LETTER TO THE EDITOR

Single-cell analysis unveils distinct transcriptional alterations and cellular origins in IgD multiple myeloma

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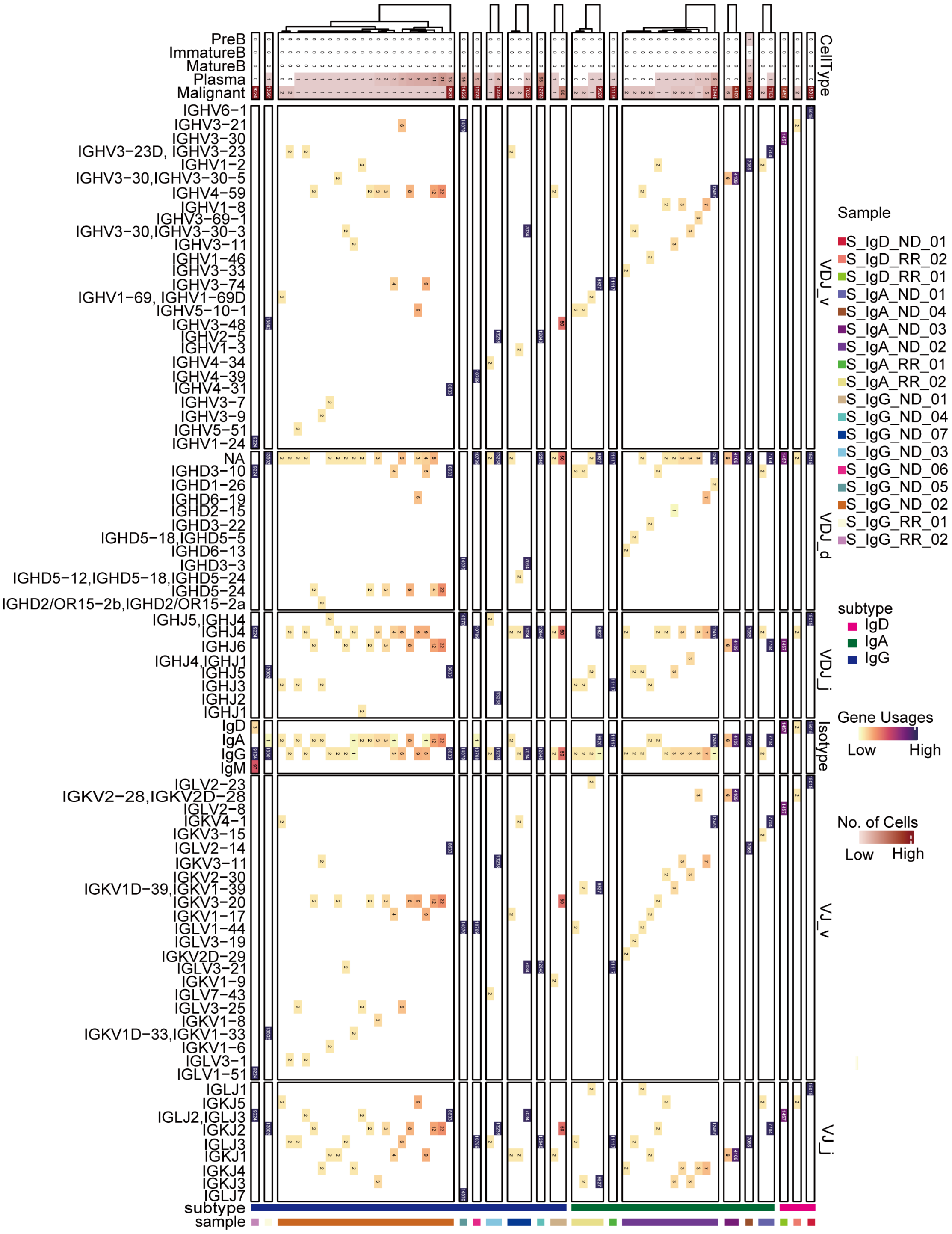
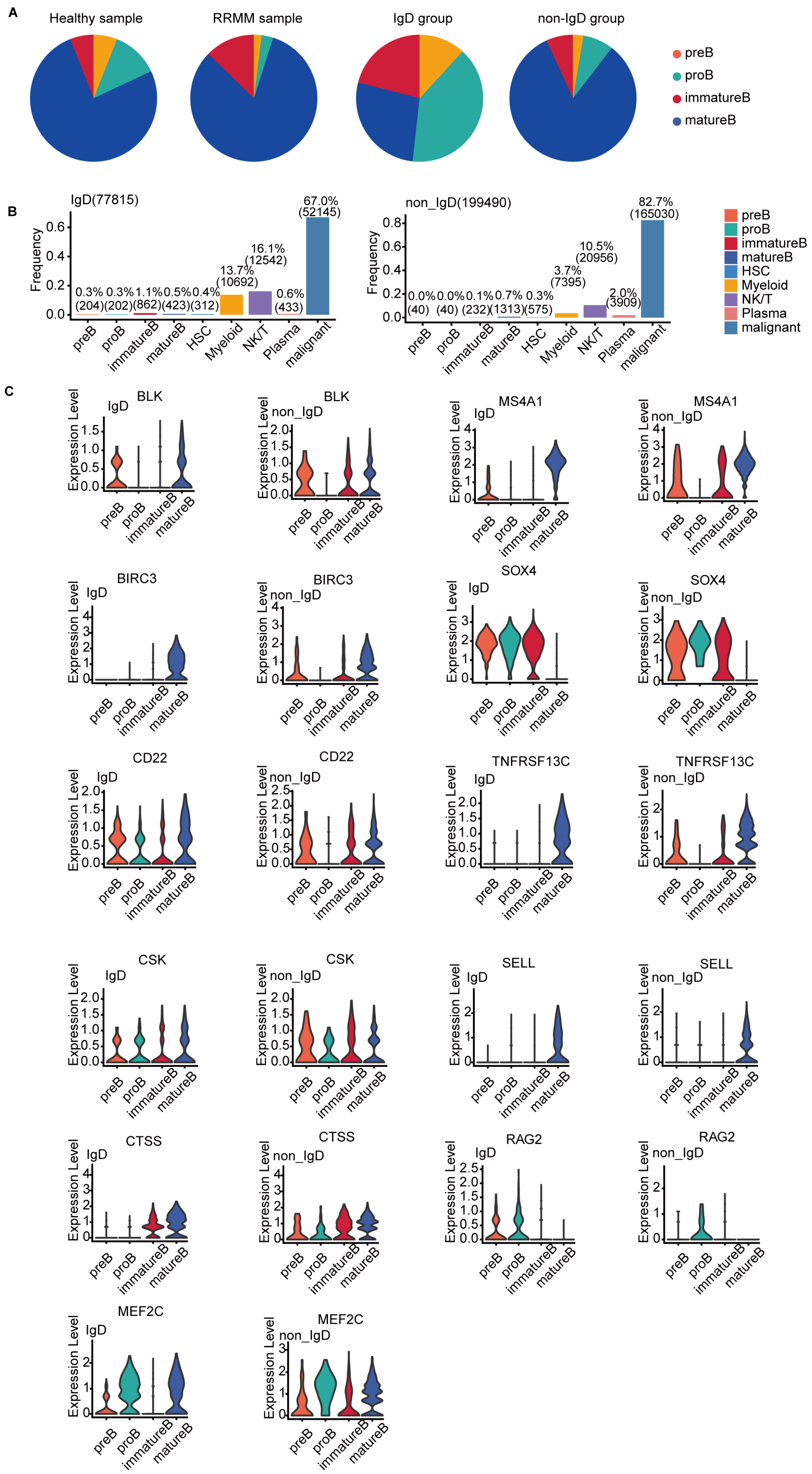
Supplemental Figures



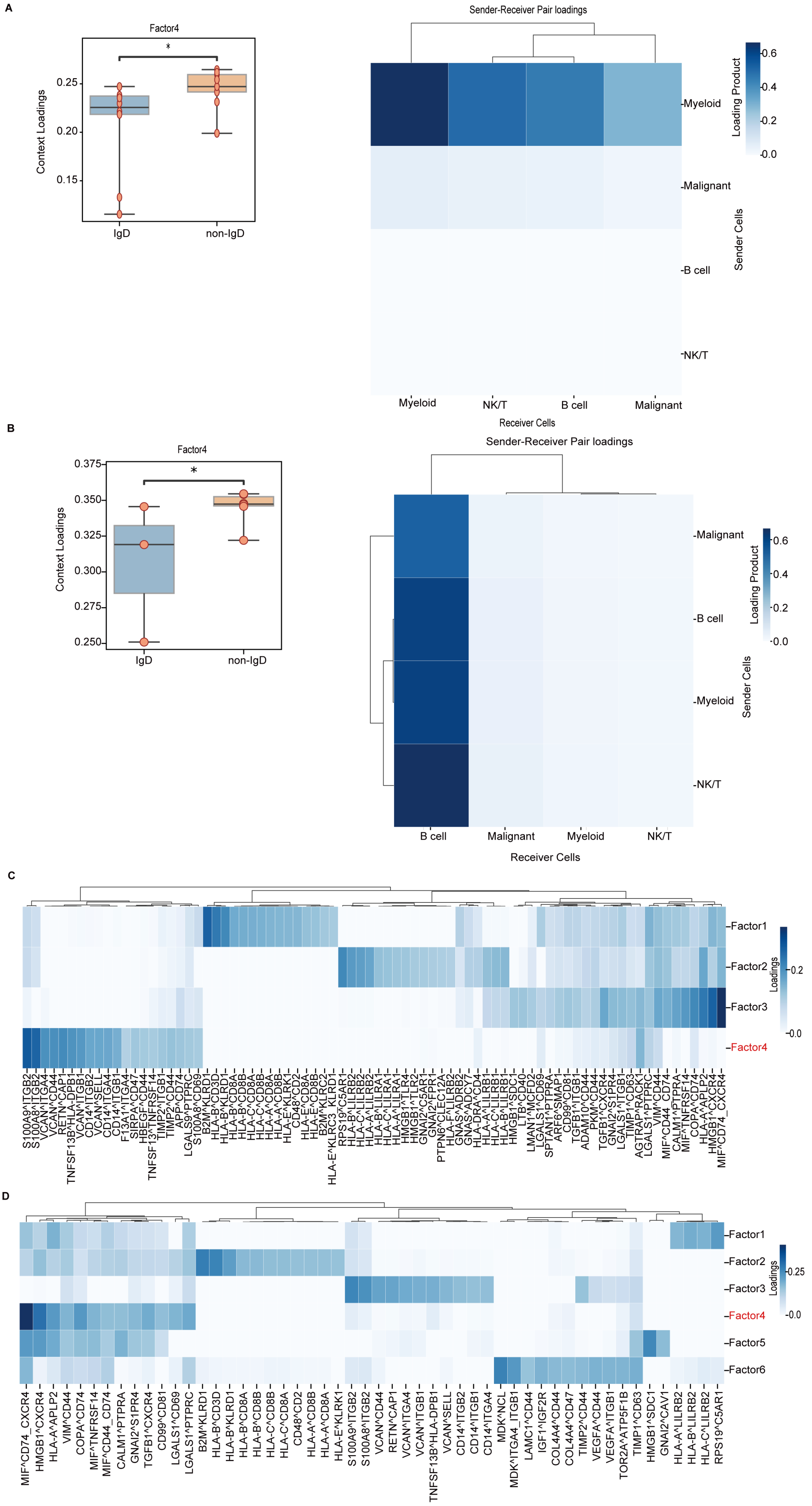
Supplemental Fig. 1. Single-cell BCR repertoire landscape of MM in sorted samples

In the top panel, cell numbers for each patient are plotted. The middle panel displays VDJ and VJ usage, isotypes, and cell numbers in a heatmap format, with MM subtypes labeled at the bottom, providing insights into the BCR profiles across different MM samples.


A
Healthy sample
RRMM sample
IgD group
non-IgD group
preB
proB
immatureB
matureB
B
IgD(77815)
Frequency
0.0
0.2
0.4
0.6
0.3% (204)
0.3% (202)
1.1% (862)
0.5% (423)
0.4% (312)
13.7% (10692)
16.1% (12542)
0.6% (433)
67.0% (52145)
preB
proB
immatureB
matureB
HSC
Myeloid
NK/T
Plasma
malignant
non_IgD(199490)
Frequency
0.0
0.2
0.4
0.6
0.8
0.0% (40)
0.0% (40)
0.1% (232)
0.7% (1313)
0.3% (575)
3.7% (7395)
10.5% (20956)
2.0% (3909)
82.7% (165030)
preB
proB
immatureB
matureB
HSC
Myeloid
NK/T
Plasma
malignant
C
BLK
MS4A1
BIRC3
SOX4
CD22
TNFRSF13C
CSK
SELL
CTSS
RAG2
MEF2C
IgD
non_IgD
Expression Level
preB
proB
immatureB
matureB

Supplemental Fig. 2. Comparison of cell proportions and genes in the B cell receptor (BCR) signaling pathway

(A) Comparison of B cell type fractions between healthy donors and patients with RRMM (adapted from https://doi.org/10.1038/s41467-021-26951-z), IgD MM, and non-IgD MM (from this study).
(B) Bar plot illustrating the proportions of various cell types (IgD MM vs. non-IgD MM)
(C) Violin plot depicting the expression levels of differentially expressed genes in immature B cells comparing IgD and non-IgD multiple myeloma (MM), with a focus on the BCR signaling pathway. Genes such as MEF2C, BLK, MS4A1, BIRC3, SOX4, CD22, TNFRSF13C, CSK, SELL, CTSS, and RAG2 are highlighted for comparison between IgD MM and non-IgD MM


A
Factor4
*
0.25
0.20
0.15
Context Loadings
IgD
non-IgD
Sender-Receiver Pair loadings
Myeloid
Malignant
B cell
NK/T
Sender Cells
Myeloid
NK/T
B cell
Malignant
Receiver Cells
0.6
0.4
0.2
0.0
Loading Product
B
Factor4
*
0.375
0.350
0.325
0.300
0.275
0.250
Context Loadings
IgD
non-IgD
Sender-Receiver Pair loadings
Malignant
B cell
Myeloid
NK/T
Sender Cells
B cell
Malignant
Myeloid
NK/T
Receiver Cells
0.6
0.4
0.2
0.0
Loading Product
C
Factor1
Factor2
Factor3
Factor4
0.2
0.0
Loadings
S100A9^ITGB2
S100A8^ITGB2
VCAN^ITGA4
VCAN^CD44
RETN^CAP1
TNFSF13B^HLA-DPB1
VCAN^ITGB1
CD14^ITGB2
VCAN^SELL
CD14^ITGA4
CD14^ITGB1
F13A1^ITGA4
SIRPA^CD47
HBEGF^CD44
TNFSF13^TNFRSF14
TIMP2^ITGB1
TIMP2^CD44
APP^CD74
LGALS9^PTPRC
S100A8^CD69
B2M^KLRD1
HLA-B^CD3D
HLA-B^KLRD1
HLA-B^CD8A
HLA-B^CD8B
HLA-C^CD8A
HLA-C^CD8B
HLA-A^CD8A
HLA-A^CD8B
HLA-E^KLRK1
CD48^CD2
HLA-E^CD8A
HLA-E^CD8B
B2M^KLRC2
HLA-E^KLRC3_KLRD1
RPS19^C5AR1
HLA-B^LILRB2
HLA-C^LILRB2
HLA-A^LILRB2
HLA-B^LILRA1
HLA-C^LILRA1
HLA-A^LILRA1
HMGB1^TLR4
HMGB1^TLR2
GNAI2^C5AR1
GNAI2^FPR1
PTPN6^CLEC12A
HLA-F^LILRB2
GNAS^ADRB2
GNAS^ADCY7
HLA-DRA^CD4
HLA-A^LILRB1
HLA-C^LILRB1
HLA-B^LILRB1
HMGB1^SDC1
LTB^CD40
LMAN1^MCFD2
LGALS1^CD69
SPTAN1^PTPRA
ARF6^SMAP1
CD99^CD81
TGFB1^ITGB1
ADAM10^CD44
PKM^CD44
TGFB1^CXCR4
GNAI2^S1PR4
LGALS1^ITGB1
TIMP1^CD63
AGTRAP^RACK1
LGALS1^PTPRC
VIM^CD44
MIF^CD44_CD74
CALM1^PTPRA
MIF^TNFRSF14
COPA^CD74
HLA-A^APLP2
HMGB1^CXCR4
MIF^CD74_CXCR4
D
Factor1
Factor2
Factor3
Factor4
Factor5
Factor6
0.25
0.0
Loadings
MIF^CD74_CXCR4
HMGB1^CXCR4
HLA-A^APLP2
VIM^CD44
COPA^CD74
MIF^TNFRSF14
MIF^CD44_CD74
CALM1^PTPRA
GNAI2^S1PR4
TGFB1^CXCR4
CD99^CD81
LGALS1^CD69
LGALS1^PTPRC
B2M^KLRD1
HLA-B^CD3D
HLA-B^KLRD1
HLA-B^CD8A
HLA-B^CD8B
HLA-C^CD8B
HLA-C^CD8A
CD48^CD2
HLA-A^CD8B
HLA-A^CD8A
HLA-E^KLRK1
S100A9^ITGB2
S100A8^ITGB2
VCAN^CD44
RETN^CAP1
VCAN^ITGA4
VCAN^ITGB1
TNFSF13B^HLA-DPB1
VCAN^SELL
CD14^ITGB2
CD14^ITGB1
CD14^ITGA4
MDK^NCL
MDK^ITGA4_ITGB1
LAMC1^CD44
IGF1^IGF2R
COL4A4^CD44
COL4A4^CD47
TIMP2^CD44
VEGFA^CD44
VEGFA^ITGB1
TOR2A^ATP5F1B
TIMP1^CD63
HMGB1^SDC1
GNAI2^CAV1
HLA-A^LILRB2
HLA-B^LILRB2
HLA-C^LILRB2
RPS19^C5AR1

Supplemental Fig. 3. Analysis of communication patterns between IgD and non-IgD MM from the LIANA and Tensor-cell2cell framework (all unsorted samples and ND unsorted samples).

(A) Left, sample loadings were statistically compared between IgD MM and non-IgD MM within the same cell-cell communication program for all unsorted samples. Right, the heatmap illustrates the cell type loadings for Factor 4 for all unsorted samples.
(B) Left, sample loadings were statistically compared between IgD MM and non-IgD MM within the same cell-cell communication program for ND unsorted samples. Right, the heatmap illustrates the cell type loadings for Factor 4 for ND unsorted samples.
(C) The heatmap displays the ligand-receptor interactions loadings across all programs for all unsorted samples.
(D) The heatmap displays the ligand-receptor interactions loadings across all programs for ND unsorted samples.