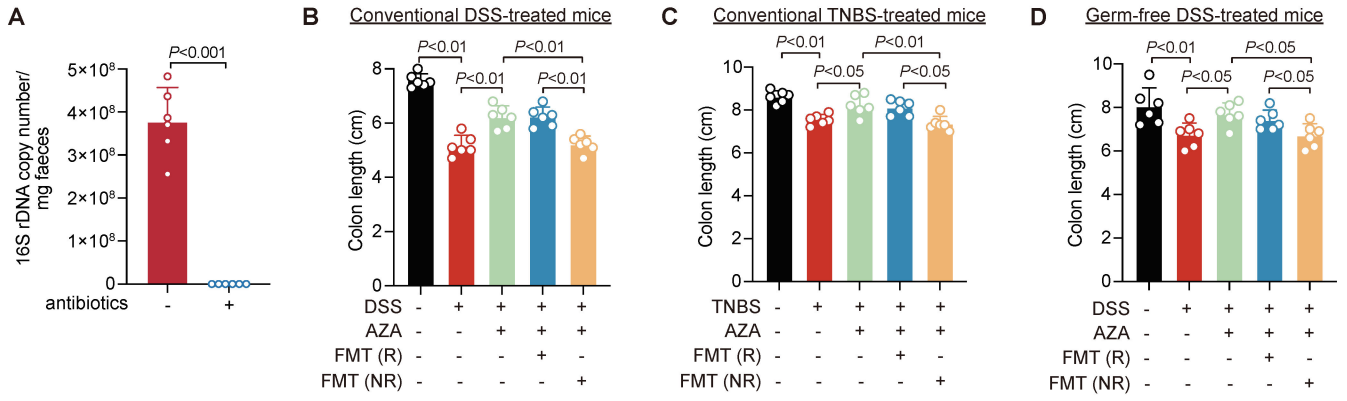**Supplemental information**

Commensal bacteria promote azathioprine therapy

failure in inflammatory bowel disease

via decreasing 6-mercaptopurine bioavailability

Yuqing Yan, Zhenhua Wang, Yi-Lu Zhou, Ziyun Gao, Lijun Ning, Ying Zhao, Baoqin Xuan, Yanru Ma, Tianying Tong, Xiaowen Huang, Muni Hu, Jing-Yuan Fang, Zhe Cui, Haoyan Chen, and Jie Hong

Supplementary Figure 1

A

P<0.001

16S rDNA copy number/ mg faeces

5×10^8
4×10^8
3×10^8
2×10^8
1×10^8
0

antibiotics   −   +

B   <u>Conventional DSS-treated mice</u>

P<0.01
P<0.01
P<0.01
P<0.01

Colon length (cm)

8
6
4
2
0

DSS	−	+	+	+	+
AZA	−	−	+	+	+
FMT (R)	−	−	−	+	−
FMT (NR)	−	−	−	−	+

C   <u>Conventional TNBS-treated mice</u>

P<0.01
P<0.05
P<0.01
P<0.05

Colon length (cm)

10
8
6
4
2
0

TNBS	−	+	+	+	+
AZA	−	−	+	+	+
FMT (R)	−	−	−	+	−
FMT (NR)	−	−	−	−	+

D   <u>Germ-free DSS-treated mice</u>

P<0.01
P<0.05
P<0.05
P<0.05

Colon length (cm)

10
8
6
4
2
0

DSS	−	+	+	+	+
AZA	−	−	+	+	+
FMT (R)	−	−	−	+	−
FMT (NR)	−	−	−	−	+

Figure S1. Gut microbes were closely associated with therapeutic failure of azathioprine (AZA) in patients with inflammatory bowel diseases. Related to Figure 1.

(**A**) The length of colon of colonic sections in conventional DSS-induced colitis, n=6/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

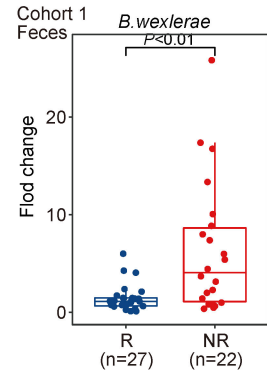(**B**) The length of colon of colonic sections in conventional TNBS-induced colitis, n=6/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**C**) The length of colon of colonic sections in germ-free DSS-induced colitis, n=6/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.
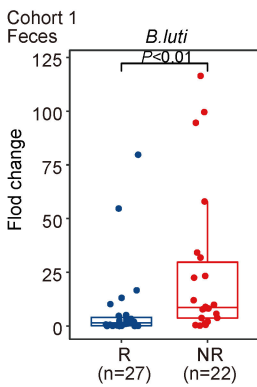
Supplementary Figure 2

Figure S2. *Blautia* bacteria could predict the effect of Azathioprine (AZA) therapy in IBD patients. Related to Figure 2.

(**A**) Top 10 strains were blasted to the sequence of *B.wexlerae/B.luti* in national library of medicine database.

(**B-C**) The amount of *B.wexlerae* (**B**) and *B.luti* (**C**) species in the feces of IBD patients of Cohort 1, R, n=27; NR, n=22, nonparametric Wilcoxon rank-sum test.

(**D**) The amount of *B.wexlerae/B.luti* species in the illum tissue of IBD patients in Cohort 1, R, n=25; NR, n=20, nonparametric Wilcoxon rank-sum test.

(**E-F**) The amount of *B.wexlerae* (**E**) and *B.luti* (**F**) in the illum tissue of IBD patients in Cohort 1, R, n=25; NR, n=20, nonparametric Wilcoxon rank-sum test.

(**G-H**) The amount of *B.wexlerae* (**G**) and *B.luti* (**H**) in the colonoscopy paraffin-embedded mucosa of IBD patients in Cohort 2, R, n=57; NR, n=34, nonparametric Wilcoxon rank-sum test.

(**I-J**) The amount of *B.wexlerae* (**I**) and *B.luti* (**J**) species in the colonoscopy paraffin-embedded mucosa of UC (R, n=36; NR, n=23) and CD (R, n=21; NR, n=11) patients in Cohort 2, nonparametric Wilcoxon rank-sum test.

(**K**) Univariate analysis was performed in Cohort 2. The bars correspond to 95% confidence intervals.

Supplementray Figure 3

Figure S3. *B.wexlerae* reduced the therapeutic effect of AZA in a dextran sulfate sodium–induced acute colitis model. Related to Figure 3.

(**A**) Schematic diagram of the DSS-induced acute colitis model treated with *B.wexlerae* and *B.luti* in C57BL/6 mice, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=9), (DSS+ *B.wexlerae*) group (n=10).

(**B-C**) The relative abundance of *B.luti* (**B**) and *B.wexlerae* (**C**) in feces of *B.luti* or *B.wexlerae*-gavaged mice, n=6/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**D and E**) The alterations in mouse body weight (**D**) and DAI (**E**) evaluation, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SEM.

(**F and G**) Gross morphology (**F**) and length (**G**) of the colon in C57BL/6 mice with and without *B.wexlerae* and *B.luti* gavaged, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**H and I**) Representative images stained with Hematoxylin and Eosin staining (**H**) and the histology scores (**I**) of colonic sections in *B.wexlerae* and *B.luti*-gavaged C57BL/6 mice, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Original magnification, ×5 (*top row*) and ×20 (*bottom row*). Data are represented as mean ± SD.

(**J-N**) Real-time PCR was performed to detect *Tnf* (**J**), *Ifng* (**K**), *Il1b* (**L**), *Il17* (**M**) and *Il6* (**N**) in different treatment of mice groups, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**O**) Statistical proportion of monocyte cells in different mice groups, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**P**) Statistical proportion of granulocyte in different mice groups, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10), (DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**Q and R**) The statistical proportion of CD4+T (**Q**) and CD8+T (**R**) in mice groups with and without *B.wexlerae* and *B.luti* gavage, control group (n=10), DSS group (n=10), (DSS+ *B.luti*) group (n=10),

(DSS+ *B.wexlerae*) group (n=9), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**S**) The colon length of mice in different mice groups, n=10/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**T**) Heatmap plot showing the relative expression of immune cell markers in colon mucosae of mice.

(**U**) The statistical proportion of CD4$^+$T and CD8$^+$T in different mice groups, n=10/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

Supplementray Figure 4

A 5 weeks old

Day 0 — Antibiotic — 7 — PBS or *B.wexlerae* — 14 — 21 — 2.5%DSS — 28 — 42 — 3%DSS — 49 — 63 — 3.5%DSS — 70 — 77

Control (n=9)
DSS (n=10)
DSS+*B.wexlerae* (n=9)

B Body weight (%) vs Day(s) — Control, DSS, DSS+*B.wexlerae*

C DAI score vs Day(s) — Control, DSS, DSS+*B.wexlerae*

D Control, DSS, DSS+*B.wexlerae*

E Colon length (cm) — P<0.001; DSS - + +; *B.wexlerae* - - +

F Control, DSS, DSS+*B.wexlerae*

G Histology Score — P<0.001; DSS - + +; *B.wexlerae* - - +

H Colon length (cm) — P<0.001; DSS - + + + +; AZA - - + + +; Heat-killed *B.wexlerae* - - - + -; *B.wexlerae* - - - - +

I B cells, Plasma, T and NK cells, Myeloid cells — mean z-score; Cd79a Cd37 Bank1 Cd19 Ighd Klf2 Jchain Mzb1 Xbp1 Cd3d Cd4 Icos Il7r Cd68 Cst3 Il1b Aif1 Fcer1g

J M-Il1b+S100a8+, M-C1q+, DC-Xcr1+, DC-Napsa+, DC-Ccr7+ — Cd68 Cd14 Il1b S100a9 S100a8 Apoe C1qa C1qb C1qc Lyz2 Aif1 Fcer1g Cxcr4 Fos Fosb Jun Klf6 Fcgr2b Osm Tnf Plac8 Pde4b Cxcl2 Clec10a Cst3 Xcr1 Sox4 Cd9 Fcgrt Napsa Ccr7

K UMAP — B cells, Plasma, T and NK cells, Myeloid — Cohort 3

L B cells, Plasma, T and NK cells, Myeloid — mean z-score; CD79A MS4A1 VPREB3 CD83 BANK1 IGHA2 IGHA1 IGKC CD3D CD3E CD7 IL32 CCL5 CST7 CD2 CD68 LYZ FCER1G C1QA C1QB C1QC

M R (n=4), NR (n=3) — Cohort 3: B cells, Plasma, T&NK cells, Myeloid

N UMAP — M-IL1B+S100A8+, M-IL1B-S100A8+, DC, pDC — Cohort 3

P M-IL1B+S100A8+
- chemokine−mediated signaling pathway
- humoral immune response
- cellular response to chemokine
- response to chemokine
- neutrophil chemotaxis
- antimicrobial humoral response
- neutrophil migration
- positive regulation of calcium ion transport
- granulocyte chemotaxis
- regulation of myoblast fusion

-log10 P value

O M-IL1B+S100A8+, M-IL1B-S100A8+, DC, pDC — CD68 CD14 S100A9 S100A8 IL1B C1QA C1QC CXCL8 TNF FOS FOSB JUN KLF6 PDE4B FCGR1A FCGRT LYZ CST3 APOE SOX4 XCR1 LAMP3 PLAC8 CLEC4C IRF7

Figure S4. *B.wexlerae* reduced the therapeutic effect of AZA and elevated the amount IL1B⁺S100A8⁺ macrophages in chronic mice colitis model. Related to Figure 4.

(**A**) Schematic diagram of the DSS-induced chronic colitis model treated with *B.wexlerae* in C57BL/6 mice, control group (n=9), DSS group (n=10), (DSS+ *B.wexlerae*) group (n=10).

(**B and C**) The alterations in mouse body weight (**B**) and DAI evaluation (**C**), control group (n=9), DSS group (n=10), (DSS+ *B.wexlerae*) group (n=10), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SEM.

(**D and E**) Gross morphology (**D**) and length (**E**) of the colon in C57BL/6 mice with and without *B.wexlerae* gavaged, control group (n=9), DSS group (n=10), (DSS+ *B.wexlerae*) group (n=10), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**F and G**) Representative images stained with Hematoxylin and Eosin staining (**F**) and the histology scores (**G**) of colonic sections in *B.wexlerae*-gavaged C57BL/6 mice. Original magnification, ×5 (*top row*) and ×20 (*bottom row*), control group (n=9), DSS group (n=10), (DSS+ *B.wexlerae*) group (n=10), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**H**) The colon length was shown in heat-killed *B.wexlerae* or *B.wexlerae*-gavaged C57BL/6 mice with AZA treatment, control group (n=9), DSS group (n=10), (DSS+AZA) group (n=10), (DSS+heat-killed *B. wexlerae*+AZA) group (n=10) and (DSS+*B. wexlerae*+AZA) group (n=10), nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**I**) Heatmap showing specific marker genes for 5 major cell clusters in chronic colitis of mice. Relative expression was defined as the gene-wise (row) z-score of normalized UMI counts across cell types (column).

(**J**) Violin plots showing marker genes across myeloid subsets in DSS-induced chronic colitis.

(**K**) UMAP of major immune cell clusters in Cohort 3.

(**L**) Heatmap showing specific marker genes for 7 major cell clusters in Cohort 3. Relative expression was defined as the gene-wise (row) z-score of normalized UMI counts across cell types (column).
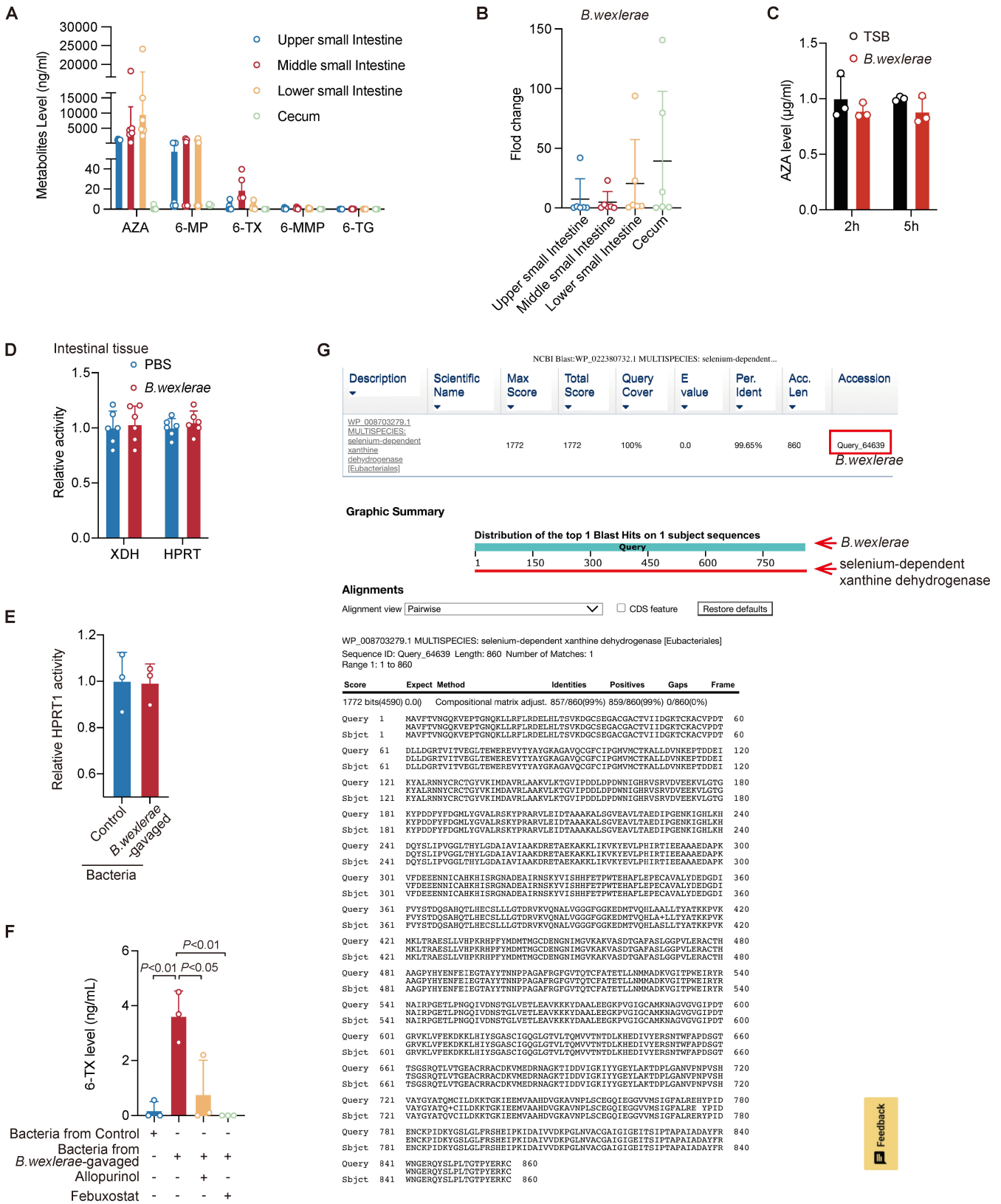
(**M**) Bar plots exhibiting the cellular sources for IBD patient cell subtypes. Blocks represent different subtype and are color-coded by their derived types. Block heights are proportional to the number of detected cells.

(**N**) UMAP of myeloid cell clusters in Cohort 3.

(**O**) Violin plots showing marker genes across myeloid subsets in IBD patients.

(P) Bar graph showing the enriched pathways in Il1B$^+$S100A8$^+$ macrophages (M-Il1B$^+$S100A8$^+$) in remission (n = 4) IBD patients compared with non-remission patients (n = 3) via gene oncology analysis.

Supplementary Figure 5

A

B *B.wexlerae*

C

D Intestinal tissue

E

F

Bacteria from Control
Bacteria from *B.wexlerae*-gavaged
Allopurinol
Febuxostat

G

NCBI Blast:WP_022380732.1 MULTISPECIES: selenium-dependent...

Description	Scientific Name	Max Score	Total Score	Query Cover	E value	Per. Ident	Acc. Len	Accession
WP_008703279.1 MULTISPECIES: selenium-dependent xanthine dehydrogenase [Eubacteriales]		1772	1772	100%	0.0	99.65%	860	Query_64639

B.wexlerae

Graphic Summary

Distribution of the top 1 Blast Hits on 1 subject sequences

← *B.wexlerae*

← selenium-dependent xanthine dehydrogenase

Alignments

Alignment view: Pairwise   ☐ CDS feature   Restore defaults

WP_008703279.1 MULTISPECIES: selenium-dependent xanthine dehydrogenase [Eubacteriales]
Sequence ID: Query_64639 Length: 860 Number of Matches: 1
Range 1: 1 to 860

Score	Expect	Method	Identities	Positives	Gaps	Frame
1772 bits(4590)	0.0()	Compositional matrix adjust.	857/860(99%)	859/860(99%)	0/860(0%)	

```
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Sbjct  1    MAVFTVNGQKVEPTGNQKLLRFLRDELHLTSVKDGCSEGACGACTVIIDGKTCKACVPDT  60

Query  61   DLLDGRTVITVEGLTEWEREVYTYAYGKAGAVQCGFCIPGMVMCTKALLDVNKEPTDDEI  120
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Sbjct  61   DLLDGRTVITVEGLTEWEREVYTYAYGKAGAVQCGFCIPGMVMCTKALLDVNKEPTDDEI  120

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Sbjct  121  KYALRNNYCRCTGYVKIMDAVRLAAKVLKTGVIPDDLDPDWNIGHRVSRVDVEEKVLGTG  180

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Sbjct  181  KYPDDFYFDGMLYGVALRSKYPRARVLEIDTAAAKALSGVEAVLTAEDIPGENKIGHLKH  240

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Sbjct  241  DQYSLIPVGGLTHYLGDAIAVIAAKDRETAEKAKKLIKVKYEVLPHIRTIEEAAAEDAPK  300

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Sbjct  721  VAYGYATQVCILDKKTGKIEEMVAAHDVGKAVNPLSCEGQIEGGVVMSIGFALRERYPID  780

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Sbjct  841  WNGERQYSLPLTGTPYERKC  860
```

Figure S5. *B.wexlerae* was closely associated with the biotransformation of azathioprine. Related to Figure 5.

(**A**) The level of the metabolites of AZA in luminal contents. Data are represented as mean ± SD.

(**B**) The abundance of *B. wexlerae* in luminal contents. Data are represented as mean ± SD.

(**C**) The level of AZA detected in the bacterial culture Tryptic Soy Broth (TSB) medium with *B.wexlerae* incubation, n=3/group, Student's T Test. Data are represented as mean ± SD.
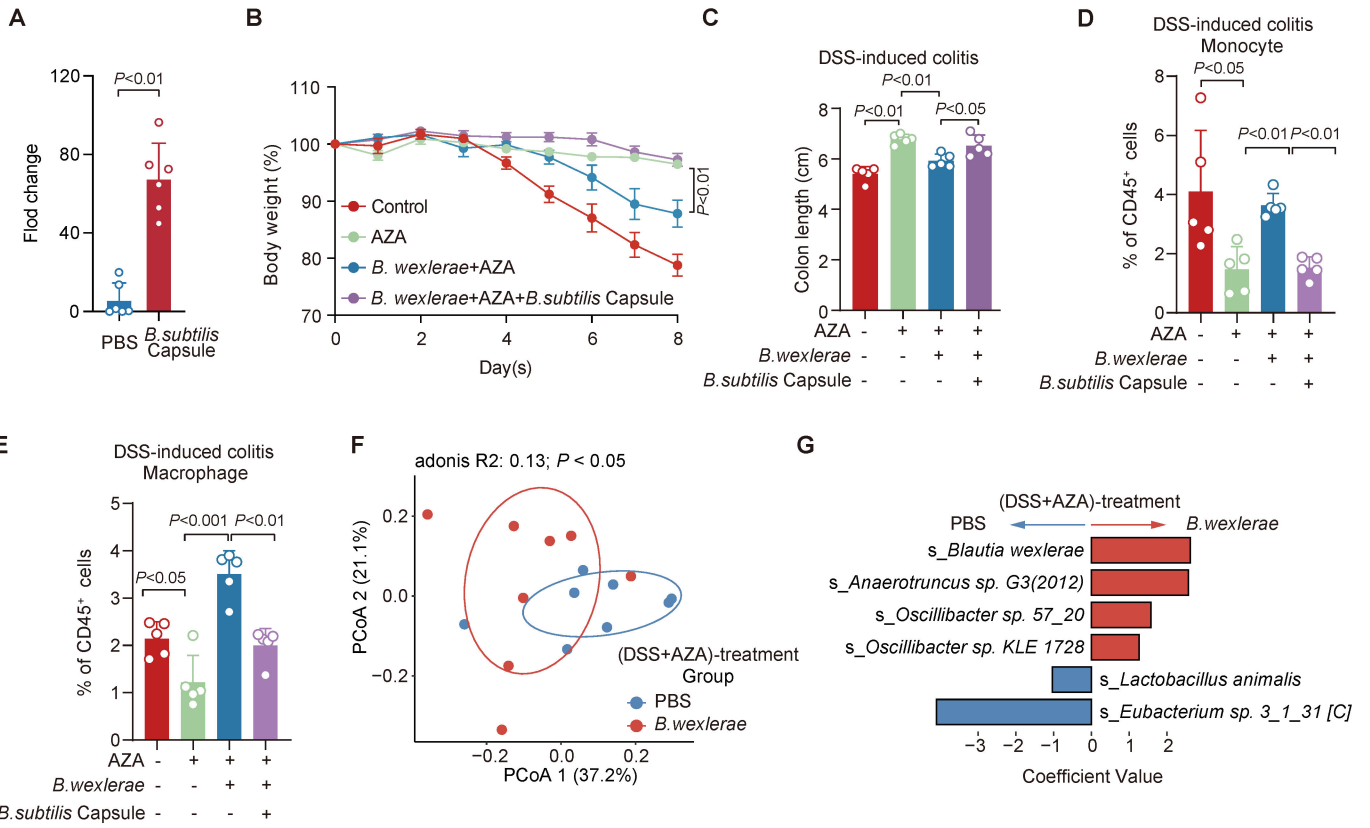
(**D**) The relative activity of XDH and HPRT1 for AZA metabolism in mice intestinal tissue. XDH (left). HPRT (right), n=6/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**E**) HPRT1 activity in the medium exposed to fecal samples under anaerobic condition, n=3/group, Student's T Test. Data are represented as mean ± SD.

(**F**) Quantitative level of 6-TX in bacterial supernatant under different treatment, n=3/group, Student's T Test. Data are represented as mean ± SD.

(**G**) The analysis of the DNA sequence data of *B.wexlerae* on NCBI Web site.

Supplementary Figure 6

Figure S6. *Bacillus Subtilis* **supplementation reversed** *B.wexlerae*-**induced AZA therapeutic failure in intestinal colitis mouse model. Related to Figure 6.**

(**A**) The relative abundance of *B. subtilis* in feces of *B.subtilis*-gavaged mice, n=5/group, nonparametric Wilcoxon rank-sum test. Data are represented as mean ± SD.

(**B**) The alterations in mouse body weight in different mice, n=5/group, Student's T Test. Data are represented as mean ± SEM.

(**C**) The length of the colon in C57BL/6 mice in different mice, n=5/group, Student's T Test. Data are represented as mean ± SD.

(**D and E**) The flow cytometry analysis of monocytes (**D**) and macrophage (**E**) was performed in DSS-induced colitis groups, n=5/group, Student's T Test.

(**F**) PCoA analysis showed that the overall fecal microbiota composition was different between PBS and *B. wexlerae* groups (n=8/group, *P* <0.05).

(**G**) Analysis of *B. wexlerae*-modulated gut bacteria at specie level in (DSS+AZA)-treated mice by Maaslin2 program, n=8/group.

Characteristics	Remission (n=27)		Non-Remission (n=22)		P
	CD (n=21)	UC (n=6)	CD (n=19)	UC (n=3)	
Demographis					
Gender, Male, n(%)	14 (66.67%)	4 (66.67%)	11 (57.89%)	2 (66.67%)	0.803
Age, years, median(min-max)	28.00 [22.00, 35.00]	44.00 [37.00, 54.00]	26.00 [18.50, 34.00]	24.00 [20.50, 29.00]	0.101
BMI, kg/m^2 ,median(min-max)	18.43 [17.50, 21.88]	21.70 [20.88, 22.45]	21.07 [19.08, 23.82]	17.19 [16.38, 19.32]	0.473
Disease activity, median(min-max)					
Duration of symptoms, months	2 (1-8)	3 (1-5)	3 (1-10)	2 (1-2)	0.285
CRP, mg/L	13.50 [9.10, 25.40]	8.45 [3.72, 12.65]	19.20 [5.45, 42.10]	5.50 [2.95, 34.70]	0.733
ESR, mm/h	34.00 [17.00, 44.00]	17.50 [16.00, 37.00]	33.00 [15.00, 44.00]	14.00 [8.00, 30.50]	0.748
Hb, g/L	123.00 [108.00, 132.00]	120.50 [109.75, 126.00]	113.00 [103.50, 129.00]	91.00 [83.00, 110.00]	0.087
CDAI	274.39 (183.4-356.64)		288.91 (224.79-353.02)		0.364
Mayo score		8 (4-9)		6 (6-8)	0.972
Disease characteristics					
Montreal L					0.060
L1 ileal, n (%)	9 (42.86%)		7 (36.84%)		
L2 colonic, n (%)	4 (19.05%)		5(15.79%)		
L3 ileocolonic, n (%)	8 (38.10%)		7 (47.36%)		
L4 isolated upper disease, n (%)	0 (0.00%)		0 (0.00%)		
Montreal B					0.577
B1 non-stricturing, non-penetrating, n (%)	15 (71.43%)		12 (63.16%)		
B2 stricturing, n (%)	6 (28.57%)		7 (36.84%)		
B3 penetrating, n (%)	0 (0.00%)		0 (0.00%)		
Montreal B perianal, n (%)					0.894
None	18 (85.71%)		16 (84.21%)		
Perianal disease	3 (14.29%)		3 (15.79%)		
Montreal E					0.487
E1 proctitis, n (%)		3 (50.00%)		2 (66.67%)	
E2 left sided colitis, n (%)		2 (33.33%)		0 (0.00%)	
E3 pancolitis, n (%)		1 (16.67%)		1 (33.33%)	

Table S1. Related to Figure 1. Demographic characteristics of Cohort 1.

Patients	Age (years)	Gender	BMI (kg/m^2)	CRP (mg/L)	ESR (mm/h)	HB (g/L)
1	27	Male	23.37	1.61	6	139
2	55	Male	24.77	3.32	36	137
3	50	Male	19.95	12.6	14	120
4	37	Female	19.81	164	97	91
5	15	Female	20.07	20.92	69	100
6	58	Female	22.49	0.59	14	128
7	27	Male	20.07	41.4	33	132
8	45	Male	22.49	0.58	9	157
9	24	Male	15.94	0.5	29	84
10	30	Female	15.15	7.26	48	116
11	19	Female	28.80	1.69	11	101
12	16	Male	20.57	70.9	65	138
13	38	Male	17.30	4.1	60	118
14	43	Female	24.97	2.13	38	103
15	19	Male	15.92	5.31	8	139
16	21	Female	20.39	22.97	49	117
17	21	Male	19.38	0.81	4	154
18	32	Female	19.92	0.5	36	124
19	28	Female	15.06	10.5	29	92
20	20	Female	16.00	0.5	7	119
21	26	Male	19.59	0.5	6	140
22	58	Female	24.52	1.82	19	123
23	62	Male	24.22	1.75	7	153
24	21	Male	21.97	23.5	32	135
25	40	Male	22.60	22.1	40	85
26	22	Male	32.87	5.85	19	161
27	43	Female	21.80	37.44	67	74
28	36	Male	19.59	0.5	18	124
29	26	Male	18.78	0.75	14	150
30	18	Male	18.04	67.87	2	157
31	17	Male	20.76	0.5	5	134
32	50	Female	23.88	5	4	124
33	13	Female	15.40	17.8	20	106
34	35	Male	18.96	15.03	16	106
35	33	Female	24.22	16.49	67	110
36	40	Male	23.15	2.77	6	172
37	19	Male	19.69	0.5	4	154
38	17	Male	23.15	5.13	17	150
39	36	Male	22.15	23.31	13	136
40	37	Male	21.51	18.3	12	142
41	22	Female	15.22	0.5	4	132
42	23	Female	20.08	0.26	5	121
43	49	Male	23.09	0.63	5	142
44	57	Female	19.81	81.6	56	84
45	50	Female	17.50	9.27	11	120
46	19	Female	15.24	2.25	6	133
47	18	Female	18.07	0.15	13	97

48	37	Male	18.94	4.48	10	123
49	37	Male	19.82	2.65	32	107
50	21	Male	22.72	9.54	67	121
51	22	Male	16.98	3.05	20	145
52	25	Male	19.27	0.64	7	138
53	23	Female	16.61	2.32	25	107
54	34	Female	17.07	0.19	13	115
55	29	Male	19.05	11.2	12	127
56	45	Female	20.20	0.54	13	121
57	30	Male	17.16	5	2	141
58	37	Male	18.29	0.31	9	122
59	27	Female	24.09	3.31	2	129
60	54	Male	19.72	60.6	64	95
61	25	Male	16.53	0.78	19	107
62	22	Female	21.23	0.5	10	107
63	27	Male	18.93	5.47	5	144
64	58	Female	17.19	28.2	64	81
65	68	Female	20.40	2.25	30	134
66	22	Female	22.94	0.5	23	142
67	19	Male	26.83	2.5	2	144
68	18	Male	19.47	9.59	29	125
69	30	Male	19.49	11.9	16	132
70	20	Male	23.38	12.2	34	134
71	29	Male	24.00	107.1	66	103
72	20	Male	27.47	10.5	16	142
73	22	Female	16.53	4.7	17	106
74	31	Male	21.86	10.2	10	119
75	30	Male	26.42	4.5	12	156
76	45	Female	20.81	2.3	19	127
77	26	Male	18.72	1.4	16	141
78	24	Male	26.83	0.5	7	167
79	25	Male	23.18	0.1	2	142
80	58	Female	15.81	14.5	51	93
81	17	Female	16.97	0.1	4	137
82	18	Female	19.29	117.4	74	109
83	30	Male	19.49	15.6	16	136
84	25	Female	17.65	17.1	34	106
85	61	Male	23.51	3.9	16	127
86	32	Male	16.33	1.7	34	123
87	36	Male	24.51	1.3	6	117
88	57	Male	25.16	22.9	34	96
89	33	Male	23.38	2.7	23	129
90	23	Male	20.09	7.7	6	134
91	16	Male	19.76	22.3	32	112

Table S2. Related to Figure 2. Clinical information on Cohort 2.

B. Wexlerae/luti abundance	Sensitivity	Specificity	YoudenIndex
Inf	1	0	1
-4.252529463	1	0.03125	1.03125
-4.581509591	0.983050847	0.03125	1.014300847
-5.537878037	0.983050847	0.0625	1.045550847
-6.489592552	0.983050847	0.09375	1.076800847
-6.689202945	0.983050847	0.125	1.108050847
-6.792258899	0.983050847	0.15625	1.139300847
-6.895759901	0.983050847	0.1875	1.170550847
-6.950245222	0.966101695	0.1875	1.153601695
-7.128705979	0.966101695	0.21875	1.184851695
-7.294996103	0.966101695	0.25	1.216101695
-7.444566886	0.966101695	0.28125	1.247351695
-7.624618531	0.949152542	0.28125	1.230402542
-7.730538051	0.949152542	0.3125	1.261652542
-7.920929591	0.949152542	0.34375	1.292902542
-8.232744058	0.93220339	0.34375	1.27595339
-8.48333184	0.915254237	0.34375	1.259004237
-8.57785225	0.915254237	0.375	1.290254237
-8.719418526	0.915254237	0.40625	1.321504237
-8.884890239	0.898305085	0.40625	1.304555085
-8.928016981	0.881355932	0.40625	1.287605932
-9.073852539	0.881355932	0.4375	1.318855932
-9.224819819	0.86440678	0.4375	1.30190678
-9.255772591	0.847457627	0.4375	1.284957627
-9.300165812	0.847457627	0.46875	1.316207627
-9.414551417	0.847457627	0.5	1.347457627
-9.495992979	0.830508475	0.5	1.330508475
-9.617959659	0.813559322	0.5	1.313559322
-9.75630951	0.813559322	0.53125	1.344809322
-9.875935237	0.796610169	0.53125	1.327860169
-10.0481027	0.779661017	0.53125	1.310911017
-10.16509756	0.762711864	0.53125	1.293961864
-10.25254282	0.745762712	0.53125	1.277012712
-10.31744608	0.728813559	0.53125	1.260063559
-10.36336073	0.728813559	0.5625	1.291313559
-10.4015983	0.728813559	0.59375	1.322563559
-10.43828297	0.728813559	0.625	1.353813559
-10.48003419	0.711864407	0.625	1.336864407
-10.52584156	0.711864407	0.65625	1.368114407
-10.57453839	0.711864407	0.6875	1.399364407
-10.65204525	0.711864407	0.71875	1.430614407
-10.70736838	0.711864407	0.75	1.461864407
-10.71593968	0.694915254	0.75	1.444915254
-10.7439766	0.677966102	0.75	1.427966102
-10.78282611	0.677966102	0.78125	1.459216102
-10.86388143	0.661016949	0.78125	1.442266949
-10.94763867	0.644067797	0.78125	1.425317797
-11.01126019	0.627118644	0.78125	1.408368644
-11.05666669	0.610169492	0.78125	1.391419492
-11.1333774	0.593220339	0.78125	1.374470339
-11.23575338	0.576271186	0.78125	1.357521186
-11.27570375	0.576271186	0.8125	1.388771186

-11.30812264	0.559322034	0.8125	1.371822034
-11.35244719	0.559322034	0.84375	1.403072034
-11.47450034	0.542372881	0.84375	1.386122881
-11.62899621	0.542372881	0.875	1.417372881
-11.81309764	0.525423729	0.875	1.400423729
-11.96199799	0.508474576	0.875	1.383474576
-12.03289175	0.491525424	0.875	1.366525424
-12.11214876	0.474576271	0.875	1.349576271
-12.15377712	0.474576271	0.90625	1.380826271
-12.28552612	0.474576271	0.9375	1.412076271
-12.43162982	0.457627119	0.9375	1.395127119
-12.54346991	0.440677966	0.9375	1.378177966
-12.64722888	0.423728814	0.9375	1.361228814
-12.6719478	0.406779661	0.9375	1.344279661
-12.83525419	0.389830508	0.9375	1.327330508
-13.11038256	0.372881356	0.9375	1.310381356
-13.31171529	0.355932203	0.9375	1.293432203
-13.53095945	0.338983051	0.9375	1.276483051
-13.71156232	0.338983051	0.96875	1.307733051
-13.83276622	0.322033898	0.96875	1.290783898
-14.0099659	0.305084746	0.96875	1.273834746
-14.14986452	0.288135593	0.96875	1.256885593
-14.236794	0.271186441	0.96875	1.239936441
-14.29691951	0.254237288	0.96875	1.222987288
-14.503613	0.237288136	0.96875	1.206038136
-14.74765524	0.220338983	0.96875	1.189088983
-14.85139498	0.203389831	0.96875	1.172139831
-14.97098176	0.186440678	0.96875	1.155190678
-15.16064946	0.169491525	0.96875	1.138241525
-15.53315783	0.152542373	0.96875	1.121292373
-15.80603775	0.13559322	0.96875	1.10434322
-15.98606396	0.118644068	0.96875	1.087394068
-16.17940013	0.101694915	0.96875	1.070444915
-16.4491094	0.101694915	1	1.101694915
-16.79678091	0.084745763	1	1.084745763
-17.02734725	0.06779661	1	1.06779661
-17.17600854	0.050847458	1	1.050847458
-17.7639548	0.033898305	1	1.033898305
-18.96923224	0.016949153	1	1.016949153

Youden Index was used to determine the optimal cut-off point. The best cut-off that maximizes the sensitivity plus the specificity is -10.71. The patients with a higher amount of *B. wexlerae/luti* (-delta CT > - 10.71) are more likely to present inflammation progression in AZA administration.

Table S3. Related to Figure 2. The sensitivity and specificity of individual *B. wexlerae/luti* abundance.

Patient	Gender	Age	Group
Patient 1	Male	17	R
Patient 2	Male	14	R
Patient 3	Male	28	R
Patient 4	Male	20	R
Patient 5	Male	27	NR
Patient 6	Female	27	NR
Patient 7	Female	68	NR

Table S4. Related to Figure 4. Overview of patient charateristics in Cohort 3.

Cohort	Source	Patients	Sample	Management
Cohort 1	Renji hospital	49 IBD patients	Feces	16s rDNA sequencing
		47 IBD patients	Illeum tissue	qPCR detection
Cohort 2	Renji hospital	91 IBD patients	Colonoscopy paraffin-embedded mucosa	qPCR detection
Cohort 3	Renji hospital	7 IBD patients	Mucosa tissue	Single-cell RNA sequencing

Table S5. Related to STAR★METHODS. Summary table of Cohort 1~3.

Gene	Forward primer	Reverse primer
Blautia wexlerae/Blautia luti	GCATAAGCGCACAGAGCT	CACATCAGACTTGCCACA
Blautia wexlerae	GCCAAAAGAGAAACAAGTCAGAGAA	GACGCAAATACATCACGAAGGAATA
Blautia luti	CATAGCGTGTCCAGTTCCGAAAG	GACCATTTTTGCAAGCTGGTACTGT
16s	GGTGAATACGTTCCCGG	TACGGCTACCTTGTTACGACTT
Mouse β-actin	AGCACTGTGTTGGCATAGAGGTC	CTTCTTGGGTATGGAATCCTGTG
Mouse Tnf-α	CATCTTCTCAAAATTCGAGTGACAA	TGGGAGTAGACAAGGTACAACCC
Mouse Ifn-γ	AGCTCTTCCTCATGGCTGTTTC	ATGTTGTTGCTGATGGCCTGA
Mouse Il-1b	CAACCAACAAGTGATATTCTCCATG	GATCCACACTCTCCAGCTGCA
Mouse Il-17	CTCCAGAAGGCCCTCAGACTAC	AGCTTTCCCTCCGCATTGACACAG
Mouse Il-6	TCTATACCACTTCACAAGTCGGA	GAATTGCCATTGCACAACTCTTT
Mouse Cd4	CTCCTTCGGCTTTCTGGGTTTCC	GCACTGGCAGGTCTTCTTCTCAC
Mouse Cd8a	CTGTCGCTGAACCTGCTGCTG	TCGGAGTTCGGGTGCCTGTG
Mouse Ptprc	GTTATCCACGCTGCTGCCTCAC	TTGGCTGCTGAATGTCTGAGTGTC
Mouse Cd19	CCATCTCCTCTCCCTGTCTCCTTC	ATTGCCTCCCTCTTCTACCTCCAC
Mouse Sdc1	CTTTGTCACGGCAGACACCTT	GACAGAGGTAAAAGCAGTCTCG
Mouse Tnfrsf17	ACCGTGTCACTTGCGATGTTCC	TGTCGTCACCAGCCCTGATCC
Mouse Ly6c	GCCGCGCCTCTGATGGATTC	ACACCAGCAGGGCAGAAAGAAAG
Mouse Ly6g	CCACCTGAGACTTCCTGCAACAC	GGCAGATGGGAAGGCAGAGATTG
Mouse Itgax	GAGCCCATCTCCCTCCAGGTG	CACAGTAGGACCACAAGCCAACAG
Mouse Ncam1	CACCGTCTTCTCCATCCATTGACC	CAGCGACTTCCACTCAGCCTTG
Mouse Itga2	CTCCTGCTGCGGCTGCTAATG	AGTTGCCTTGTGGGTTCGTAAGC
pycA	GTCTTCCGTTCAGGAAAGGC	GATCTCCCGTTTGGATCGGCTC

Table S6. Related to STAR★METHODS. The sequences of primers used in this study.