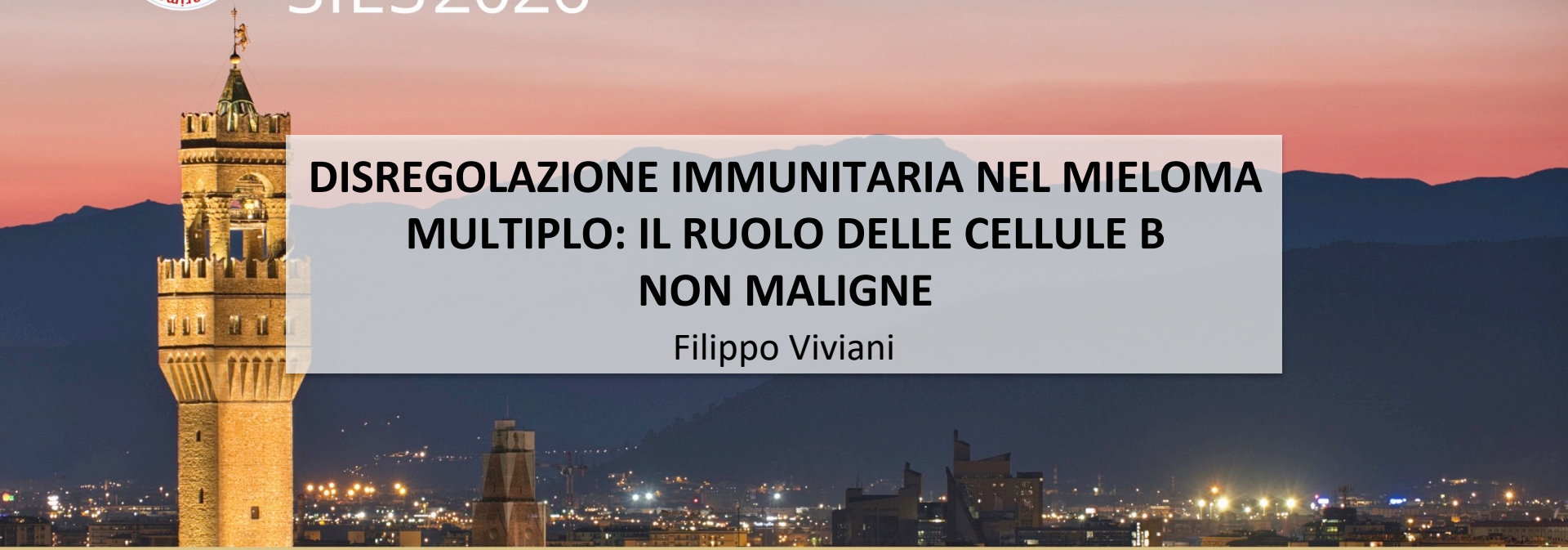
XIX CONGRESSO NAZIONALE SIES 2026

# DISREGOLAZIONE IMMUNITARIA NEL MIELOMA MULTIPLO: IL RUOLO DELLE CELLULE B NON MALIGNE

Filippo Viviani



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Palazzo degli Affari

# Disclosures of Filippo Viviani

| Company name | Research support | Employee | Consultant | Stockholder | Speakers bureau | Advisory board | Other |
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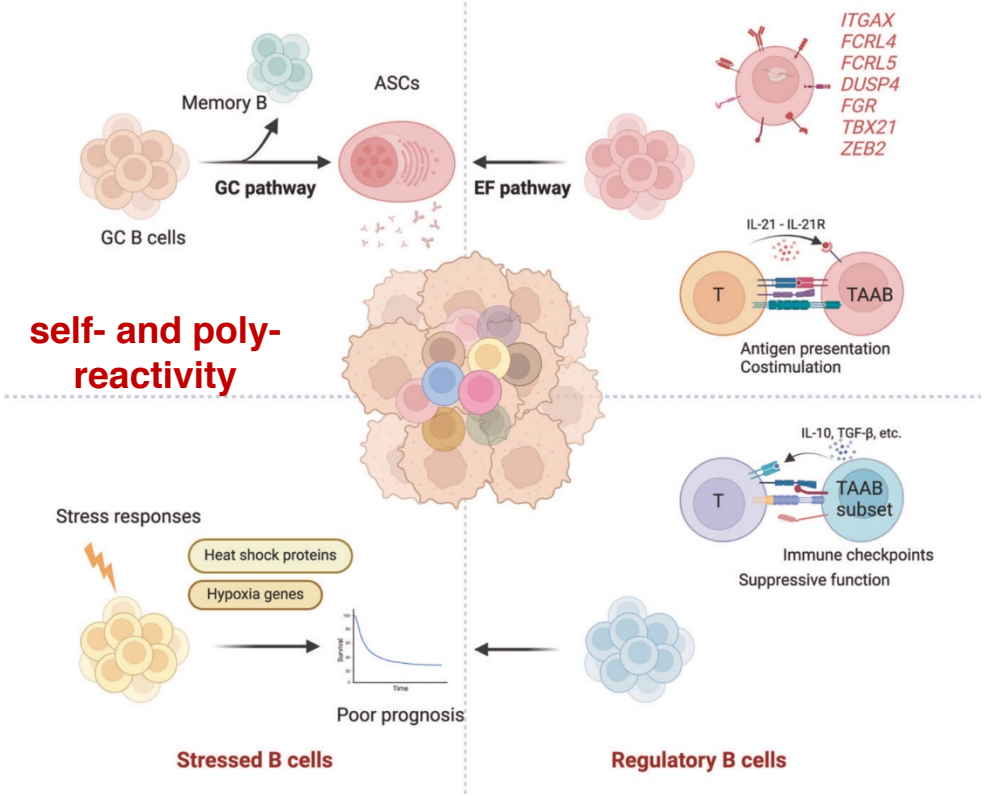
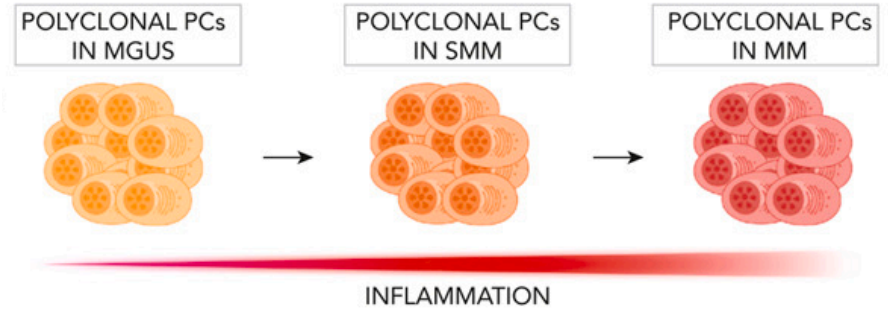
# Multi-omics data highlight different roles of B cells in cancer development




Xiao F, et al. Cell Mol Immunol. 2024; Fitzsimons E, et al. Cancer Cell. 2024; Ma J, et al. Science. 2024; Yang Y, et al. Cell. 2024.

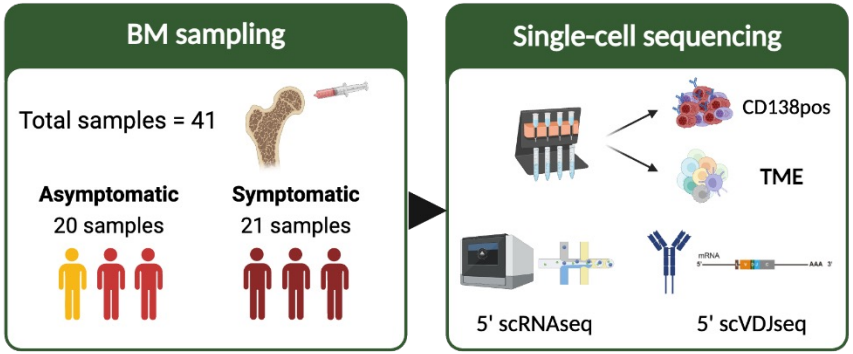
# Aim of the study

Polyclonal «healthy» plasma cells of MM TME show deranged functions pathways which are absent in healthy donors

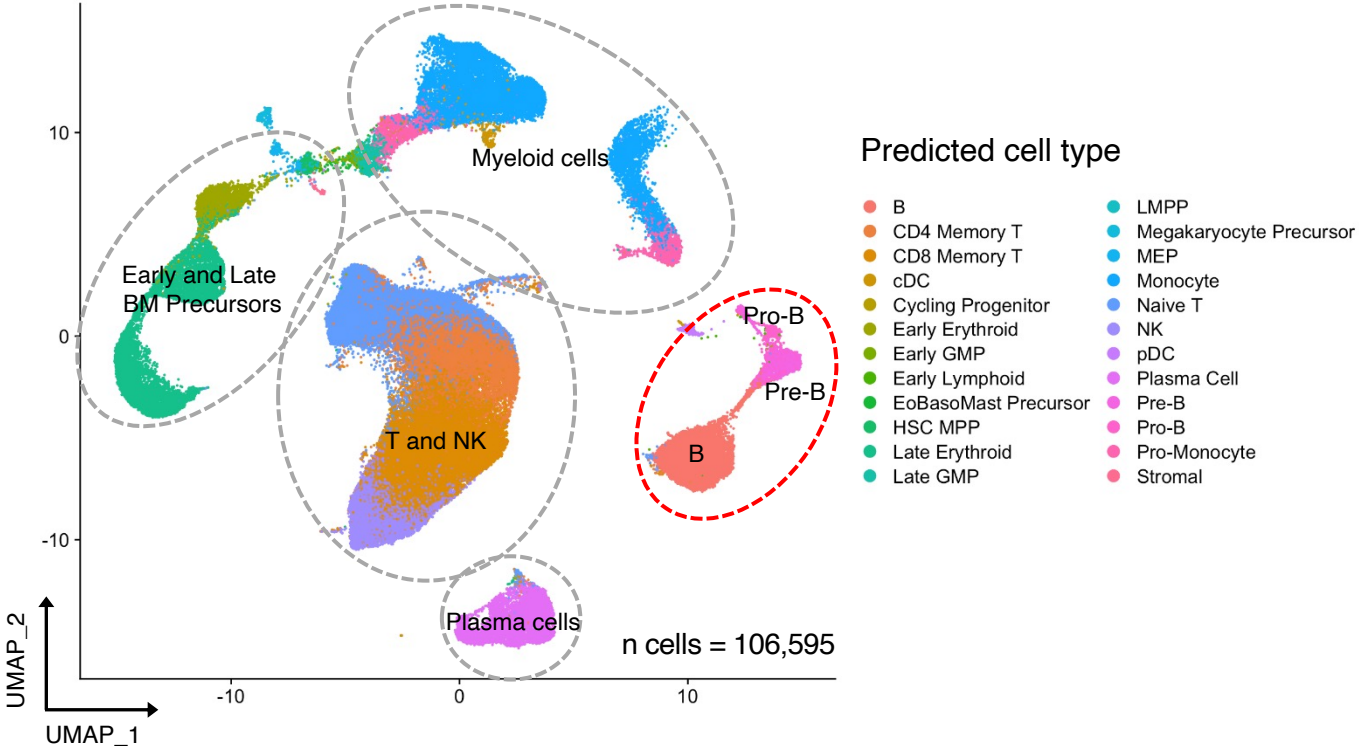



Detect early signs of B cell dysfunction and features linked to disease progression

# Material and Methods



# Tumor microenvironment landscape and B cell selection



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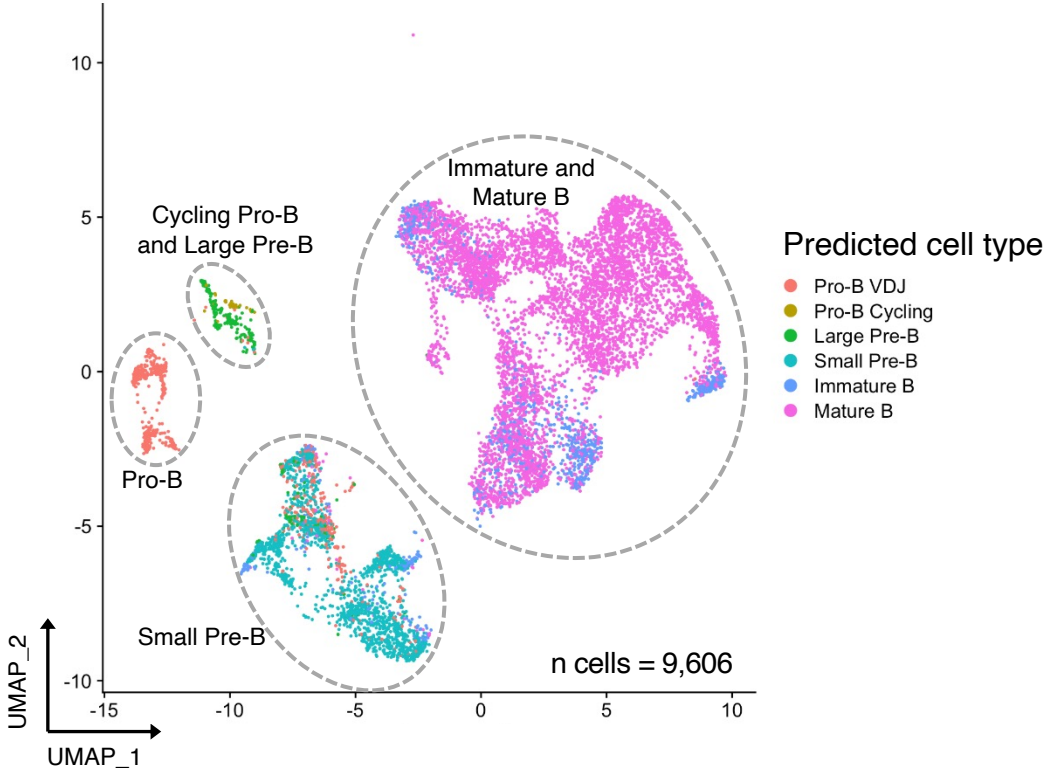
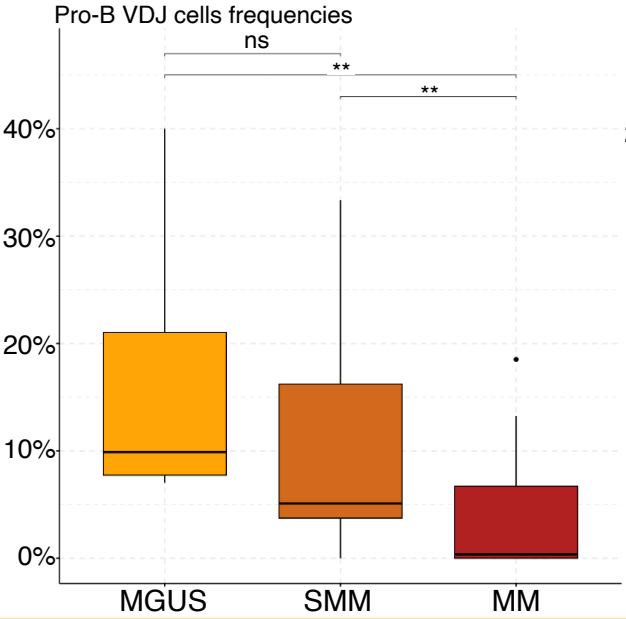
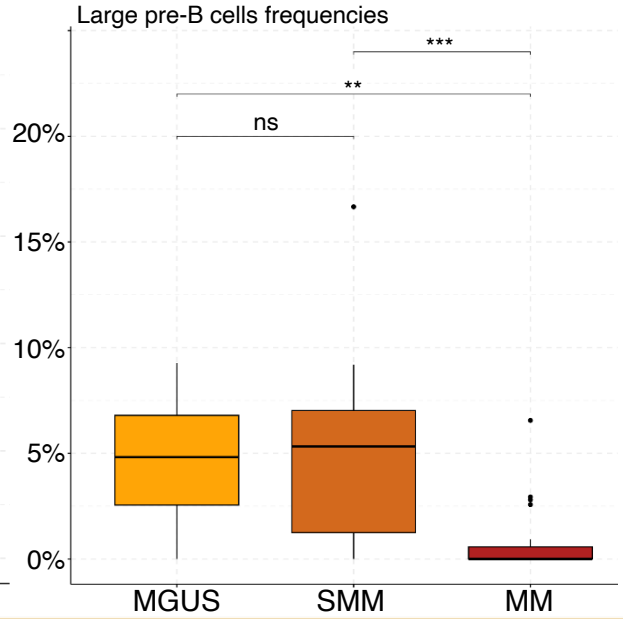
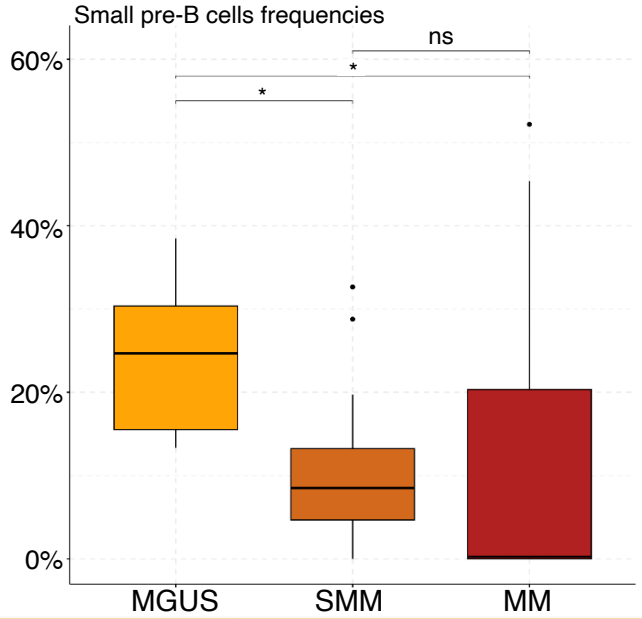


# Early-stage B cells are reduced in overt Multiple Myeloma

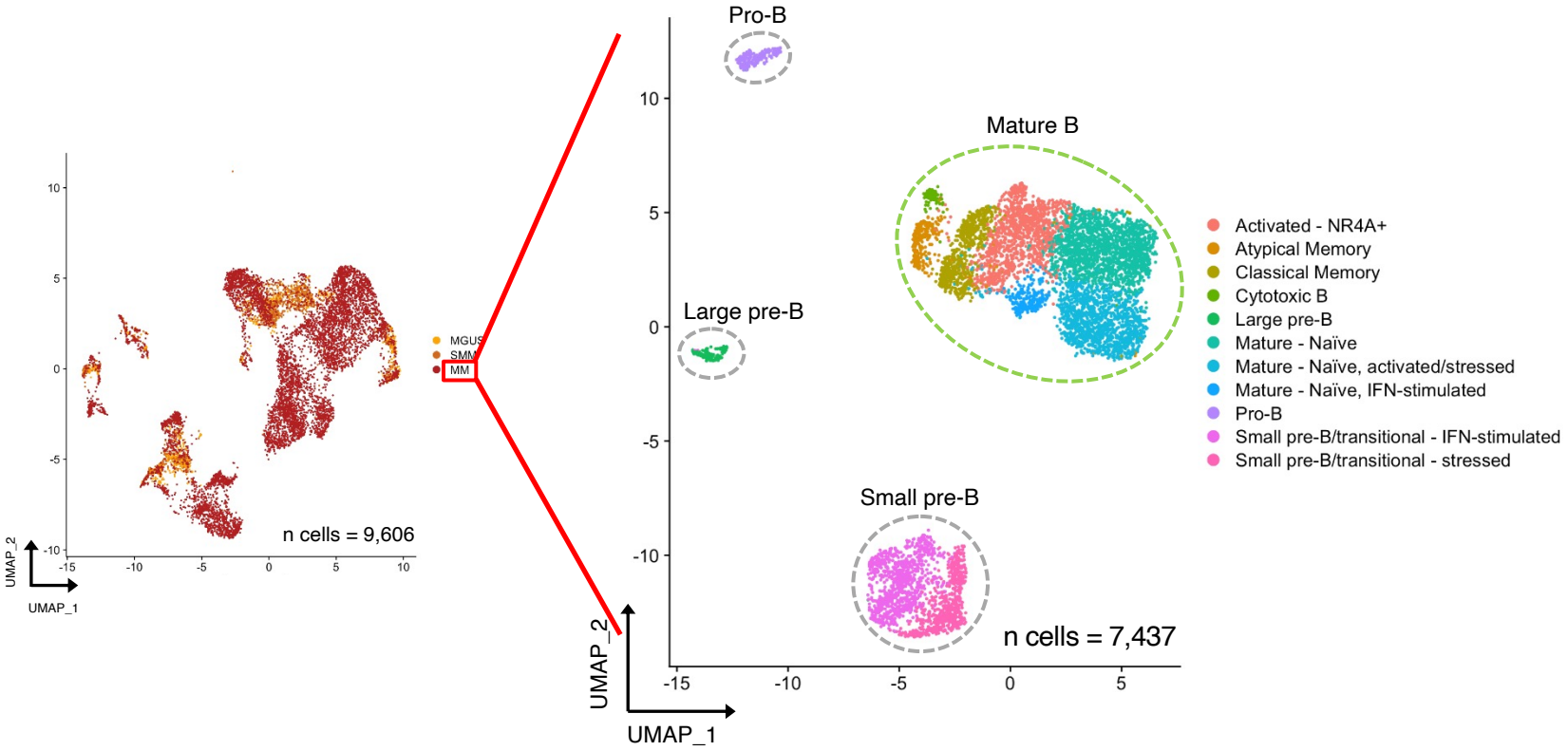
| | Pro-B VDJ | Pro-B Cycling | Large Pre-B | Small Pre-B | Immature B | Mature B | Total |
|---|---|---|---|---|---|---|---|
| **MGUS** | 112 (13.6%) | 4 (0.5%) | 44 (5.4%) | 207 (25.2%) | 77 (9.4%) | 378 (46%) | 822 |
| **SMM** | 146 (10.8%) | 10 (0.7%) | 70 (5.2%) | 157 (11.7%) | 65 (4.8%) | 899 (66.7%) | 1347 |
| **MM** | 410 (5.5%) | 18 (0.2%) | 147 (2%) | 1124 (15.1%) | 905 (12.2%) | 4833 (65%) | 7437 |
| **Total pts** | 668 | 32 | 261 | 1488 | 1047 | 6110 | **9606** |



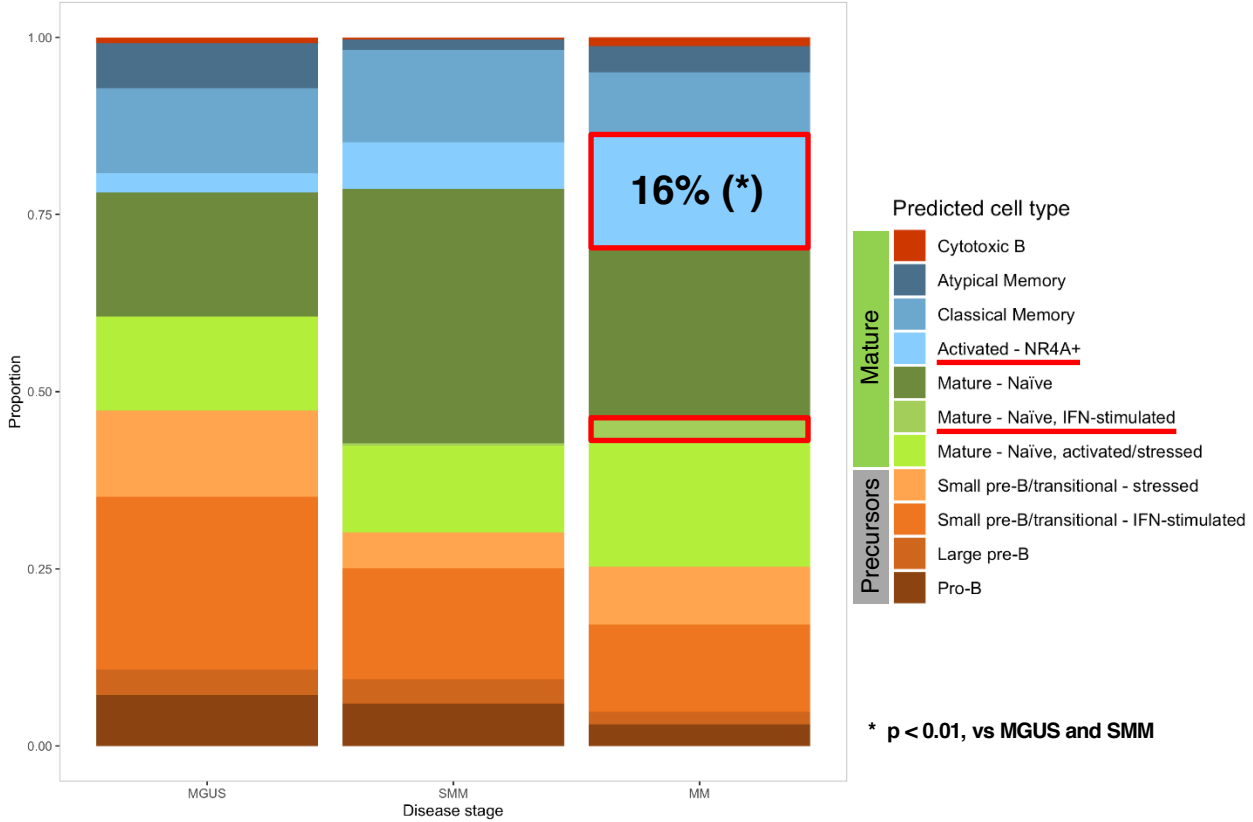



# Multiple Myeloma B cells show different functional clustering



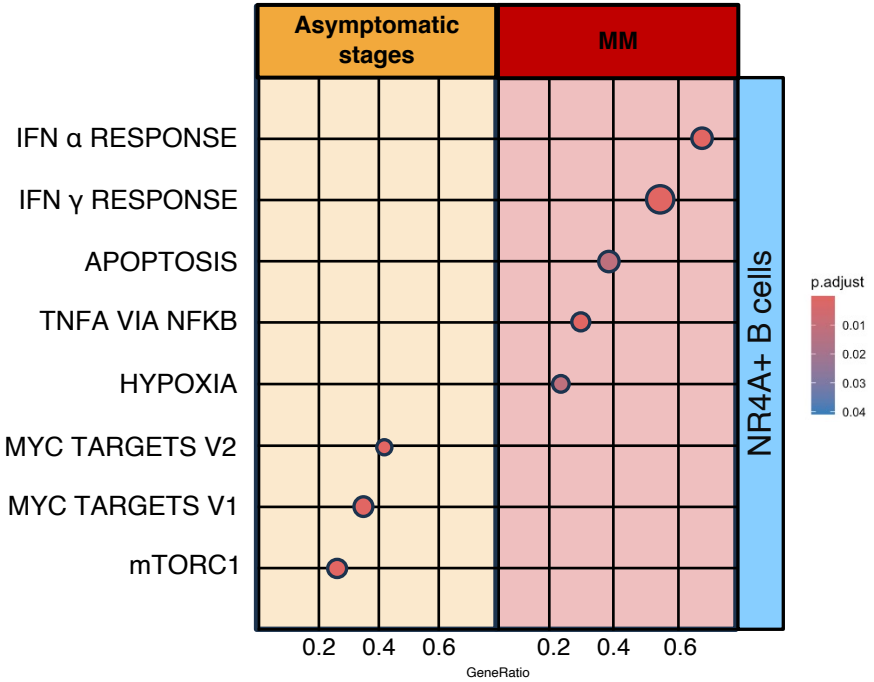
# Marker genes highlight IFN-stimulated and NR4A+ mature B subsets

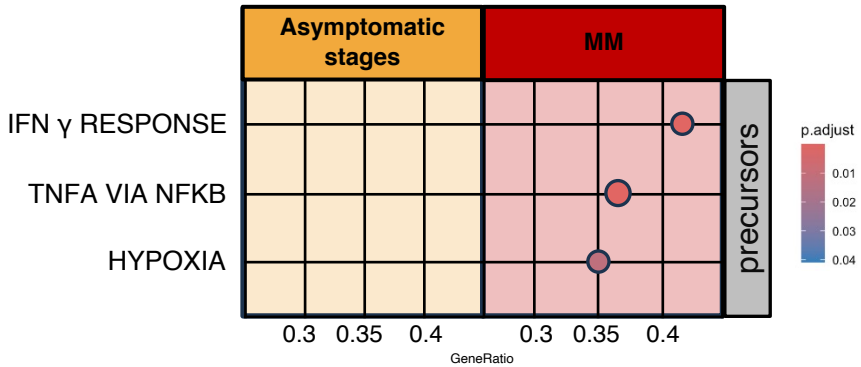
# Activated NR4A+ and IFN-stimulated subsets expand in symptomatic disease



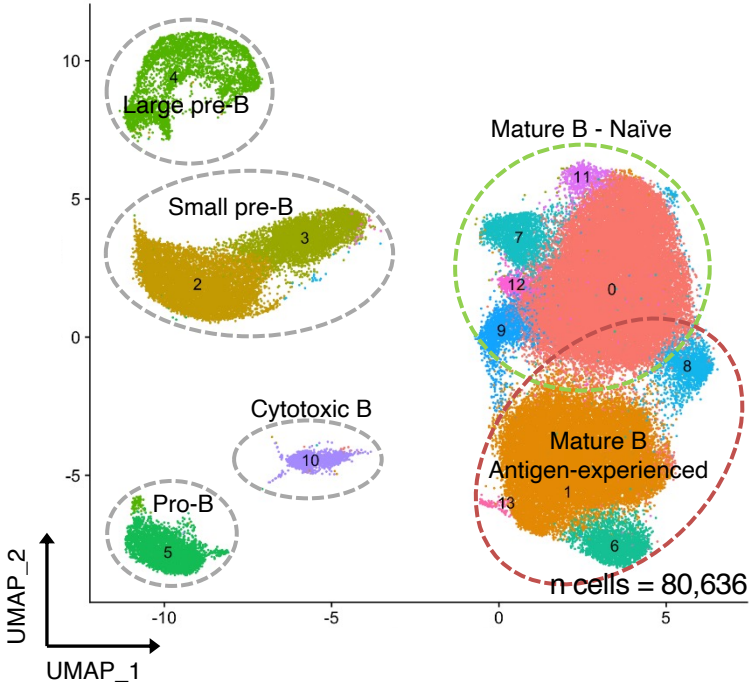

* $p < 0.01$, vs MGUS and SMM

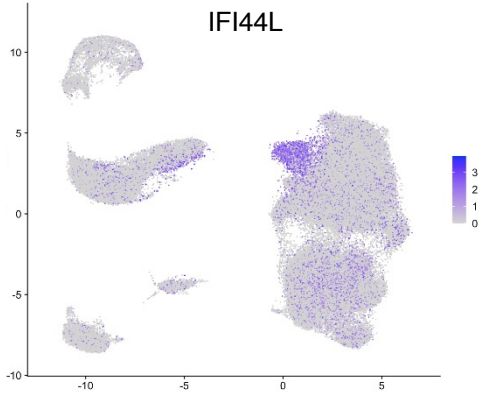
# Precursor B cells in MM herald the derangement of activated B cells

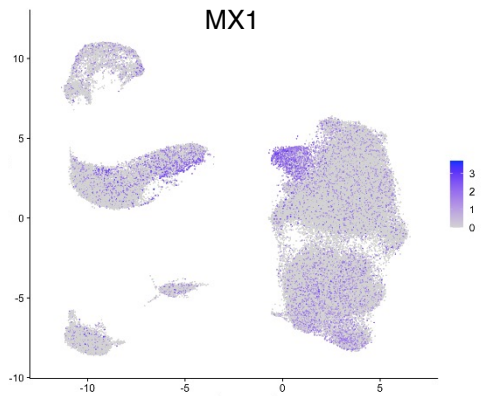


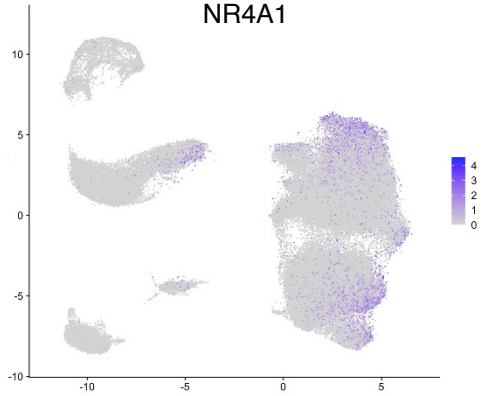



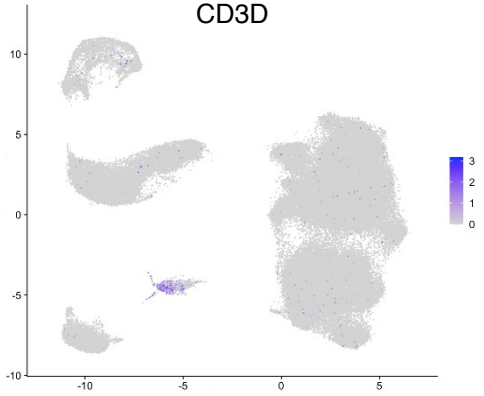
# NR4A+ and IFN-stimulated validation in a MM external dataset



# Conclusions

- Precursor stages of B cells are significantly reduced in overt myeloma, suggesting an impaired development
- In MM, NR4A+ and IFN-stimulated B cell expansion reflects an activated and stimulated microenvironment
- Impaired B cell precursors anticipate dysfunctional signalling observed in mature and activated stages
- Asymptomatic stages retain pathways related to physiologic B cell function and proliferation (Ab-secreting cells development, germinal center-like reactivity)

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