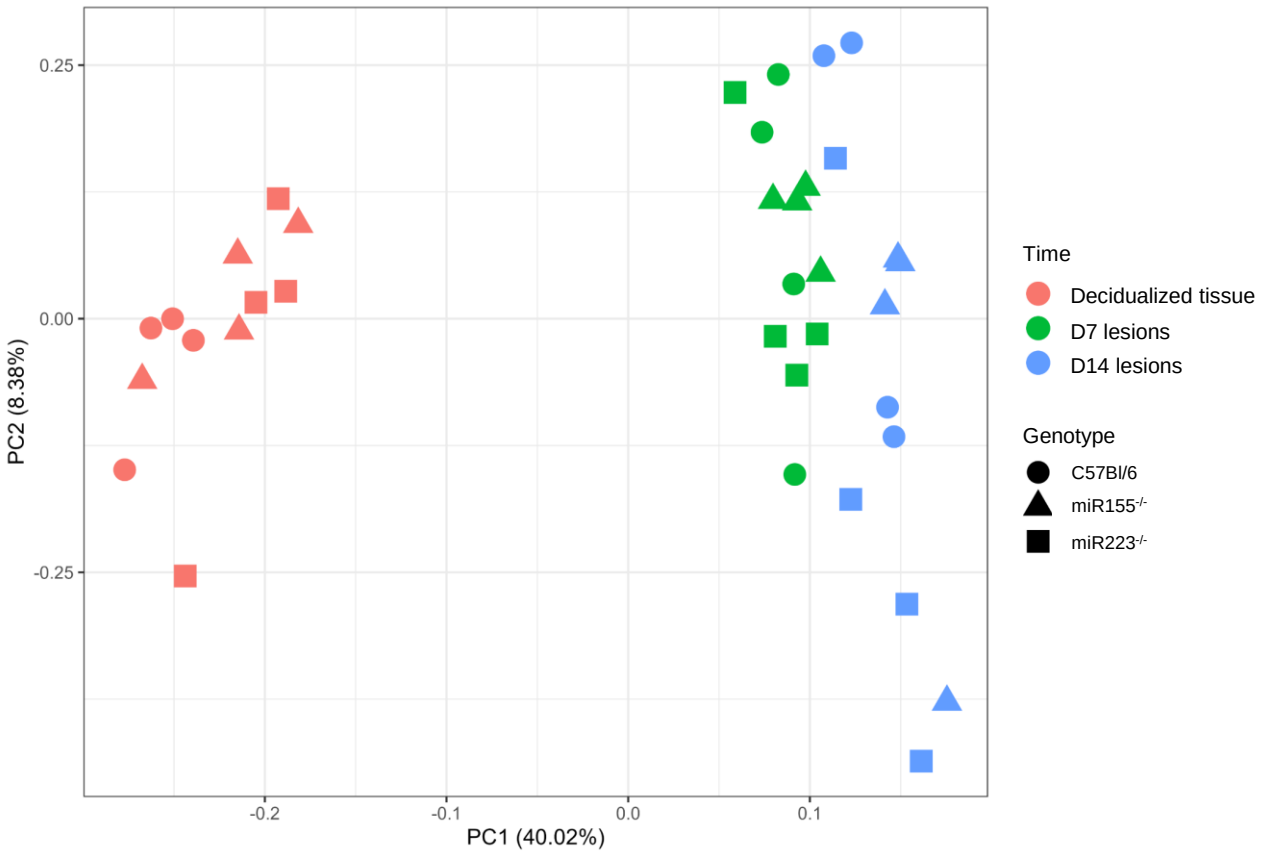

Fig. S1. Principal component analysis plot for all 36 samples used in the analysis. A principal component analysis (PCA) plot was constructed to further explore the relationships amongst the 36 different samples in the dataset, and provides additional evidence of the clear separation between decidualized endometrial samples and lesion samples, reinforcing the robustness of the observed distinctions.

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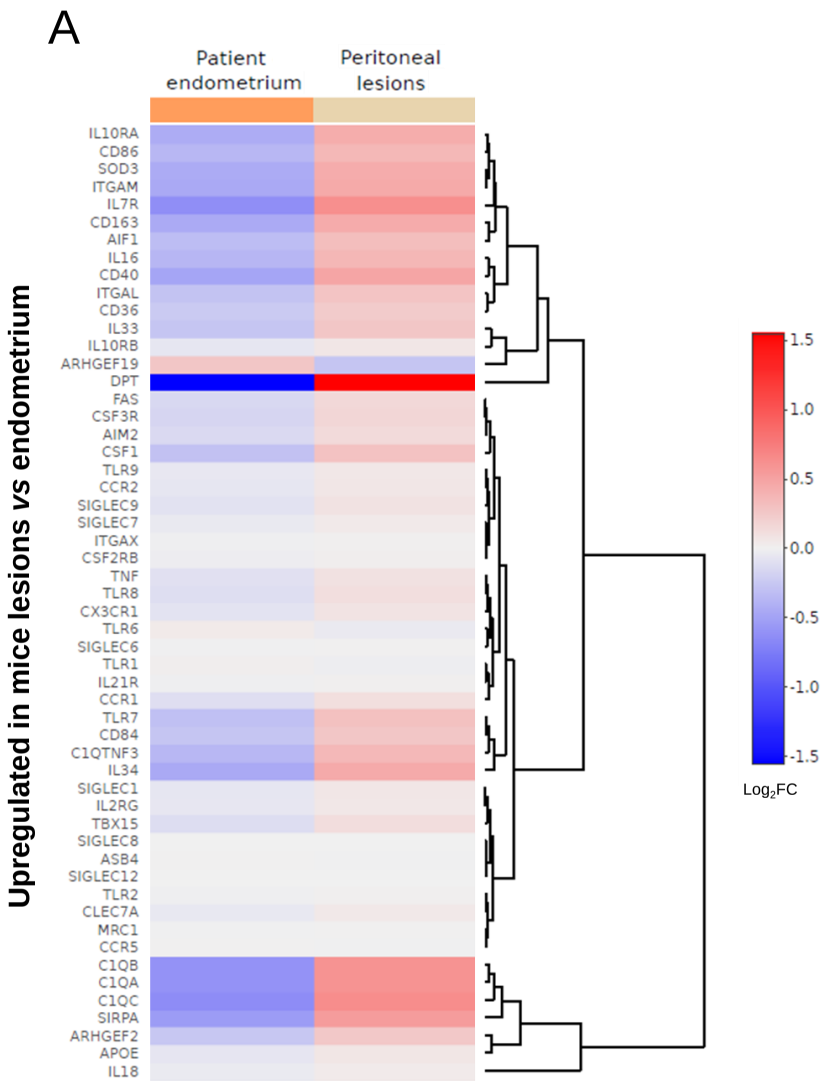
A
Patient endometrium
Peritoneal lesions
Upregulated in mice lesions vs endometrium
IL10RA
CD86
SOD3
ITGAM
IL7R
CD163
AIF1
IL16
CD40
ITGAL
CD36
IL33
IL10RB
ARHGEF19
DPT
FAS
CSF3R
AIM2
CSF1
TLR9
CCR2
SIGLEC9
SIGLEC7
ITGAX
CSF2RB
TNF
TLR8
CX3CR1
TLR6
SIGLEC6
TLR1
IL21R
CCR1
TLR7
CD84
C1QTNF3
IL34
SIGLEC1
IL2RG
TBX15
SIGLEC8
ASB4
SIGLEC12
TLR2
CLEC7A
MRC1
CCR5
C1QB
C1QA
C1QC
SIRPA
ARHGEF2
APOE
IL18
1.5
1.0
0.5
0.0
-0.5
-1.0
-1.5
Log2FC

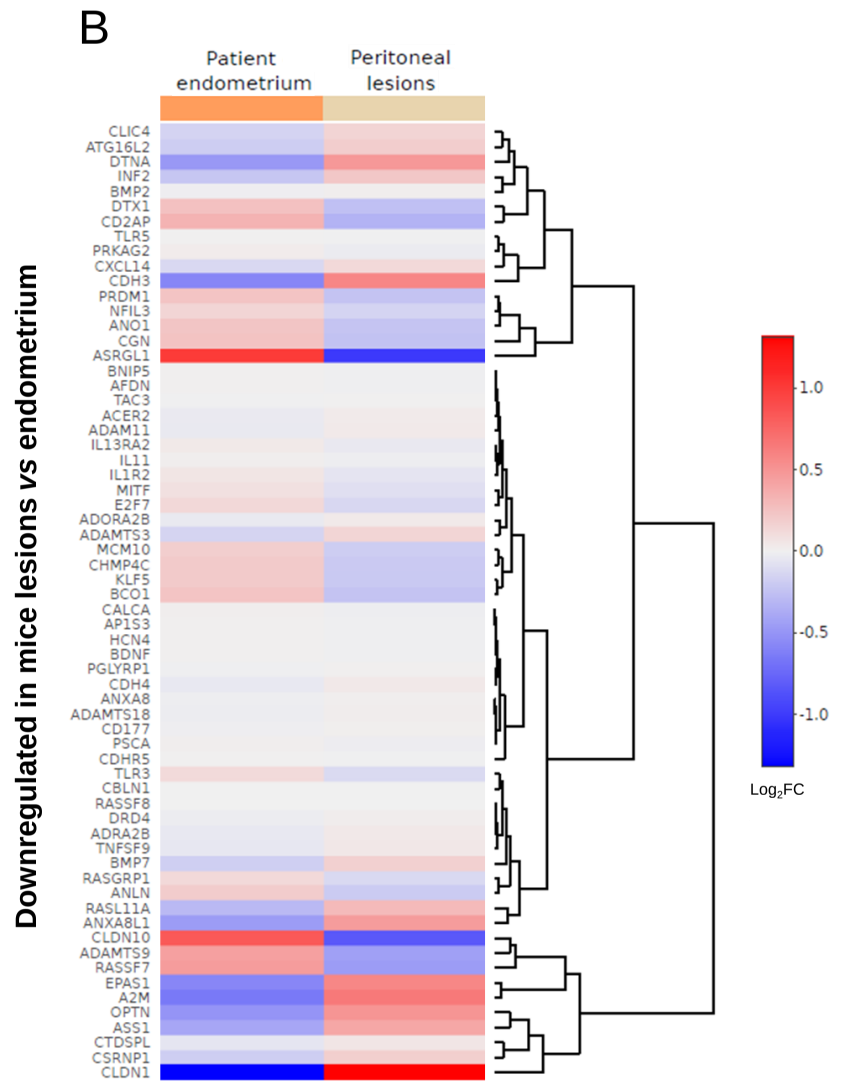
B
Patient endometrium
Peritoneal lesions
Downregulated in mice lesions vs endometrium
CLIC4
ATG16L2
DTNA
INF2
BMP2
DTX1
CD2AP
TLR5
PRKAG2
CXCL14
CDH3
PRDM1
NFIL3
ANO1
CGN
ASRGL1
BNIP5
AFDN
TAC3
ACER2
ADAM11
IL13RA2
IL11
IL1R2
MITF
E2F7
ADORA2B
ADAMTS3
MCM10
CHMP4C
KLF5
BCO1
CALCA
AP1S3
HCN4
BDNF
PGLYRP1
CDH4
ANXA8
ADAMTS18
CD177
PSCA
CDHR5
TLR3
CBLN1
RASSF8
DRD4
ADRA2B
TNFSF9
BMP7
RASGRP1
ANLN
RASL11A
ANXA8L1
CLDN10
ADAMTS9
RASSF7
EPAS1
A2M
OPTN
ASS1
CTDSPL
CSRNP1
CLDN1
1.0
0.5
0.0
-0.5
-1.0
Log2FC

Fig. S2. Expression of human orthologues corresponding to mouse genes from our dataset. A selection of DEGs common to both Day 7 (D7) and Day 14 (D14) versus endometrium (log2FC ≥ ± 2, FDR ≤ 0.05) were identified and converted into human orthologous genes using BioMart. The expression of orthologous genes was evaluated in publicly available human datasets comparing patient endometrium and peritoneal lesions, utilizing the EndometDB database (https://endometdb.utu.fi/) and presents as **(A)** Heatmap depicting the expression levels of human orthologues corresponding to upregulated mouse genes, and **(B)** Heatmap depicting the expression levels of human orthologues corresponding to downregulated mouse genes.

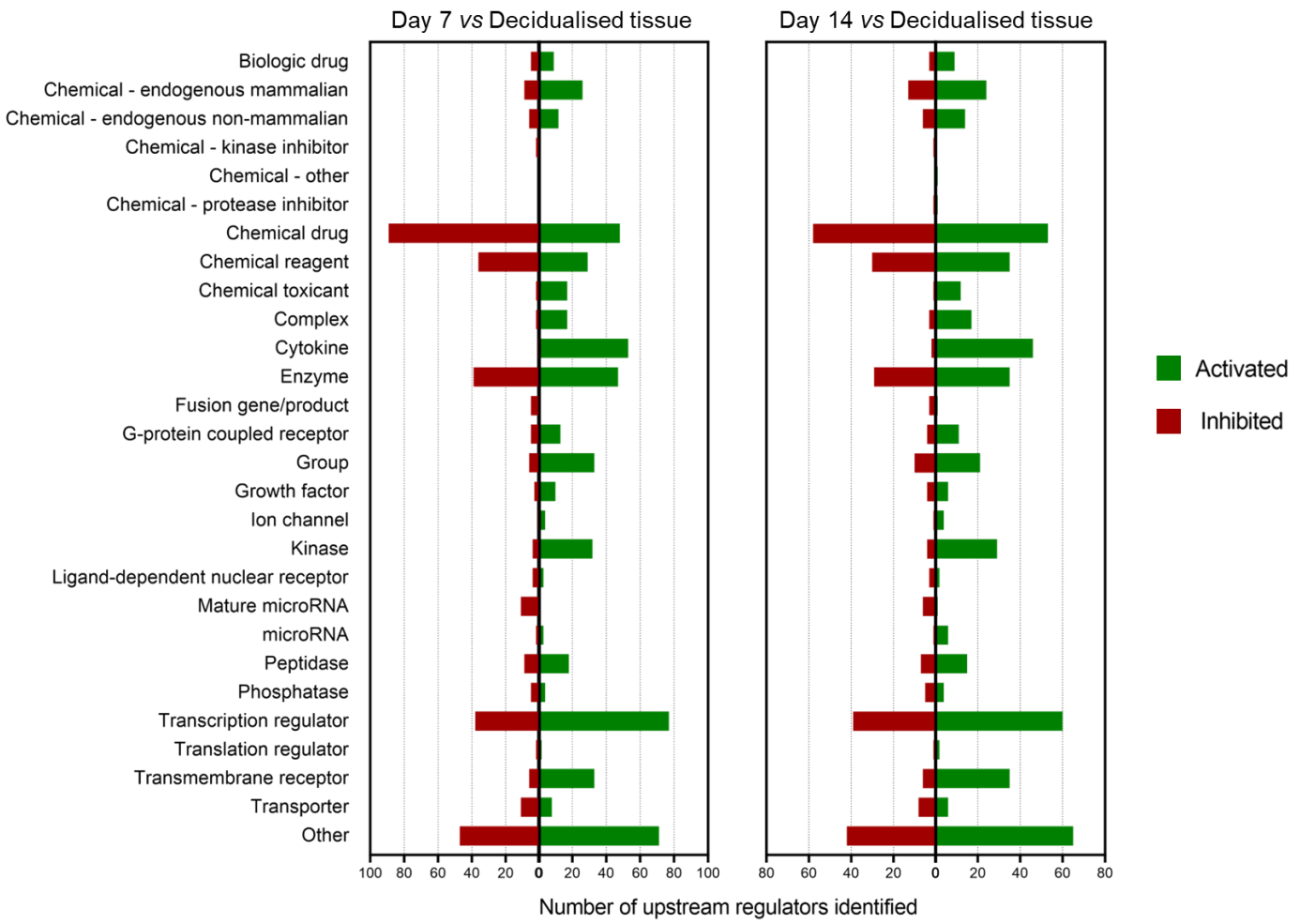

Fig. S3. Classification of molecules predicted to be upstream of genes regulated in Day 7 and Day 14 endometriosis-like lesions vs decidualized endometrium identified by IPA. Predicted upstream regulators were grouped into 28 molecular categories. All upstream regulators have a *Z*- activation score of ≥ +2 or ≤ -2, and corresponding *p*-value of ≤ 0.05.

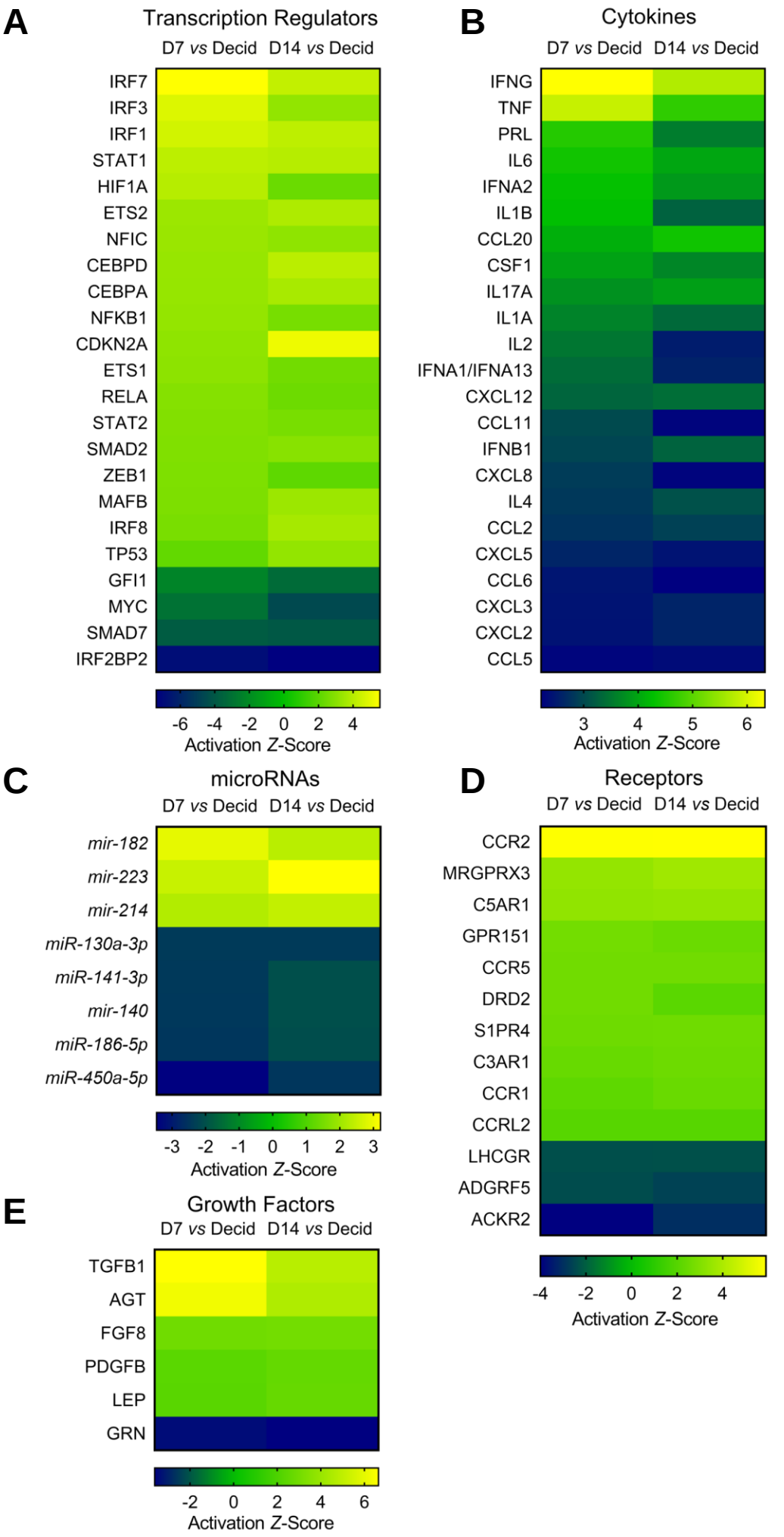
A
Transcription Regulators
D7 vs Decid
D14 vs Decid
IRF7
IRF3
IRF1
STAT1
HIF1A
ETS2
NFIC
CEBPD
CEBPA
NFKB1
CDKN2A
ETS1
RELA
STAT2
SMAD2
ZEB1
MAFB
IRF8
TP53
GFI1
MYC
SMAD7
IRF2BP2
-6 -4 -2 0 2 4
Activation Z-Score
B
Cytokines
D7 vs Decid
D14 vs Decid
IFNG
TNF
PRL
IL6
IFNA2
IL1B
CCL20
CSF1
IL17A
IL1A
IL2
IFNA1/IFNA13
CXCL12
CCL11
IFNB1
CXCL8
IL4
CCL2
CXCL5
CCL6
CXCL3
CXCL2
CCL5
3 4 5 6
Activation Z-Score
C
microRNAs
D7 vs Decid
D14 vs Decid
mir-182
mir-223
mir-214
miR-130a-3p
miR-141-3p
mir-140
miR-186-5p
miR-450a-5p
-3 -2 -1 0 1 2 3
Activation Z-Score
D
Receptors
D7 vs Decid
D14 vs Decid
CCR2
MRGPRX3
C5AR1
GPR151
CCR5
DRD2
S1PR4
C3AR1
CCR1
CCRL2
LHCGR
ADGRF5
ACKR2
-4 -2 0 2 4
Activation Z-Score
E
Growth Factors
D7 vs Decid
D14 vs Decid
TGFB1
AGT
FGF8
PDGFB
LEP
GRN
-2 0 2 4 6
Activation Z-Score

Fig. S4. Predicted upstream regulators of genes identified in D7 and D14 endometriosis-like lesions compared to decidualized endometrium. Upstream regulators of pathways were identified by IPA [*Z*- score of ≥ +2 or ≤ -2] and heatmaps were generated to show comparisons between Day 7 lesions *vs* Decidualized endometrium (Decid) and Day 14 lesions *vs* Decidualized endometrium (Decid) for the categories of **(A)** transcription regulators, **(B)** cytokines, **(C)** microRNAs **(D)** receptors, and **(E)** growth factors. Note: This list is not exhaustive; complete list of upstream regulators are available in the Supplementary Material (Table S6 and S7).

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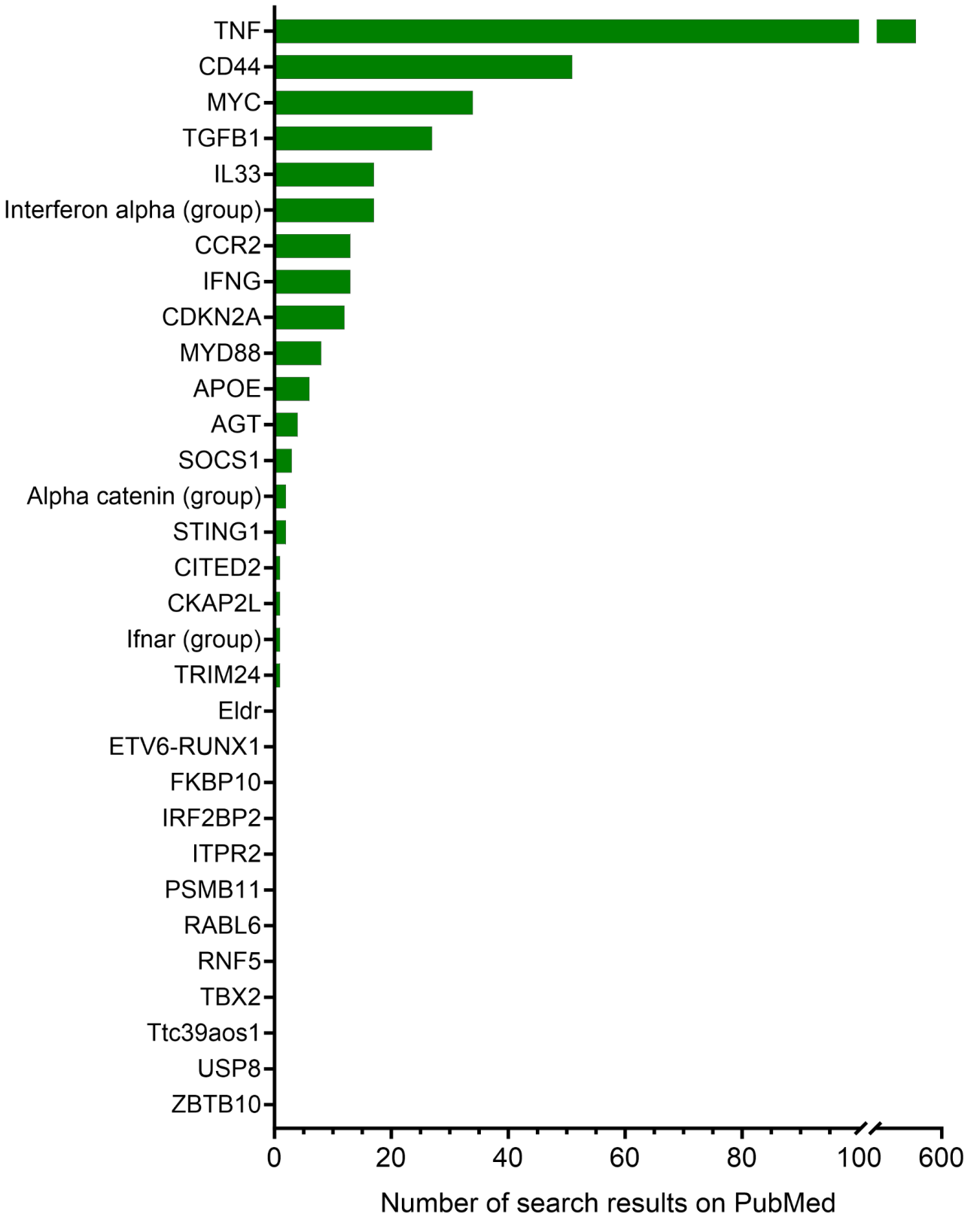
TNF
CD44
MYC
TGFB1
IL33
Interferon alpha (group)
CCR2
IFNG
CDKN2A
MYD88
APOE
AGT
SOCS1
Alpha catenin (group)
STING1
CITED2
CKAP2L
Ifnar (group)
TRIM24
Eldr
ETV6-RUNX1
FKBP10
IRF2BP2
ITPR2
PSMB11
RABL6
RNF5
TBX2
Ttc39aos1
USP8
ZBTB10
0
20
40
60
80
100
600
Number of search results on PubMed

Fig. S5. Number of published studies in the scientific literature reporting top predicted endogenous upstream regulators in comparisons between endometriosis-like lesions and decidualized endometrium. Data depict the number of search results returned via the PubMed Search Engine for individual top 10 activated and inhibited endogenous upstream regulators of endometriosis (see Figure 6A in main paper for details). PubMed searches were performed using the search terms 'molecule symbol' AND 'endometriosis'.

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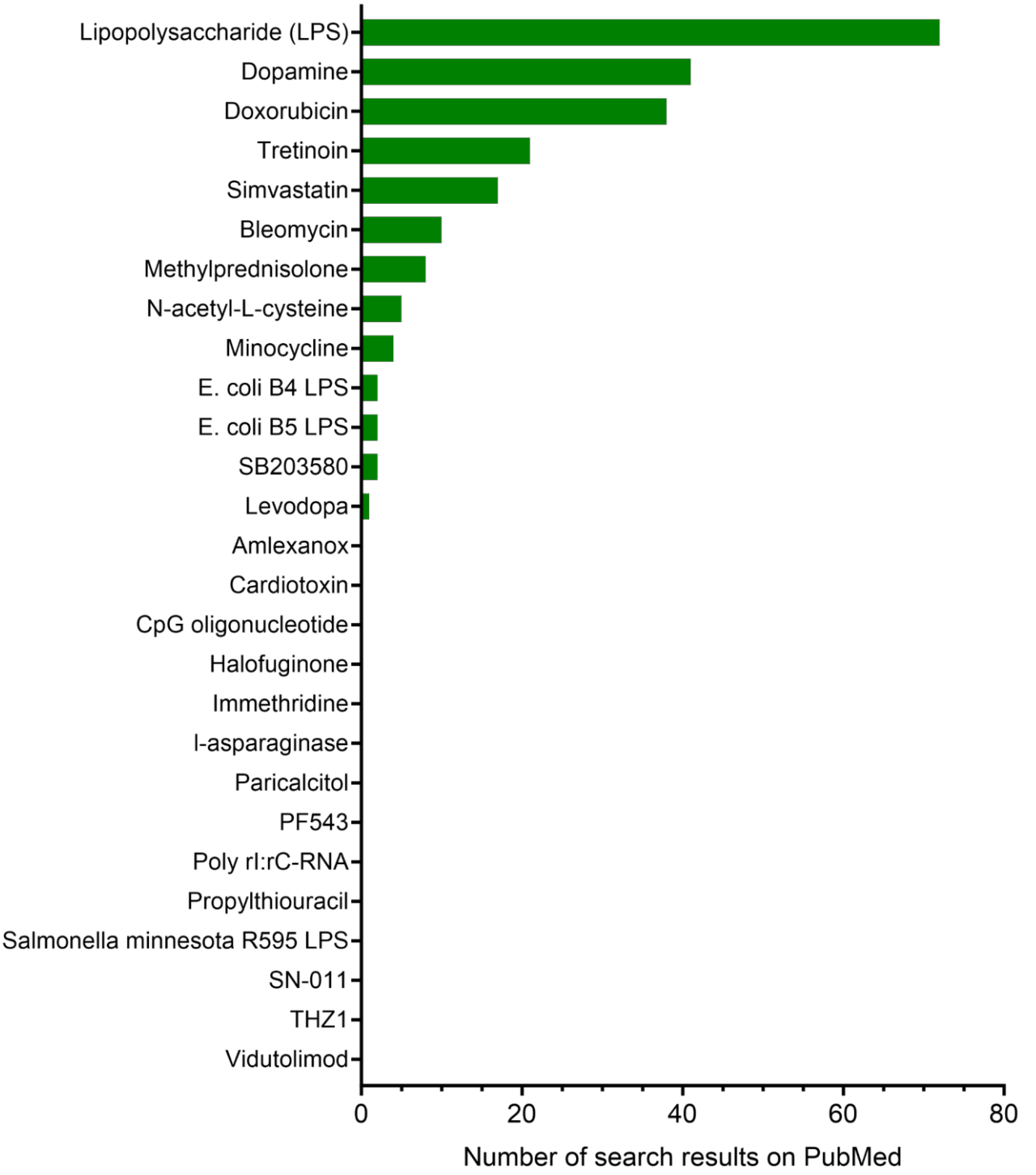

Fig. S6. Number of published studies in the scientific literature reporting top predicted non-endogenous upstream regulators in comparisons between endometriosis-like lesions and decidualized endometrium. Data depict the number of search results returned via the PubMed Search Engine for individual top 10 activated and inhibited non-endogenous upstream regulators of endometriosis (see Figure 6B in main paper for details). PubMed searches were performed using the search terms ‘molecule symbol’ AND ‘endometriosis’.

Table S1. Differentially Expressed Genes (DEGs) identified in D7 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S2. Differentially Expressed Genes (DEGs) identified in D14 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S3. Differentially Expressed Genes (DEGs) identified in D14 *vs* D7 endometriosis-like lesions from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S4. Ingenuity Canonical Pathways identified in D7 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S5. Ingenuity Canonical Pathways identified in D14 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S6. Upstream regulators identified in D7 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S7. Upstream regulators identified in D14 endometriosis-like lesions *vs* decidualized endometrium from C57Bl/6 mice.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Table S8. Number of reads generated per RNA sample.

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data

Available for download at
https://journals.biologists.com/dmm/article-lookup/doi/10.1242/dmm.050566#supplementary-data