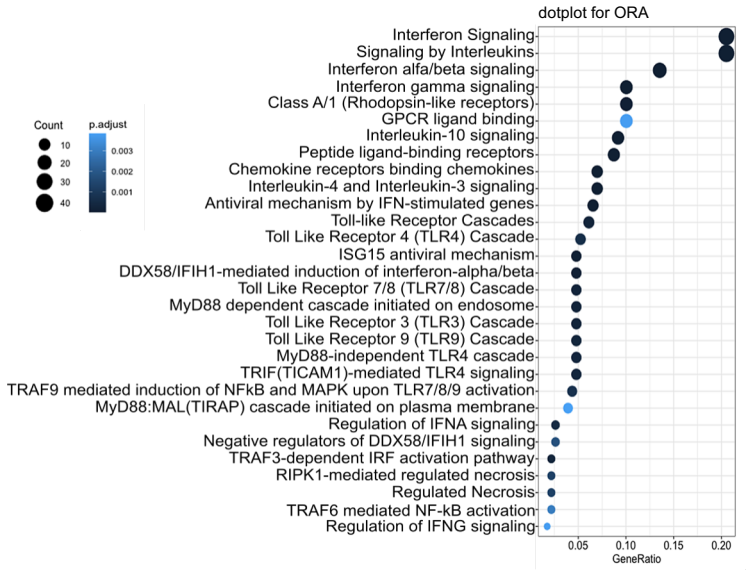
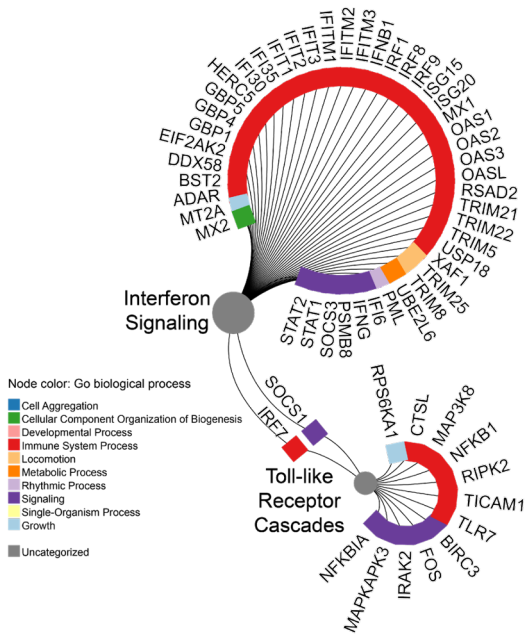
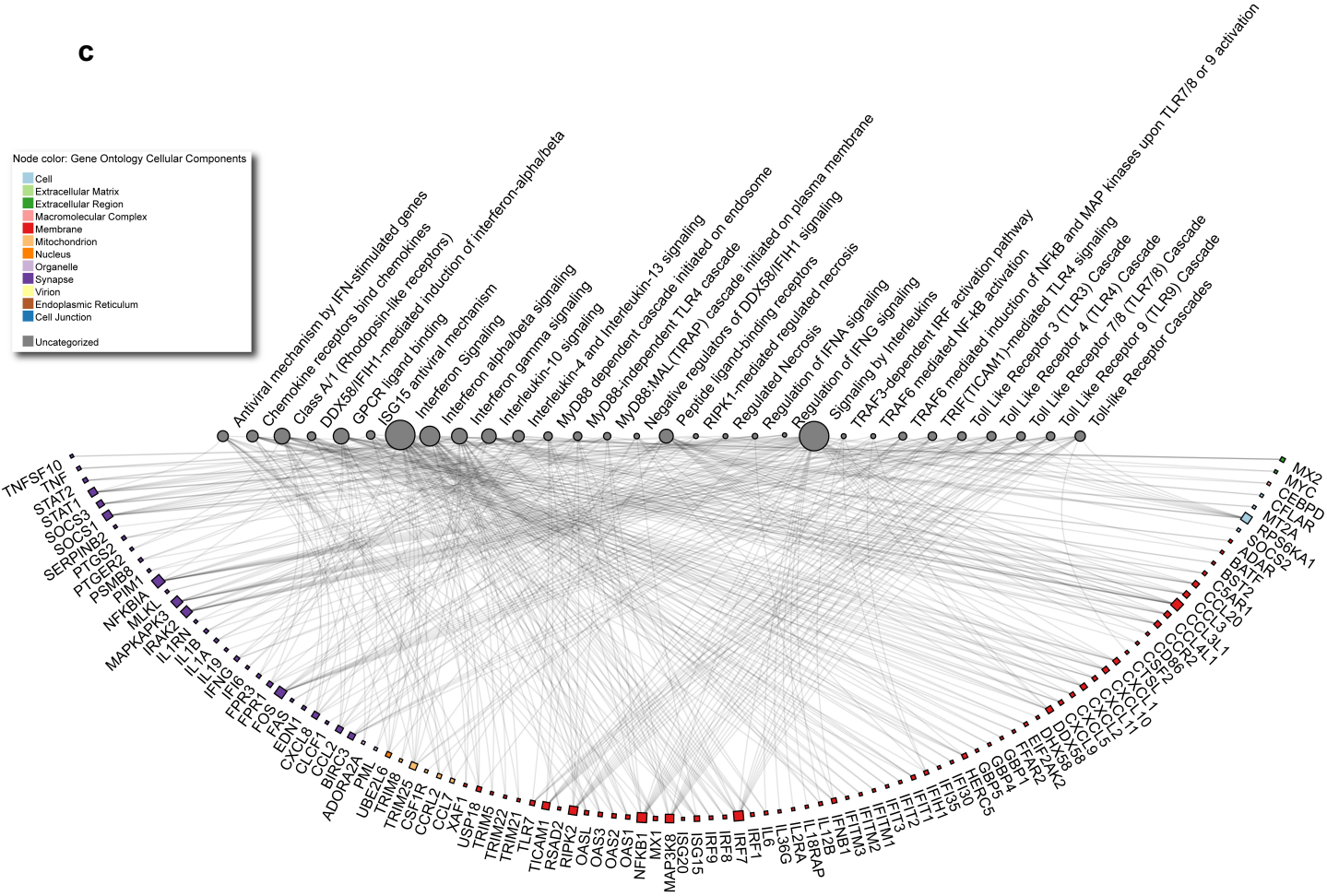
a


dotplot for ORA
Count
10
20
30
40
p.adjust
0.003
0.002
0.001
Interferon Signaling
Signaling by Interleukins
Interferon alfa/beta signaling
Interferon gamma signaling
Class A/1 (Rhodopsin-like receptors)
GPCR ligand binding
Interleukin-10 signaling
Peptide ligand-binding receptors
Chemokine receptors binding chemokines
Interleukin-4 and Interleukin-13 signaling
Antiviral mechanism by IFN-stimulated genes
Toll-like Receptor Cascades
Toll Like Receptor 4 (TLR4) Cascade
ISG15 antiviral mechanism
DDX58/IFIH1-mediated induction of interferon-alpha/beta
Toll Like Receptor 7/8 (TLR7/8) Cascade
MyD88 dependent cascade initiated on endosome
Toll Like Receptor 3 (TLR3) Cascade
Toll Like Receptor 9 (TLR9) Cascade
MyD88-independent TLR4 cascade
TRIF(TICAM1)-mediated TLR4 signaling
TRAF9 mediated induction of NFkB and MAPK upon TLR7/8/9 activation
MyD88:MAL(TIRAP) cascade initiated on plasma membrane
Regulation of IFNA signaling
Negative regulators of DDX58/IFIH1 signaling
TRAF3-dependent IRF activation pathway
RIPK1-mediated regulated necrosis
Regulated Necrosis
TRAF6 mediated NF-kB activation
Regulation of IFNG signaling
0.05
0.10
0.15
0.20
GeneRatio

b

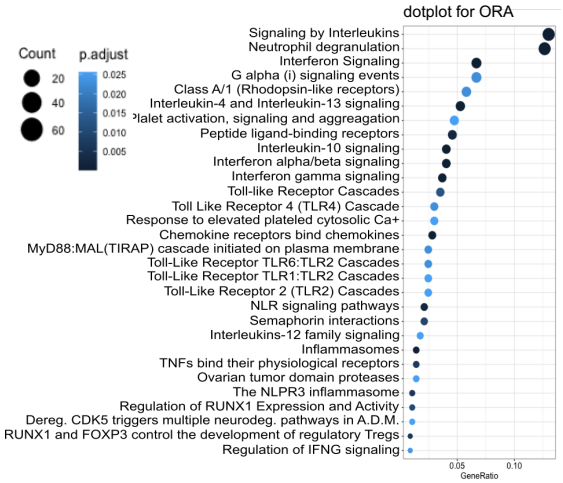

Interferon Signaling
Toll-like Receptor Cascades
Node color: Go biological process
Cell Aggregation
Cellular Component Organization of Biogenesis
Developmental Process
Immune System Process
Locomotion
Metabolic Process
Rhythmic Process
Signaling
Single-Organism Process
Growth
Uncategorized

c

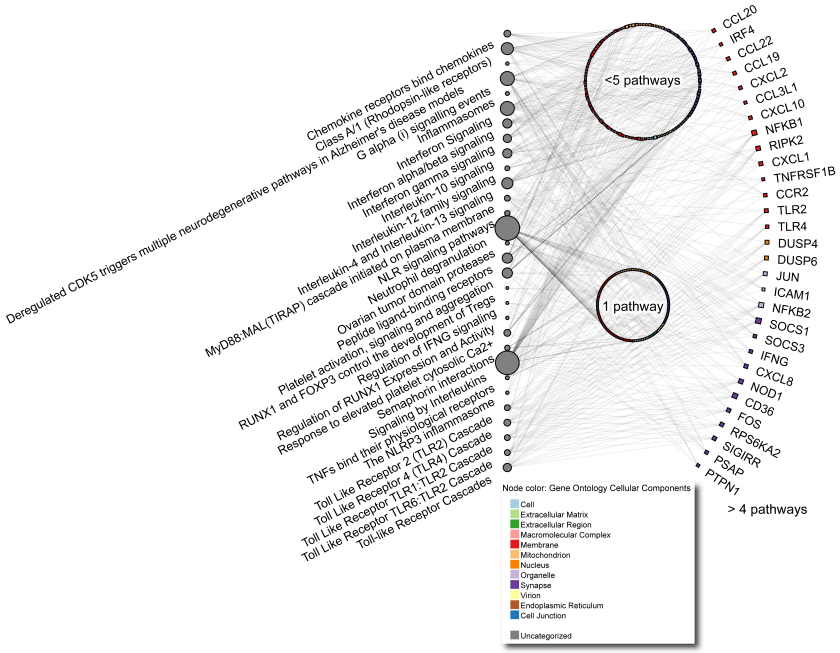

Node color: Gene Ontology Cellular Components
Cell
Extracellular Matrix
Extracellular Region
Macromolecular Complex
Membrane
Mitochondrion
Nucleus
Organelle
Synapse
Virion
Endoplasmic Reticulum
Cell Junction
Uncategorized
Antiviral mechanism by IFN-stimulated genes
Chemokine receptors bind chemokines
Class A/1 (Rhodopsin-like receptors)
DDX58/IFIH1-mediated induction of interferon-alpha/beta
GPCR ligand binding
ISG15 antiviral mechanism
Interferon Signaling
Interferon alpha/beta signaling
Interferon gamma signaling
Interleukin-10 signaling
Interleukin-4 and Interleukin-13 signaling
MyD88 dependent cascade initiated on endosome
MyD88-independent TLR4 cascade
MyD88:MAL(TIRAP) cascade initiated on plasma membrane
Negative regulators of DDX58/IFIH1 signaling
Peptide ligand-binding receptors
RIPK1-mediated regulated necrosis
Regulated Necrosis
Regulation of IFNA signaling
Regulation of IFNG signaling
Signaling by Interleukins
TRAF3-dependent IRF activation pathway
TRAF6 mediated NF-kB activation
TRAF6 mediated induction of NFkB and MAP kinases upon TLR7/8 or 9 activation
TRIF(TICAM1)-mediated TLR4 signaling
Toll Like Receptor 3 (TLR3) Cascade
Toll Like Receptor 4 (TLR4) Cascade
Toll Like Receptor 7/8 (TLR7/8) Cascade
Toll Like Receptor 9 (TLR9) Cascade
Toll-like Receptor Cascades

Suppl. Fig. 1. Functional clustering of DEGs associates TLR and IFN signaling pathways. **a,** Dot plot showing the 30 most enriched signaling pathways obtained by ORA of DEGs (dataset GSE42606) using ClusterProfiler. Y-axis contains enriched pathways while the size of circles represents the number of genes (count) enriching each category and color (from blue to black) indicates how significant (when p-value < 0.05) enriched is the pathway. **b,** Network of TLR- and IFN-associated genes enriching signaling pathways showed in the dot plot (a). The network includes genes upregulated and downregulated (**Suppl. Table S4**) when comparing resting with *C. albicans*-infected PBMCs. The size of circles represents the number (counts) of genes that enrich the pathway, and colored squares represent the cell location of genes. **c,** Network demonstrating interactions between pathways and their associated genes revealed by ORA. Circular nodes represent pathways and the circle size is associated with the number of genes that enrich each pathway, while colored squares represent the cell location of genes. The interaction network was build using the NAViGaTOR software. *DEGs, Differentially Expressed Genes; IFN, Interferon; ORA, Over-representation Analysis; TLR, Toll-like Receptor.*

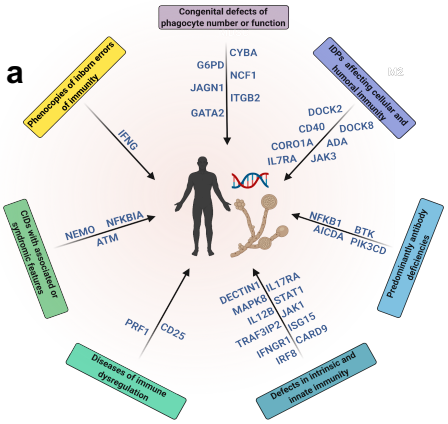
a

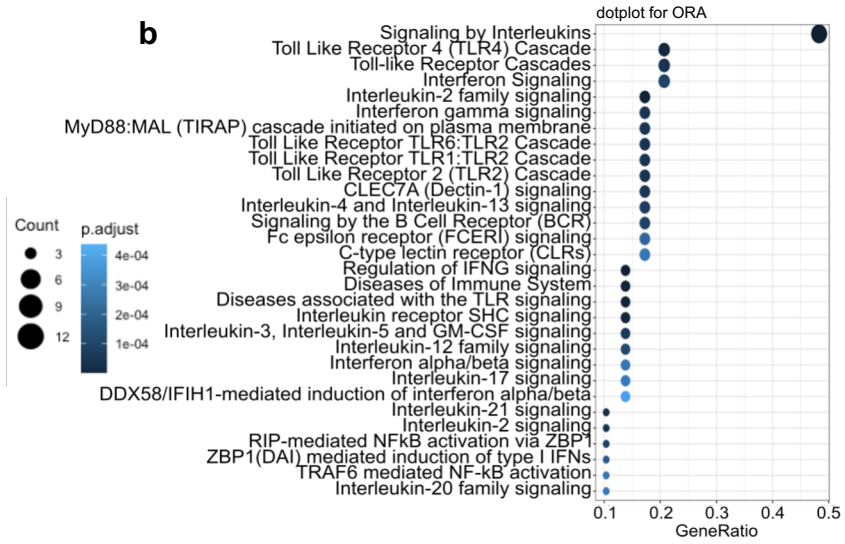

dotplot for ORA
Count
20
40
60
p.adjust
0.025
0.020
0.015
0.010
0.005
Signaling by Interleukins
Neutrophil degranulation
Interferon Signaling
G alpha (i) signaling events
Class A/1 (Rhodopsin-like receptors)
Interleukin-4 and Interleukin-13 signaling
Platelet activation, signaling and aggregation
Peptide ligand-binding receptors
Interleukin-10 signaling
Interferon alpha/beta signaling
Interferon gamma signaling
Toll-like Receptor Cascades
Toll Like Receptor 4 (TLR4) Cascade
Response to elevated plateled cytosolic Ca+
Chemokine receptors bind chemokines
MyD88:MAL(TIRAP) cascade initiated on plasma membrane
Toll-Like Receptor TLR6:TLR2 Cascades
Toll-Like Receptor TLR1:TLR2 Cascades
Toll-Like Receptor 2 (TLR2) Cascades
NLR signaling pathways
Semaphorin interactions
Interleukins-12 family signaling
Inflammasomes
TNFs bind their physiological receptors
Ovarian tumor domain proteases
The NLPR3 inflammasome
Regulation of RUNX1 Expression and Activity
Dereg. CDK5 triggers multiple neurodeg. pathways in A.D.M.
RUNX1 and FOXP3 control the development of regulatory Tregs
Regulation of IFNG signaling
0.05
0.10
GeneRatio

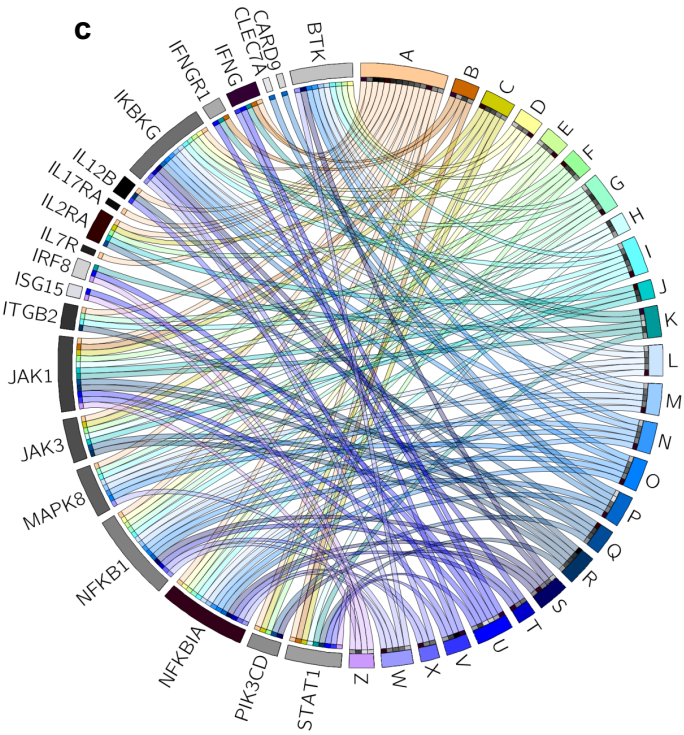
b


Chemokine receptors bind chemokines
Class A/1 (Rhodopsin-like receptors)
Deregulated CDK5 triggers multiple neurodegenerative pathways in Alzheimer's disease models
G alpha (i) signaling events
Inflammasomes
Interferon Signaling
Interferon alpha/beta signaling
Interferon gamma signaling
Interleukin-10 signaling
Interleukin-12 family signaling
Interleukin-13 signaling
Interleukin-4 and Interleukin-13 signaling
MyD88:MAL(TIRAP) cascade initiated on plasma membrane
NLR signaling pathways
Neutrophil degranulation
Ovarian tumor domain proteases
Peptide ligand-binding receptors
Platelet activation, signaling and aggregation
RUNX1 and FOXP3 control the development of Tregs
Regulation of RUNX1 Expression and Activity
Response to elevated platelet cytosolic Ca2+
Regulation of IFNG signaling
Semaphorin interactions
Signaling by Interleukins
TNFs bind their physiological receptors
The NLRP3 inflammasome
Toll Like Receptor 2 (TLR2) Cascade
Toll Like Receptor 4 (TLR4) Cascade
Toll Like Receptor TLR1:TLR2 Cascade
Toll Like Receptor TLR6:TLR2 Cascade
Toll-like Receptor Cascades
<5 pathways
1 pathway
> 4 pathways
CCL20
IRF4
CCL22
CCL19
CXCL2
CCL3L1
CXCL10
NFKB1
RIPK2
CXCL1
TNFRSF1B
CCR2
TLR2
TLR4
DUSP4
DUSP6
JUN
ICAM1
NFKB2
SOCS1
SOCS3
IFNG
CXCL8
NOD1
CD36
FOS
RPS6KA2
SIGIRR
PSAP
PTPN1
Node color: Gene Ontology Cellular Components
Cell
Extracellular Matrix
Extracellular Region
Macromolecular Complex
Membrane
Mitochondrion
Nucleus
Organelle
Synapse
Virion
Endoplasmic Reticulum
Cell Junction
Uncategorized

Suppl. Fig. 2. Induction of TLR and IFN signaling pathways by *Candida auris*. a, Dot plot showing the 30 most enriched signaling pathways obtained by ORA of DEGs using ClusterProfiler. Y-axis contains enriched pathways while the size of circles represents the number of genes (count) enriching each category and color (from blue to black) indicating how significantly enriched (when p-value <0.05) is the pathway. **b,** Network demonstrating interactions between pathways and their associated genes revealed by ORA. Circular nodes represent pathways, circle size is associated with the number of genes enriching each pathway, while colored squares represent the cell location of genes. Genes interacting with more than 5 pathways are named. The interaction network was build using the NAViGaTOR software.







A Signaling by Interleukins
B Regulation of IFNG signaling
C Interleukin-2 family signaling
D Diseases of Immune System
E Diseases associated with the TLR signaling cascade
F Interleukin receptor SHC signaling
G Toll Like Receptor 4 (TLR4) Cascade
H Interleukin-21 signaling
I Toll-like Receptor Cascades
J Interleukin-2 signaling
K Interferon gamma signaling
L MyD88:MAL(TIRAP) cascade initiated on plasma membrane
M Toll Like Receptor TLR6:TLR2 Cascade
N Toll Like Receptor TLR1:TLR2 Cascade
O Toll Like Receptor 2 (TLR2) Cascade
P CLEC7A (Dectin-1) signaling
Q Interleukin-3, Interleukin-5 and GM-CSF signaling
R Interleukin-4 and Interleukin-13 signaling
S Signaling by the B Cell Receptor (BCR)
T RIP-mediated NFkB activation via ZBP1
U Interferon Signaling
V Interleukin-12 family signaling
X ZBP1(DAI) mediated induction of type I IFNs
W Fc epsilon receptor (FCERI) signaling
Z Interferon alpha/beta signaling

Suppl. Fig. 3. Inborn errors of immunity confirm the interplay of TLR- and IFN-associated genes. a, Overview (created using BioRender.com) of genes associated with inborn errors of immunity that are also found among the DEGs across the 7 datasets of WBCs, PBMCs, and moDCs (**Suppl. Table S16**). **b,** Dot plot showing the 30 most enriched signaling pathways obtained by ORA of DEGs seen in (**a**). Y-axis contains enriched pathways while the size of circles represents the number of genes (count) enriching each category and color (from blue to black) indicates how significantly enriched (when p-value <0.05) is each pathway. **c,** GOPlot displaying genes causing inborn errors of immunity and enriched pathways. *DEGs, Differentially Expressed Genes; moDCs, Monocyte-Derived Dendritic Cells; IFN, Interferon; ORA, Over-representation Analysis; PBMCs, Peripheral Blood Mononuclear Cells; TLR, Toll-like Receptor; WBCs, White Blood Cells.*