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Supplemental Information

Translocation of Viable Gut Microbiota to Mesenteric Adipose Drives Formation of Creeping Fat in Humans

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Table S1. CD and UC Patient metadata, related to Figure 1

		Crohn's disease (n=11)	Ulcerative colitis (n=13)
Gender	Male	7	7
Race	European ancestry/Jewish	3	3
	European ancestry	6	7
	Asian	1	0
	Pacific Islander	1	0
	Hispanic	0	1
	Other	0	2
Family history of IBD	Yes	1	5
	No	10	8
Median age (min. - max.)		49 (18-75)	37 (20-72)
Median age at diagnosis (min.- max.)		35 (7-60)	26 (11-60)
Median duration of disease (min.- max.)		15 (9-19)	5 (1-25)
Previous IBD surgery	Yes	7	0
	No	4	13
Montreal classification	A1	3	
	A2	5	
	A3	3	
	B1	0	
CD†	B2	11	
	B3	4	
	L1	2	
	L2	0	
	L3	9	
	p	1	
	E1		0
UC	E2		1
	E3		12
Indication for surgery	Strictures	7	0
	Strictures w/ fistulae	2	0
	Medically refractory	0	13
	Obstruction	2	0
Smoker	Never	5	10
	Current	0	0
	Ex-smoker	5	3
	N/A	1	0
Medications*	Aminosalicylates	1	7
	Corticosteroids	3	8
	Immunomodulators	7	6
	Biologics	9	12

† Patients may be classified in more than one "B" category

* Patients could be on more than one class of medication

Montreal Classification:	**CD**	**UC**
	A1- below 16 y	E1- Ulcerative proctitis
	A2- between 17 and 40 y	E2- Left sided UC (distal UC)
	A3- above 40 y	E3- Extensive UC (pancolitis)
	L1- ileal	
	L2- colonic	
	L3- ileocolonic	
	B1- non-stricturing, non-penetrating	
	B2- stricturing	
	B3- penetrating	
	p- perianal disease modifier	

Table S2. Metagenomic read counts per sample, related to Figure 2.

H- MAT = control adipose
H- MUC = control mucosa
CD CrF = CD creeping fat
CD INV MUC = CD involved mucosa
CD MAT = CD uninvolved adipose
CD UN MUC = CD uninvolved mucosa

Sample IDs	Reads Per Sample (after 0.01% relative abundance filtering and decontamination)
H3.MAT	0
CD4.INV.MUC	438
H3.MUC	1713
H1.MUC	1807
H2.MUC	2502
H4.MAT	4097
CD1.MAT	4914
CD1.INV.MUC	7025
CD1.CrF	7164
H1.MAT	9158
CD4.CrF	9824
CD3.MAT	14714
CD4.UN.MUC	16472
CD2.MAT	18233
CD4.MAT	19741
H2.MAT	21498
CD1.UN.MUC	22158
CD2.CrF	34624
CD3.CrF	337415
CD3.INV.MUC	1014248
CD3.UN.MUC	1038967
CD2.UN.MUC	4401798
CD2.INV.MUC	17529985
H4.MUC	19680723

Table S3. Adonis PERMANOVA of beta diversity measures from metagenomic sequencing identifies sample type (tissue source- MAT or mucosa and CD or H) and participant ID (inter-individual differences) as most significant parameters defining bacterial diversity, related to Figure 2.

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Weighted UniFrac	Sample Type	5	3.08997458	0.61799492	2.45866441	0.21636313	0.02
	Participant ID	6	8.67791511	1.44631919	5.75411449	0.60763634	0.001
	Residuals	10	2.51353912	0.25135391		0.17600054	
	Total	21	14.2814288			1	

		Df	SumsOfSqs	MeanSqs	F.Model	R2	Pr(>F)
Unweighted UniFrac	Sample Type	5	1.48612759	0.29722552	1.33938695	0.23969334	0.028
	Participant ID	6	2.49487688	0.41581281	1.87377673	0.40239167	0.001
	Residuals	10	2.21911612	0.22191161		0.35791499	
	Total	21	6.20012059			1	

Table S4. Bacterial isolates recovered from CD and UC mesenteric adipose, related to Figure 3

List of cultivable organism from mesenteric adipose tissue
Actinomyces odontolyticus
Alistipes finegoldii
Arabia massiliensis 94% (Paraeggerthella 100% by RDP)
Bacteroides caccae
Bacteroides cellulosilyticus
Bacteroides fragilis
Bacteroides ovatus
Bacteroides thetaiotaomicron
Bacteroides uniformis
Bacteroides vulgatus
Bifidobacterium bifidum
Bifidobacterium longum
Bifidobacterium pseudolongum
Bilophila wadsworthia
Blautia coccoides
Blautia hansenii
Blautia obeum
Blautia sp. KLE 1732 97%
Cetobacterium somerae
Citrobacter freundii
Clostridium baratii
Clostridium bolteae
Clostridium botulinum
Clostridium chauvoei
Clostridium innocuum
Clostridium perfringens
Clostridium spiroforme
Clostridium symbiosum
Collinsella aerofaciens
Desulfovibrio desulfuricans
Dorea longicatena
Eggerthella lenta
Eisenbergiella tayi
Enterococcus faecalis
Enterococcus gilvus
Enterococcus hermanniensis
Erysipelatoclostridium ramosum
Erysipelotrichaceae 97% Coprobacillus 90%
Escherichia/Shigella
Eubacterium oxidoreducens
Eubacterium sp. Marseille (BLAST:98%)/Unclassified Lachnospiraceae (RDP: 100%)
Faecalicatena contorta
Flavonifractor plautii
Fusobacterium nucleatum
Fusobacterium ulcerans
Gardnerella vaginalis
Gemella sanguinis
Haemophilus parainflluenzae
Hungatella hathewayi
Klebsiella oxytoca
Klebsiella pneumoniae
Klebsiella spp.
Lachnoclostridium sp.
Lactobacillus gasseri
Lactobacillus rhamnosus GG
Massiliomicrobiota timonensis
Massiliomicrobiota timonensis
Merdimonas faecis 95% (Unclassified Lachnospiraceae)
Morganella morganii
Oscillibacter ruminantium
Parabacteroides distasonis
Parabacteroides johnsonii
Parabacteroides merdae
Parvimonas sp.
Phascolarctobacterium 100%; Phascolarctobacterium succinatutens YIT 12067 91%
Proteus mirabilis
Rothia mucilaginosa
Ruminococcus gnavus
Ruminococcus torques
Staphylococcus capitis
Staphylococcus epidermidis
Staphylococcus haemolyticus
Staphylococcus saccharolyticus
Streptococcus anginosus
Streptococcus australis
Streptococcus lutetiensis
Streptococcus parasanguinis
Streptococcus sanguinis
Tyzzerella nexilis
Unclassified Enterococcus
Unclassified Erysipelotrochaceae
Veillonella atypica
Veillonella parvula

Table S9. Primers used in the study, related to Key Resources Table in STAR Methods

Target gene	Primers		Reference
Bacterial 16S (full length)	27F: AGAGTTTGATCMTGGCTCAG	1492R: TACGGYTACCTTGTTACGACTT	Macrogen
Bacterial 16S (V4 region)	515F: GTGYCAGCMGCCGCGGTAA	806R: GGACTACNVGGGTWTCTAAT	Walters et al., 2016
Fungal ITS (full length)	ITS1: TCCGTAGGTGAACCTGCGG	ITS4: TCCTCCGCTTATTGATATGC	White et al., 1990
Fungal ITS (ITS1 region)	ITS1F: CTTGGTCATTTAGAGGAAGTA	ITS2: GCTGCGTTCTTCATCGATGC	White et al., 1990
Human GAPDH	F: CTCTGCTCCTCCTGTTCGAC	R: TTAAAAGCAGCCCTGGTGAC	Maeß et al., 2010
Human Claudin3	F: CACGCGAGAAGAAGTACACG	R: CCTGCGTCTGTCCCTTAGAC	Yao et al., 2015
Human Claudin4	F: CATCTCCTCTGTTCCGGGTA	R: ATCCACTCTGCACTTCCCAG	This study
Human Claudin7	F: GCAAAATGTACGACTCGGTG	R: CACAAACATGGCCAGGAAG	This study
Human E-cadherin	F: GCCGAGAGCTACACGTTCAC	R: GTCGAGGGAAAAATAGGCTG	Gleeson et al., 2020
Human Junctional adhesion molecule-A	F: TCATATTGGCGATCCTGTTG	R: AGGCACAGGACAACTTCACA	Gleeson et al., 2020
Human Zonula occludens-1	F: ACAGCAATGGAGGAAACAGC	R: CCCCACTCTGAAAATGAGGA	Gleeson et al., 2020
Human Mucin-1	F: CCCTCCCAGTGTGCAAATAAG	R: GAACGGTGTCGTCGAAACAG	This study
Human Tricellulin	F: GGCAGCTCGGAGACATAGAG	R: TTTGCTGTTCTCAGTTCCTTGA	This study
Human RPL37A	F: ATTGAAATCAGCCAGCACGC	R: AGGAACCACAGTGCCAGATCC	Maeß et al., 2010
Human CD80	F: CTCTTGGTGCTGGCTGGTCTTT	R: GCCAGTAGATGCGAGTTTGTGC	Kooreman et al., 2017
Human CD86	F: CCATCAGCTTGTCTGTTTCATTCC	R: GCTGTAATCCAAGGAATGTGGTC	Kooreman et al., 2017
Human CD163	F: GTCGCTCATCCCGTCAGTCATC	R: GCCGCTGTCTCTGTCTTCGC	Wheeler et al., 2018
Human CD206	F: ACCTCACAAGTATCCACACCATC	R: CTTTCATCACCACACAATCCTC	Wheeler et al., 2018
Human TNF-α	F: ATGAGCACTGAAAGCATGATCC	R: GAGGGCTGATTAGAGAGAGGTC	Cappon et al., 2010
Human β-Actin	F: ATTGCCGACAGGATGCAGAA	R: GCTGATCCACATCTGCTGGAA	Maeß et al., 2010
Human Collagen I	F: GTCACCCACCGACCAAGAAACC	R: AAGTCCAGGCTGTCCAGGGATG	Ekwueme et al., 2016
Human Hyaluronan synthase I	F: TCAGCCCAAGATTCTTCAGTC	R: GAACGAGGAGAAAGCAGGAC	Zhang et al., 2009
Murine Hprt1	F: AGCCTAAGATGAGCGCAAGT	R: TTACTAGGCAGATGGCCACA	Arimochi et al., 2016
Murine Fatty acid binding protein 4	F: GAATTCGATGAAATCACCGCA	R: CTCTTTATTGTGGTCGACTTTCCA	Arimochi et al., 2016
Murine Peroxisome proliferator activated receptor gamma	F: GTGCCAGTTTCGATCCGTAG	R: GGCCAGCATCGTGTAGATGA	Arimochi et al., 2016
Murine Adiponectin	F: GCACTGGCAAGTTCTACTGCAA	R: GTAGGTGAAGAGAACGGCCTTGT	Arimochi et al., 2016
Murine CCAAT/enhancer-binding protein alpha	F: CAAGAACAGCAACGAGTACCG	R: GTCACTGGTCAACTCCAGCAC	Arimochi et al., 2016
Murine Fatty acid synthase	F: AGAGATCCCGAGACGCTTCT	R: GCCTGGTAGGCATTCTGTAGT	Alcala et al., 2017
Murine Collagen IV	F: TTAAAGGACTCCAGGGACCAC	R: CCCACTGAGCCTGTCACAC	Alcala et al., 2017
Murine Collagen VI	F: TCTTGAACGTGTGGCTAACC	R: T CTTTTCTCCAGAAGAACCAGG	Pan et al., 2013