Expanded View Figures

Figure EV1. *Dectin-3*$^{-/-}$ mice have increased tumor burden and impaired immune responses upon AOM-DSS treatment than WT mice. Related to Fig 1.

Mice were treated as described in Fig 1A.

A Clinical colitis scores were evaluated on day 56.
B Tumor tissues were stained for cleaved-caspase 3. The percentages of positive cells were quantified.
C, D Colonic LP cells and mLNs were isolated from each mouse. The proportion of immune cells was determined by flow cytometry.
E, F Relative expression of *Il-6*, *Il-22*, *Cxcl1*, *TNF-α* and *Il-17* in mLNs cells and tumors from tumor-bearing WT and *Dectin-3*$^{-/-}$ mice were detected using qPCR.
G Cytokine and chemokine production in the serum of WT and Dectin-3$^{-/-}$ tumor-bearing mice was determined by a multiple cytokine detection assay.

Data information: Data with error bars are represented as mean ± SD. Each panel is a representative experiment of at least three independent biological replicates.
*$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ as determined by unpaired Student's *t*-test.

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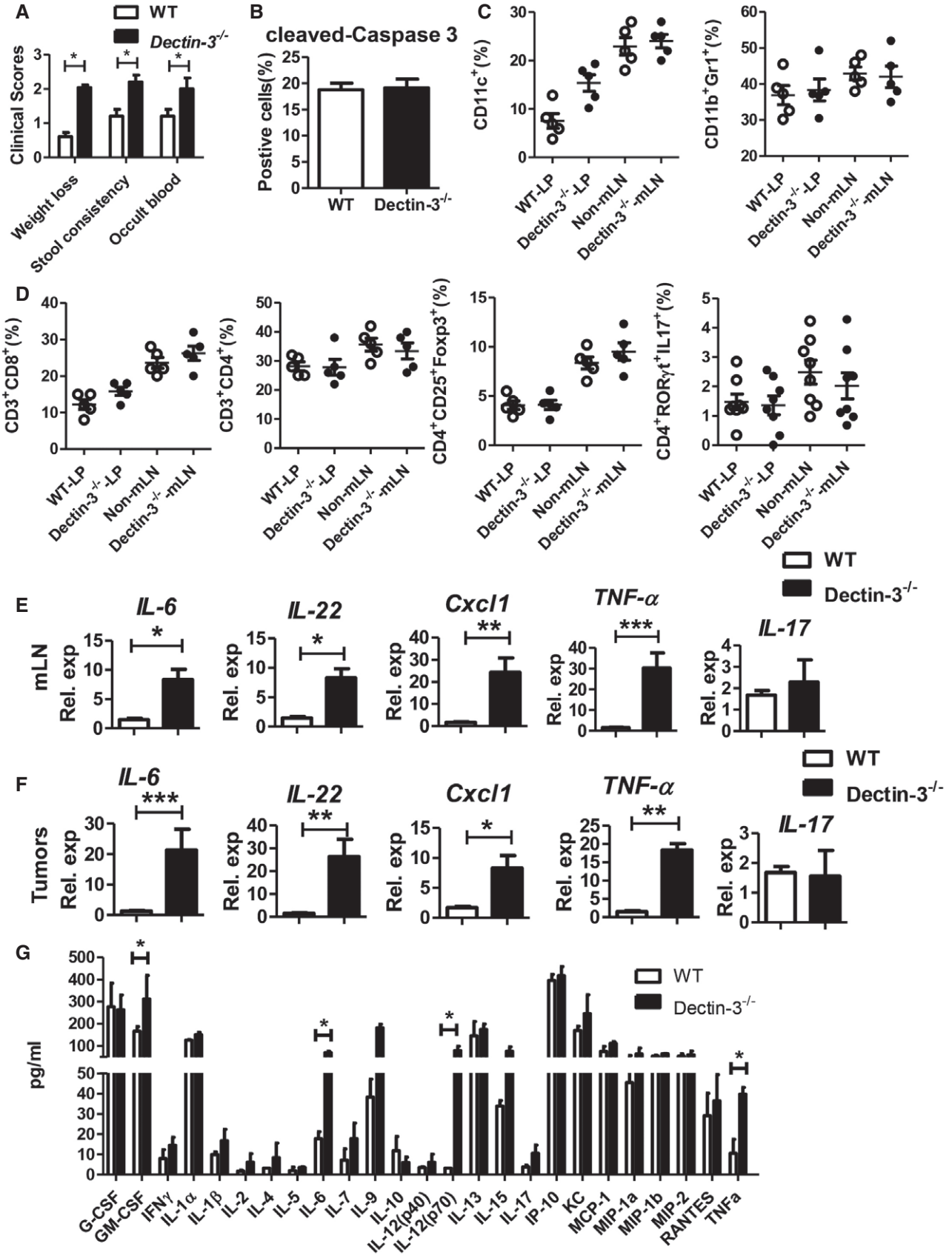

Figure EV1.

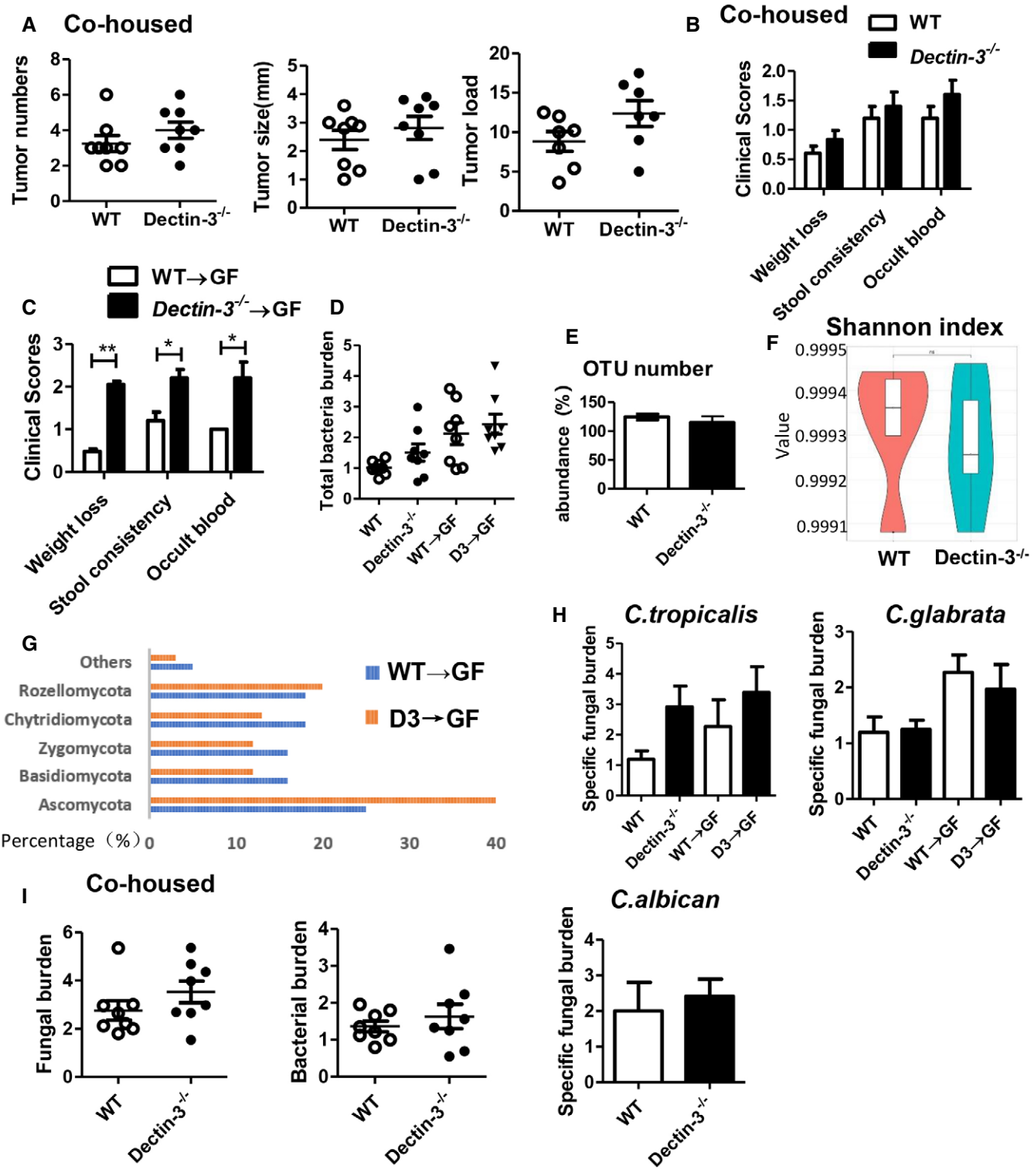
A
Co-housed
Tumor numbers
Tumor size(mm)
Tumor load
WT
Dectin-3-/-
B
Co-housed
WT
Dectin-3-/-
Clinical Scores
Weight loss
Stool consistency
Occult blood
C
WT→GF
Dectin-3-/-→GF
D
Total bacteria burden
E
OTU number
abundance (%)
F
Shannon index
Value
G
Others
Rozellomycota
Chytridiomycota
Zygomycota
Basidiomycota
Ascomycota
WT→GF
D3→GF
Percentage (%)
H
C.tropicalis
C.glabrata
Specific fungal burden
I
Co-housed
Fungal burden
Bacterial burden
C.albican

Figure EV2.

Figure EV2. Feces from tumor-bearing *Dectin-3*$^{-/-}$ mice promote CAC. Related to Fig 2.

A WT and *Dectin-3*$^{-/-}$ mice were co-housed for at least 4 weeks before and throughout the CAC experiments (n = 8, each group). After induction of tumorigenesis, mice were euthanized and colons were removed. Tumor number, tumor size, and tumor load in colons were measured.

B Mice were treated as described in Fig EV2A. Clinical colitis scores were evaluated on day 56.

C Mice were treated as described in Fig 2A. Clinical colitis scores were evaluated on day 56.

D Mice were treated as described in Figs 1A and 2A. Feces were collected from colons in each mouse. Total bacteria burden in feces were quantified using qPCR.

E Mice were treated as described in Fig 1A. Fungal ITS2 rDNA gene sequence was performed in each group. OTU numbers were counted.

F Shannon analysis related to alpha diversity was used. The central band presents the mean value. The box represents the 25th–75th percentile, and the whisker plots represent the minimum and maximum percentiles.

G Mice were treated as described in Fig 2A. Fungal ITS2 rDNA gene sequence was performed in each group. Fungal-taxon-based analysis at the phylum level in feces of mice.

H Specific fungal burden of *C. tropicalis and C. glabrata* in the feces were quantified using qPCR.

I Mice were treated as described in Fig EV2A. Total fungal burden, bacteria burden, and specific burden of *C. albicans* in feces were quantified using qPCR.

Data information: Data with error bars are represented as mean ± SD. Each panel is a representative experiment of at least three independent biological replicates.
*P < 0.05, **P < 0.01 as determined by unpaired Student's t-test.

Figure EV3. Up-regulation of IL-22 in *Dectin-3*$^{-/-}$ mice contributes to CAC development. Related to Fig 3.

A GF mice were orally gavaged with *C. albicans* (twice a week, 1 × 10^7) during administration with AOM-DSS (n = 8, each group). After induction of tumorigenesis (100 days), mice were euthanized and colons were removed. Tumor number, tumor size, and tumor load in colons were measured. Total fungal burden of colon was detected by using qPCR. Clinical colitis scores were evaluated on day 56.

B WT and *Dectin-3*$^{-/-}$ mice were treated with fluconazole during administrated with AOM-DSS (n = 8, each group). Tumor number, tumor size, and tumor load in colons were measured. Total fungal burden of colon was detected by using qPCR.

C WT and *Dectin-3*$^{-/-}$ mice were treated with antibiotics during administrated with AOM-DSS (n = 8, each group). Tumor number, tumor size, and tumor load in colons were measured. Total fungal burden of colon was detected by using qPCR.

D *Dectin-3*$^{-/-}$ mice were oral transferred with feces (400 ml each time, twice a week) from tumor-bearing WT mice during administrated with AOM-DSS (n = 8, each group). After induction of tumorigenesis, mice were euthanized and colons were removed. Tumor number, tumor size, and tumor load in colons were measured.

E, F Mice were treated as described in Fig EV3D. Fungal ITS2 rDNA gene sequence was performed in each group. Principal component analyses (PCA) based on fungal composition and Shannon analysis related to alpha diversity were used. F: samples are from Dectin-3$^{-/-}$ mice, P: samples are from Dectin-3$^{-/-}$ mice treated with WT feces.

G Fungal-taxon-based analysis at the genus level in feces of mice. 1 *Candidan* 2 *Fusarium* 3 *Kazachstania* 4 *Thermomyces* 5 *Phaeococcomyces* 6 *Mycosphaerella* 7 *Penicillium* 8 *Aspergillus* 9 *Coprinellus* 10 *Cryptococcus* 11 *Mortierella* 12 *Guehomyces* 13 *Preussia* 14 *Chaetomium*.

H ELISA results for binding assays of Dectin-3 with α-mannans. Plates were coated with α-mannans and then were added with 100 ml/well recombinant Dectin-3 at indicated concentrations.

Data information: Data with error bars are represented as mean ± SD. Each panel is a representative experiment of at least three independent biological replicates.
*P < 0.05, **P < 0.01, ***P < 0.001 as determined by Student's t-test.

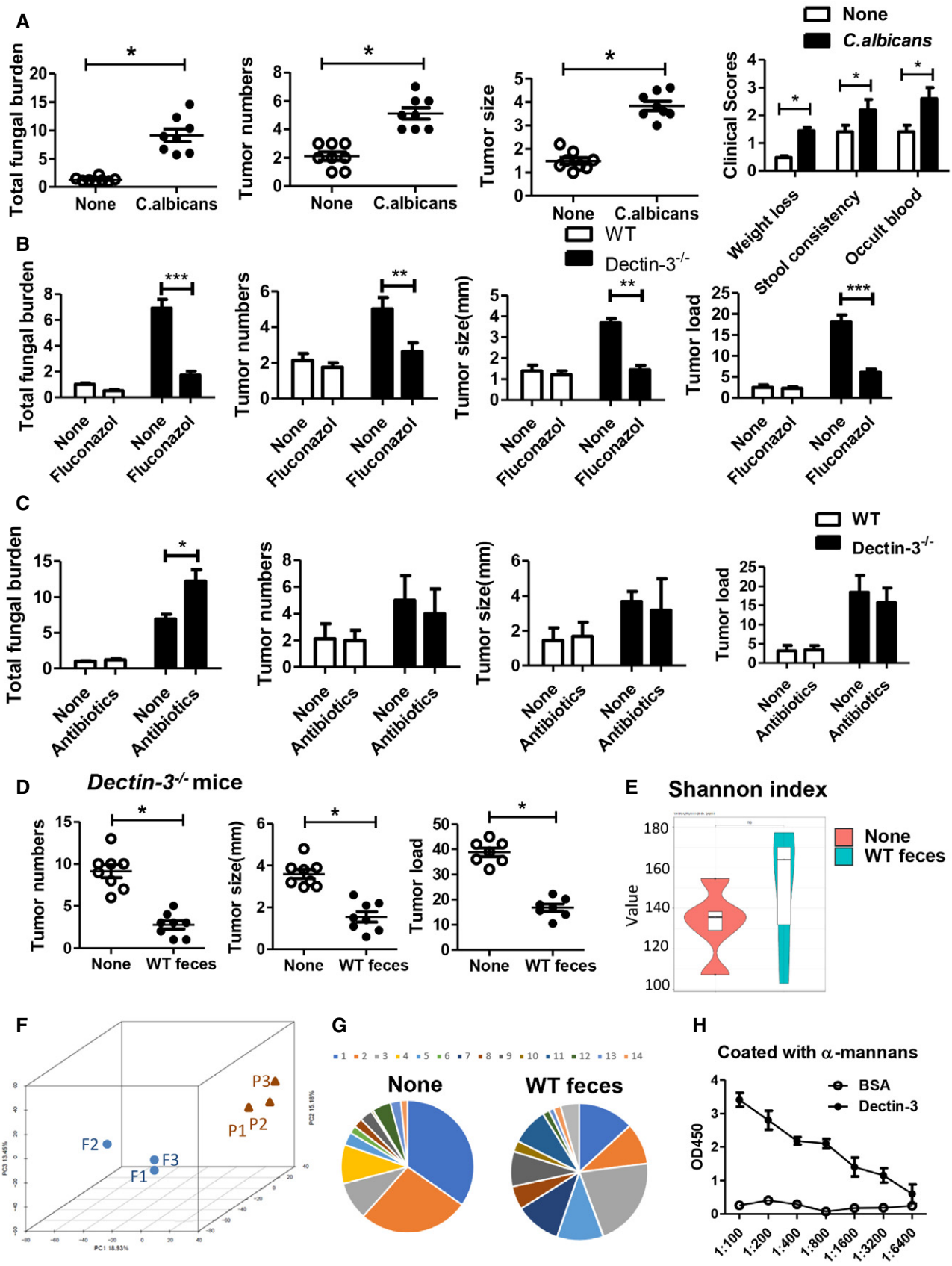
A
Total fungal burden
Tumor numbers
Tumor size
None
C.albicans
Clinical Scores
Weight loss
Stool consistency
Occult blood
B
WT
Dectin-3-/-
Total fungal burden
Tumor numbers
Tumor size(mm)
Tumor load
None
Fluconazol
C
Total fungal burden
Tumor numbers
Tumor size(mm)
Tumor load
None
Antibiotics
D
Dectin-3-/- mice
Tumor numbers
Tumor size(mm)
Tumor load
None
WT feces
E
Shannon index
Value
None
WT feces
F
P1
P2
P3
F1
F2
F3
G
None
WT feces
H
Coated with α-mannans
BSA
Dectin-3
OD450
1:100
1:200
1:400
1:800
1:1600
1:3200
1:6400

Figure EV3.

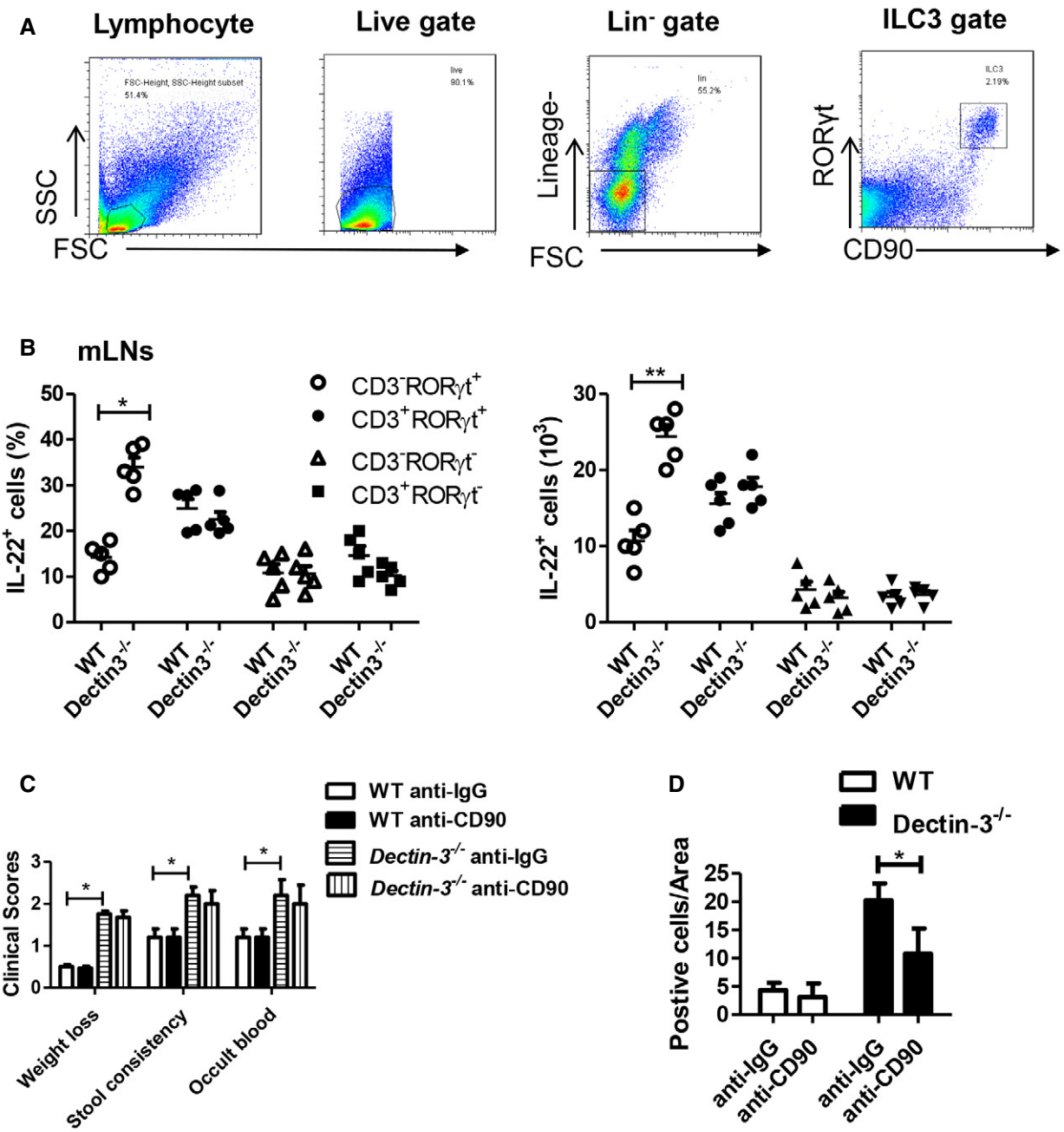

Figure EV4. IL-22 is mainly produced by RORγt$^+$ ILC3. Related to Fig 4.

A Gating strategy for ILC3. Live, Lin-, CD90hi lymphocytes expressing RORγt (ILC3) were gated to analyze ILC3 function.

B Mice were treated as described in Fig 1A. mLNs were isolated from each mouse. The proportions of IL-22$^+$ cells in CD3$^-$RORγt$^+$, CD3$^-$RORγt$^-$, CD3$^+$RORγt$^-$, and CD3$^+$RORγt$^+$ and the absolute number of IL-22$^+$ cells were determined by flow cytometry.

C, D Mice were treated as described in Fig 4E. Clinical colitis scores were evaluated on day 56. Colon tissues were stained for p-STAT3. The percentage of p-STAT3-positive tumor cells was quantified.

Data information: Data with error bars are represented as mean ± SD. Each panel is a representative experiment of at least three independent biological replicates. *$P < 0.05$, **$P < 0.01$ as determined by Student's t-test.

Figure EV5. *Candida albicans* induce glycolysis and IL-7 production in macrophages. Related to Fig 5.

A Mice were treated as described in Fig 2A. Primary macrophage were isolated from LP in WT and *Dectin-3*$^{-/-}$ tumor-bearing mice. mRNA expression of glycolysis-relative genes was detected by using qPCR.

B–F BMDMs were acquired from WT and *HIF-1*$^{-/-}$ mice and were stimulated with *C. albicans* for 24 h. Glucose uptake, pyruvate level, lactate production, and ATP level were determined using assay kit. ECAR and OCR were also examined. mRNA expression of glycolysis-relative genes was detected by using qPCR.

G Primary macrophage were isolated from LP tissues in indicated mice. mRNA expressions of *IL-7* and *TNF-α* were detected by qPCR.

H WT-derived BMDMs were stimulated with *C. albicans*, curdlan, or α-mannan in combination with or without 2-DG (2.5 mM) for 24 h. mRNA expression of *TNF-α* was detected by using qPCR.

Data information: Data with error bars are represented as mean ± SD. Each panel is a representative experiment of at least three independent biological replicates. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ as determined by Student's *t*-test.

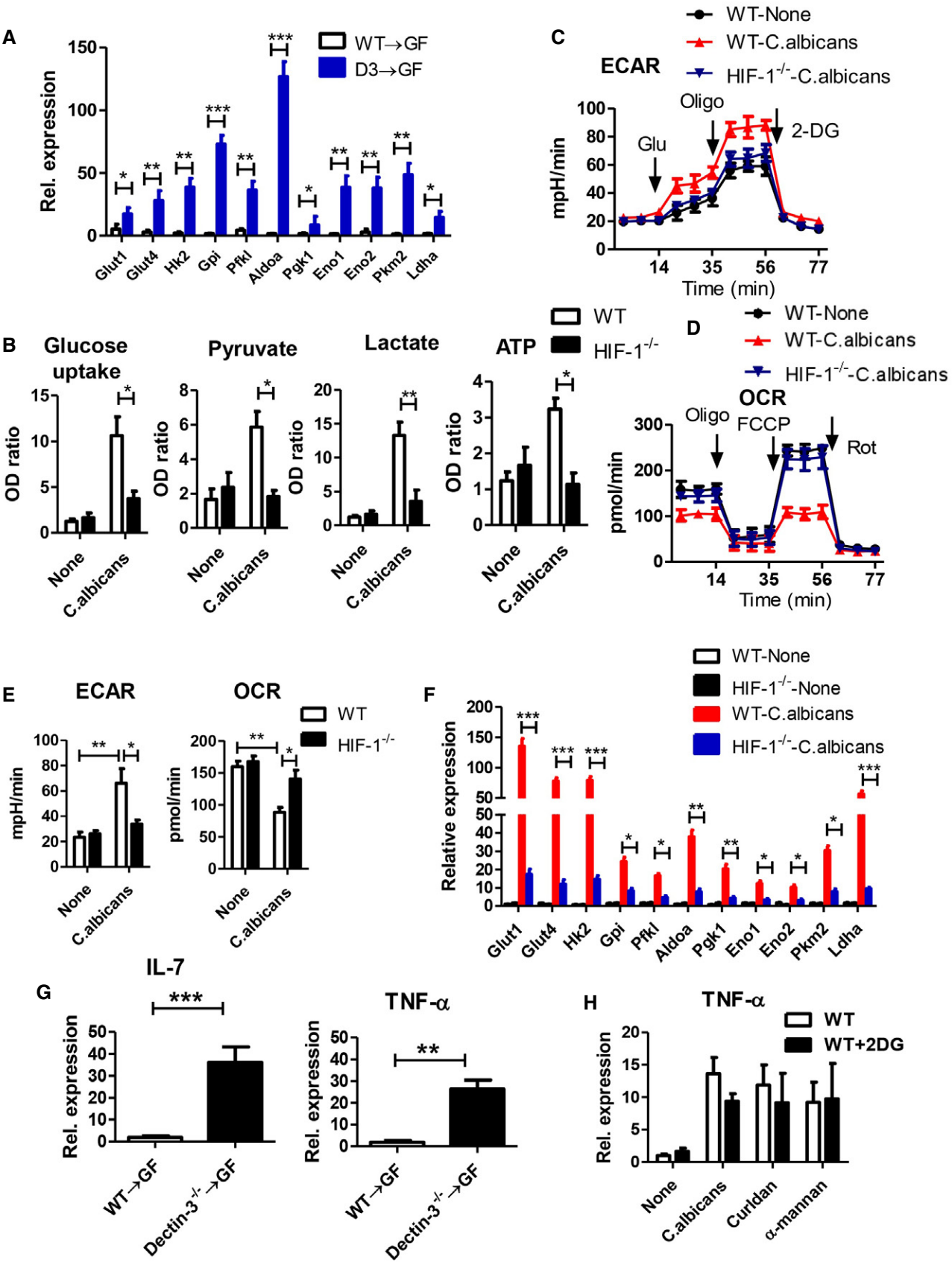

Figure EV5.