35.0- 48.0)	55.0(48.0- 61.0)	48.0 (40.0- 64.0)	48.0 (32.0- 63.0)	50.5 (36.0- 66.0)	58.0 (31.0- 69.0)	0.054
BMI (kg/m ²), n=62	23.1 (16.3- 31.9)	25.5 (19.5- 27.8)	24.9 (24.9- 24.9)	25.2 (19.1- 48.3)	29.6 (20.4- 39.1)	28.5 (16.4- 41.7)	28.5 (21.1- 40.8)	0.309
Creatinine (mg/dL), n=88	0.9 (0.4-5.6)	0.9 (0.6-3.3)	0.8 (0.6-1.0)	0.7 (0.3-2.0)	0.8 (0.4-8.1)	0.9 (0.5-3.1)	0.7 (0.5-5.5)	0.914
Bilirubin (mg/dL), n=88	20.1 (5.2- 30.9)	9.7 (3.1- 22.3)	10.5 (3.1- 21.4)	15.5 (4.9- 36.6)	18.3 (4.3- 38.6)	17.8 (8.4- 32.1)	8.1 (2.5-31.6)	0.014
AST (IU/L), n=88	102.0 (67.0- 406.0)	139.5 (56.0- 170.0)	159.0 (105.0- 290.0)	117.0 (63.0- 170.0)	205.0 (38.0- 339.0)	197.5 (51.0- 456.0)	144.5 (57.0- 274.0)	0.018
ALT (IU/L), n=88	34.0 (20.0- 120.0)	52.0 (26.0- 174.0)	61.0 (30.0- 216.0)	33.0 (21.0- 75.0)	48.0 (15.0- 118.0)	60.5 (19.0- 134.0)	44.0 (25.0- 124.0)	0.172
Albumin (g/dL), n=84	2.9 (2.2-4.1)	1.8 (1.3-2.7)	2.2 (1.9-3.4)	2.7 (2.1-3.3)	2.7 (1.8-3.9)	2.1 (1.6-3.2)	2.3 (1.5-3.2)	2.89e-04
INR, n=87	1.7 (1.4-3.5)	2.2 (1.7-2.7)	1.2 (1.0-2.1)	2.1 (1.6-2.6)	1.8 (1.3-4.4)	1.6 (1.2-2.3)	1.9 (1.1-3.7)	0.064
GGT (IU/L), n=45	115.0 (33.0- 783.0)	109.5 (88.0- 131.0)	2615.0 (88.0- 3632.0)	242.0 (120.0- 917.0)	536.5 (135.0- 2660.0)	698.0 (288.0- 1519.0)	2116.0 (2116.0- 2116.0)	0.011
Platelet count (10 ⁹ /L), n=84	126.0 (21.0- 295.0)	73.0 (32.0- 326.0)	134.0 (42.0- 194.0)	128.0 (51.0- 189.0)	153.0 (22.0- 333.0)	115.0 (13.0- 447.0)	103.0 (49.0- 414.0)	0.842
Steroids, n (%), n=86	5 (29.4)	2 (40.0)	2 (28.6)	4 (36.4)	6 (37.5)	9 (64.3)	2 (12.5)	0.147
Antibiotics n (%), n=86	6 (35.3)	4 (80.0)	3 (42.9)	8 (72.7)	7 (43.8)	4 (28.6)	9 (56.3)	0.204
Infections, n (%), n=71	7 (46.7)	0 (0.0)	1 (16.7)	2 (22.2)	1 (7.7)	3 (21.4)	3 (23.1)	0.391
MELD, median (range), n=87	23.0 (19.0- 46.0)	26.5 (16.0- 33.0)	18.0 (12.0- 26.0)	24.0 (19.0- 29.0)	26.0 (15.0- 40.0)	23.0 (19.0- 34.0)	22.5 (13.0- 40.0)	0.087
MELD > 21, n (%)	15 (88.2)	5 (83.3)	3 (42.9)	9 (81.8)	13 (76.5)	9 (69.2)	9 (56.2)	0.234
Maddrey's DF, median (range), n=72	90.1 (39.7- 234.4)	66.1 (25.6- 99.1)	15.2 (-8.4- 69.1)	54.7 (33.0- 140.4)	54.7 (8.0- 140.3)	117.6 (35.1- 200.1)	42.5 (-0.6- 145.4)	0.001
Maddrey's DF > 32, n (%)	15 (100.0)	5 (83.3)	3 (42.9)	11 (100.0)	13 (76.5)	2 (100.0)	9 (64.3)	0.008
ABIC, median (range), n=87	8.3 (6.0- 11.0)	6.6 (6.5-9.0)	7.5 (6.6-9.3)	8.3 (6.7-9.6)	8.3 (5.6-10.5)	7.8 (5.9-9.8)	8.5 (5.7-10.4)	0.225
Liver cirrhosis, n (%), n=51	11 (68.8)	2 (66.7)	3 (50.0)	1 (50.0)	5 (41.7)	4 (100.0)	7 (87.5)	0.276
30 day mortality rate, n (%), n=81	2 (11.8)	1 (20.0)	1 (14.3)	1 (9.1)	1 (9.1)	2 (14.3)	1 (6.2)	0.963
90 day mortality rate, n (%), n=60	4 (28.6)	1 (25.0)	1 (25.0)	3 (50.0)	1 (12.5)	3 (23.1)	2 (18.2)	0.827

*Significance is indicated in bold.

Antibiotics include prophylactic antibiotics. Values are presented as median with range in brackets for continuous variables or number and percentage in brackets for categorical variables. Percentages are calculated based on the actual number of patients in each group where the respective data was available. The number of subjects for which the respective data was available is indicated in the first column. Kruskal-Wallis test and two-sided Fisher's exact test were used to determine *P* values for continuous and categorical variables, respectively.

UK, United Kingdom; USA, United States of America; BMI, body mass index; AST, aspartate aminotransferase; ALT, alanine aminotransferase; INR, international normalized ratio; GGT, gamma-glutamyl transferase; MELD, model for end-stage liver disease; DF, discriminant function; ABIC, Age, serum bilirubin, INR, and serum creatinine score

Supplementary Table 8: Characteristics of donor patients for fecal transplantation of germ-free mice

Patient	#1	#2	#3	#4	#5	#6	#7
Cytolysin	Positive	Positive	Negative	Negative	Positive	Negative	Negative
Age (years)	35	41	51	39	61	53	69
Gender	Male	Male	Male	Female	Male	Male	Male
BMI (kg/m ²)	27.5	41.7	N/A	39.1	23.8	N/A	40.8
Center	Mexico	USA Midwest	Spain	USA East	France	Spain	USA West
Infection	N/A	No	No	Yes	No	No	No
Antibiotics	Yes	No	No	Yes	No	No	No
Steroids	Yes	Yes	No	No	No	No	No
Pentoxifylline	Yes	No	No	No	No	No	Yes
Stage of fibrosis	4	N/A	N/A	N/A	4	0	4
Died within 180 days	Yes	Yes	No	No	Yes	No	No
MELD	33	29	13	15	22	14	18

Antibiotics include prophylactic antibiotics.

BMI, body mass index; MELD, model for end-stage liver disease; N/A, not applicable

Supplementary Table 9: All primers used in this study

Gene	Primer	Sequence
16S rRNA (total bacteria)	F	5'-GTGSTGCAYGGYTGTCTCGTCA-3'
	R	5'-ACGTCRTCCMCACCTTCCTC-3'
<i>E. faecalis</i> 16S rRNA	F	5'-CGCTTCTTTCTCCTCCCGAGT-3'
	R	5'-GCCATGCGGCATAAACTG-3'
<i>E. faecalis</i> <i>cylL_L</i>	F	5'-CTGTTGCGGCGACAGCT-3'
	R	5'-CCACCAACCCAGCCACAA-3'
<i>E. faecalis</i> <i>cylL_S</i>	F	5'-GTAAAATAAGTAAAATCAAGAAAACCTATTACTC-3'
	R	5'-CAAAAGAAGGACCAACAAGTTCTAATT-3'
Mouse 18S	F	5'-AGTCCCTGCCCTTTGTACACA-3'
	R	5'-CGATCCCAGGGCCTCACTA-3'
Mouse <i>Acta2</i>	F	5'-GTTCAAGTGGTGCCTCTGTCA-3'
	R	5'-ACTGGGACGACATGGAAAAG-3'
Mouse <i>Adh1</i>	F	5'-GGGTTCTCAACTGGCTATGG-3'
	R	5'-ACAGACAGACCGACACCTCC-3'
Mouse <i>Col1a1</i>	F	5'-TAGGCCATTGTGTATGCAGC-3'
	R	5'-ACATGTTTCTGCTTTGTGGACC-3'
Mouse <i>Cxcl1</i>	F	5'-TGCACCCAAACCGAAGTC-3'
	R	5'-GTCAGAAGCCAGCGTTCACC-3'
Mouse <i>Cxcl2</i>	F	5'-AAAGTTTGCCTTGACCCTGAA-3'
	R	5'-CTCAGACAGCGAGGCACATC-3'
Mouse <i>Cyp2e1</i>	F	5'-CTTAGGGAAAACCTCCGCAC-3'
	R	5'-GGGACATTCTGTGTTCCAG-3'
Mouse <i>Il1b</i>	F	5'-GGTCAAAGGTTTGGAAGCAG-3'
	R	5'-TGTGAAATGCCACCTTTTGA-3'