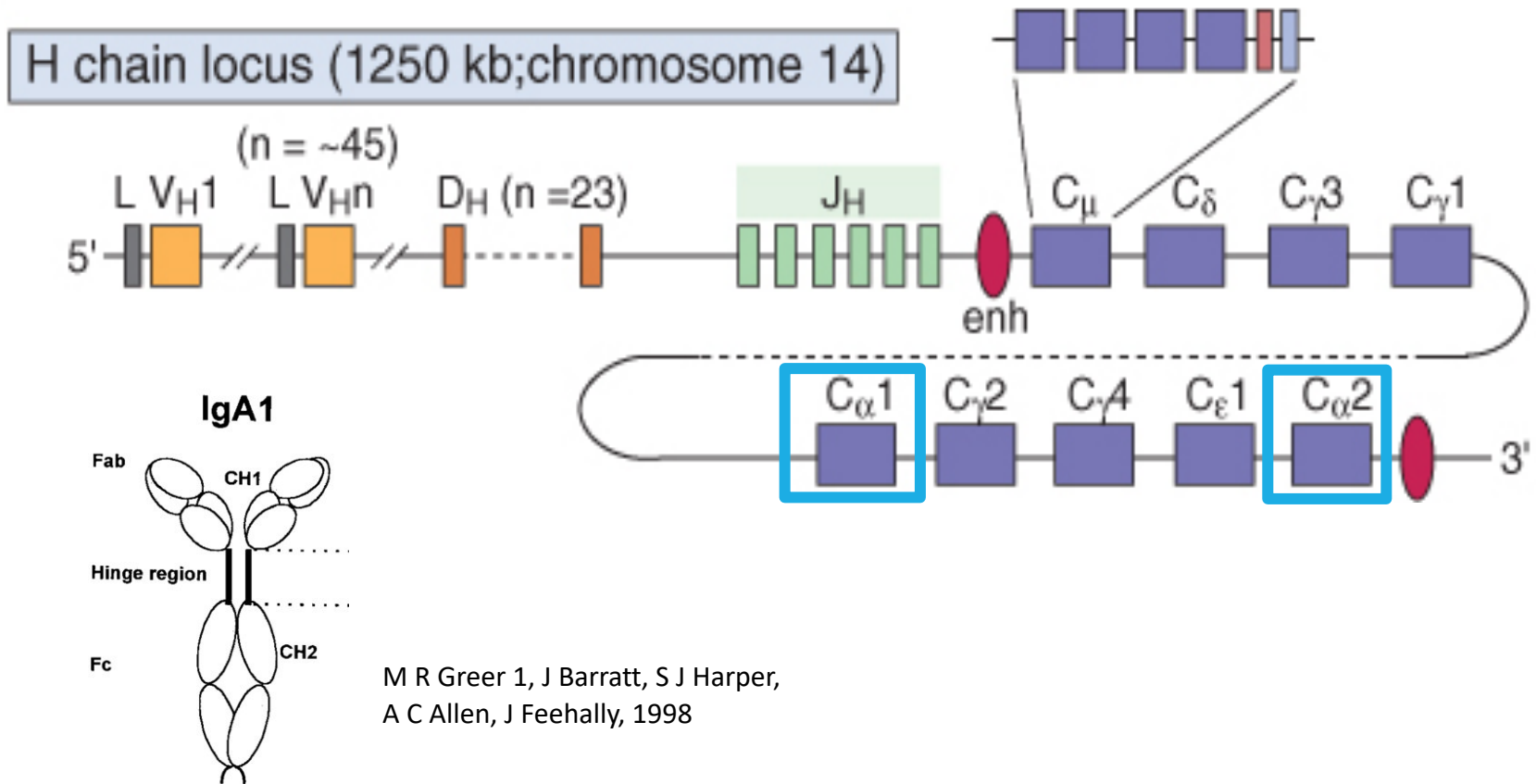


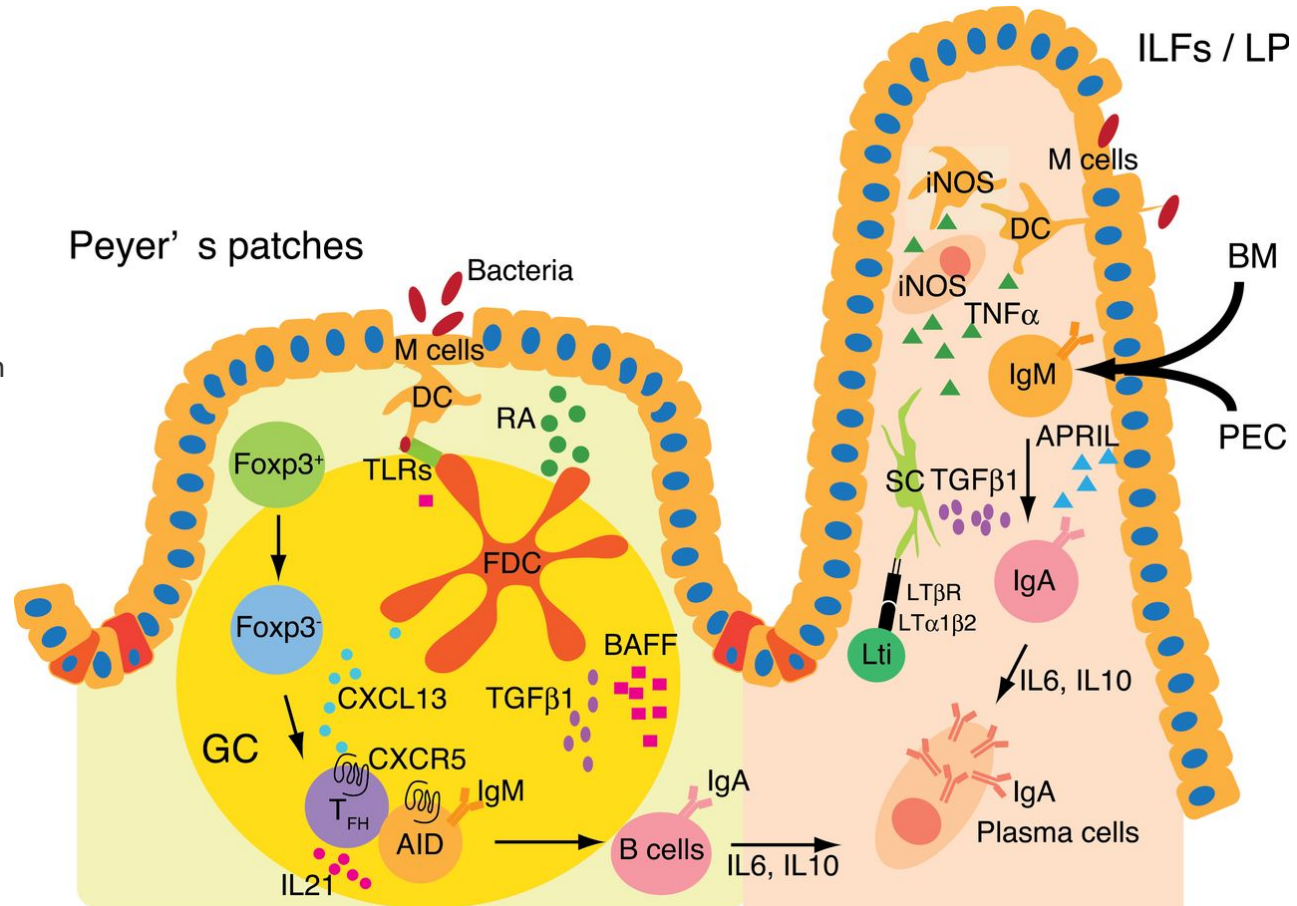
# IgA clonal lineage analysis reveals class switch dynamics in human gut

Hadas Neuman, Giuliana Magri, Andrea Cerutti & Ramit Mehr



# IgA can be induced in GC or in the ILF/lamina propria

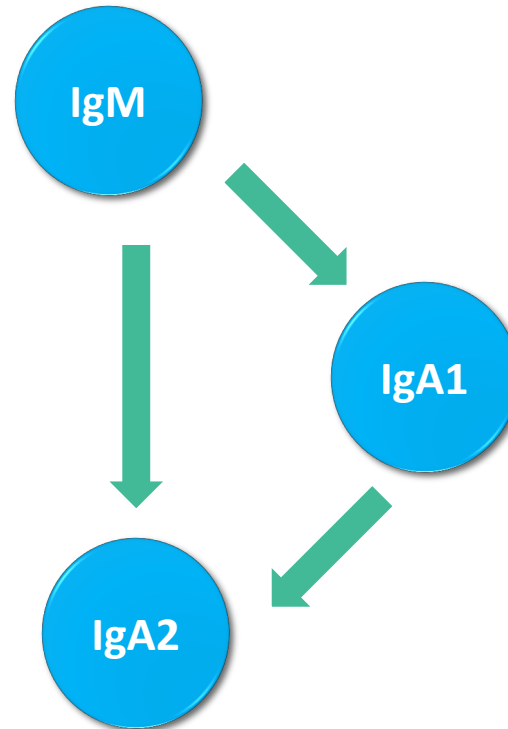
Suzuki & Nakajima, 2014  
 Int Immunol, Volume 26,  
 Issue 9, September 2014,  
 Pages 489–494,  
<https://doi.org/10.1093/in-timm/dxu059>



# Research Questions

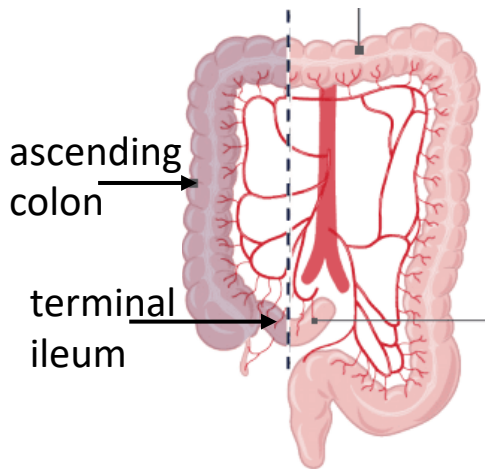
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- Does most switching into IgA2 go directly from IgM (or IgG), or **sequentially** via IgA1?
- Does this switching occur **mostly within GCs** or outside them?

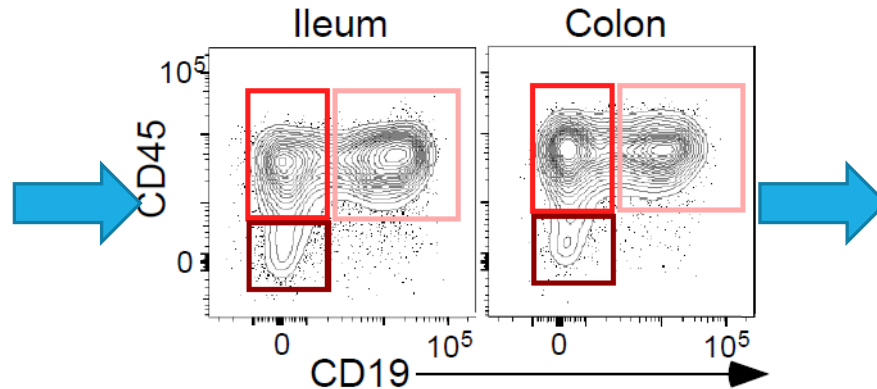


# Data: HTS of amplified Ig genes from human ileum & colon biopsies

right hemicolectomy



<https://www.ccalliance.org/blog/patient-support/types-of-colorectal-cancer-resection-surgeries>



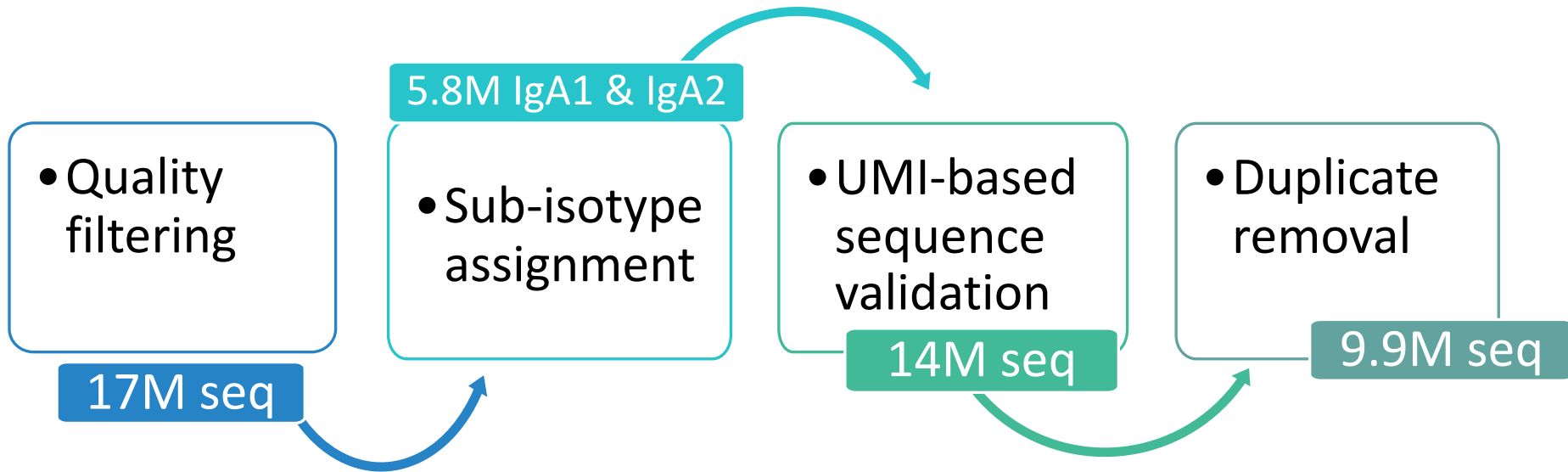
<https://www.illumina.com/systems/sequencing-platforms/miseq.html>

18,499,579 sequences were received

Dr. Giuliana Magri & Prof. Andrea Cerutti

# Data processing

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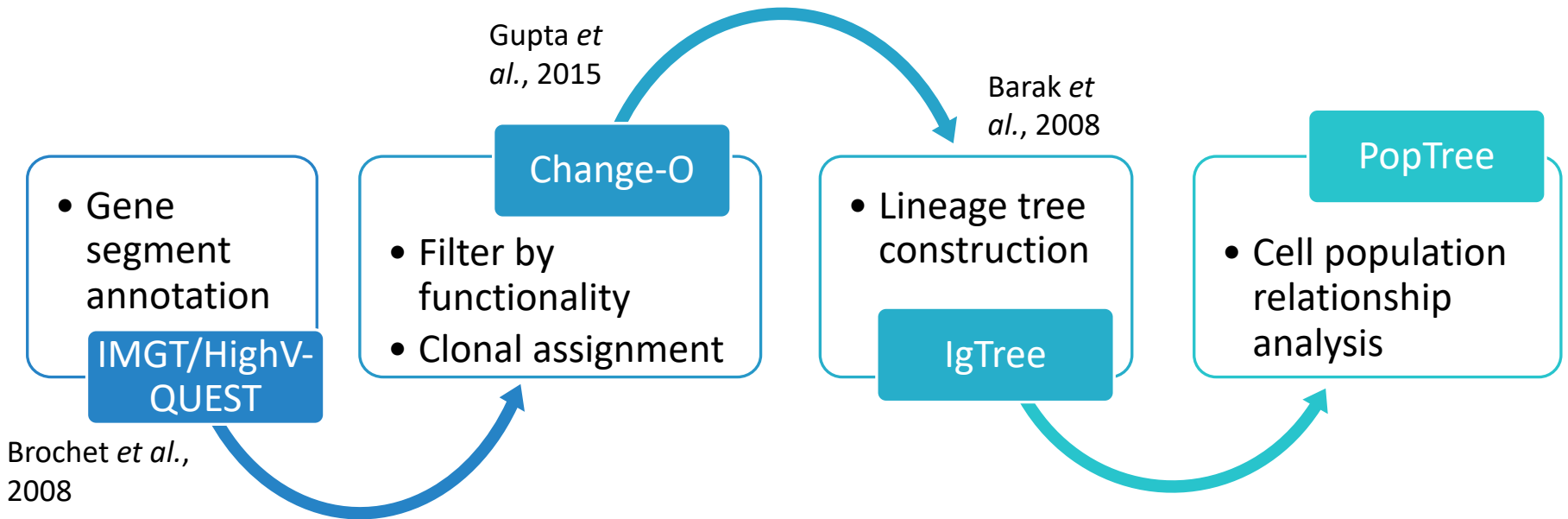


**Most steps were done using pRESTO**

Vander Heiden et al., 2014

# Data analysis

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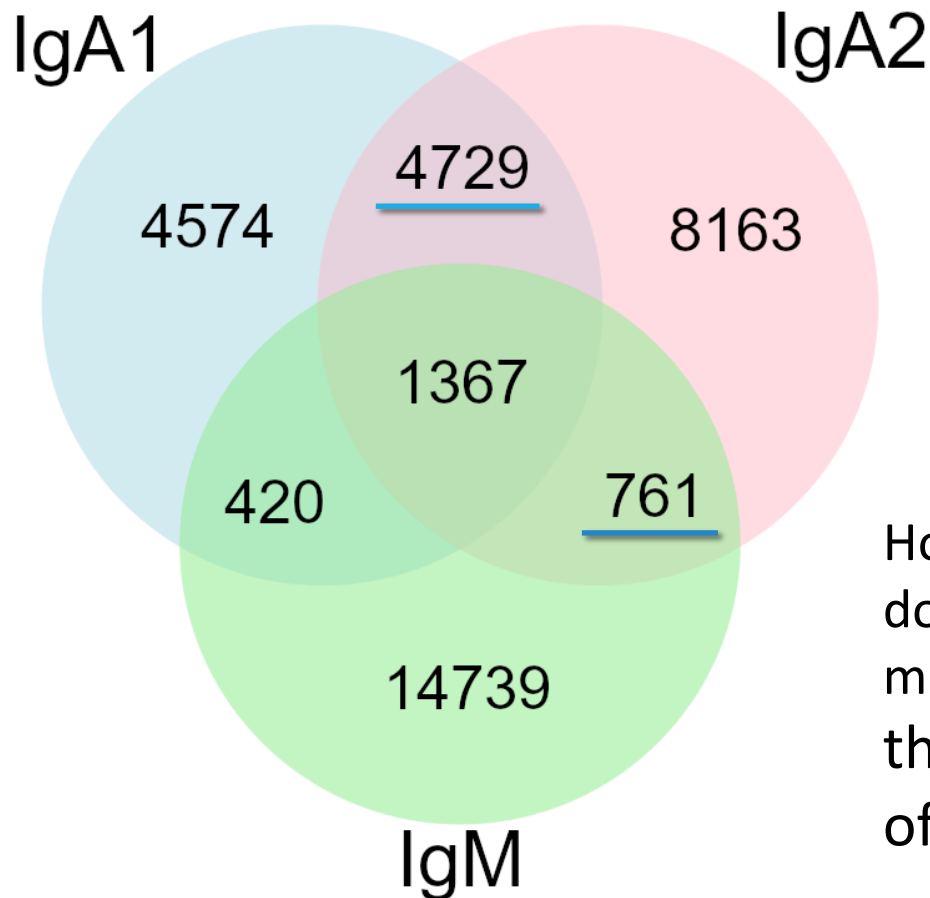


**274,706 trees were constructed and analyzed**

More clones were shared between IgA1 and IgA2 than between IgM and IgA2

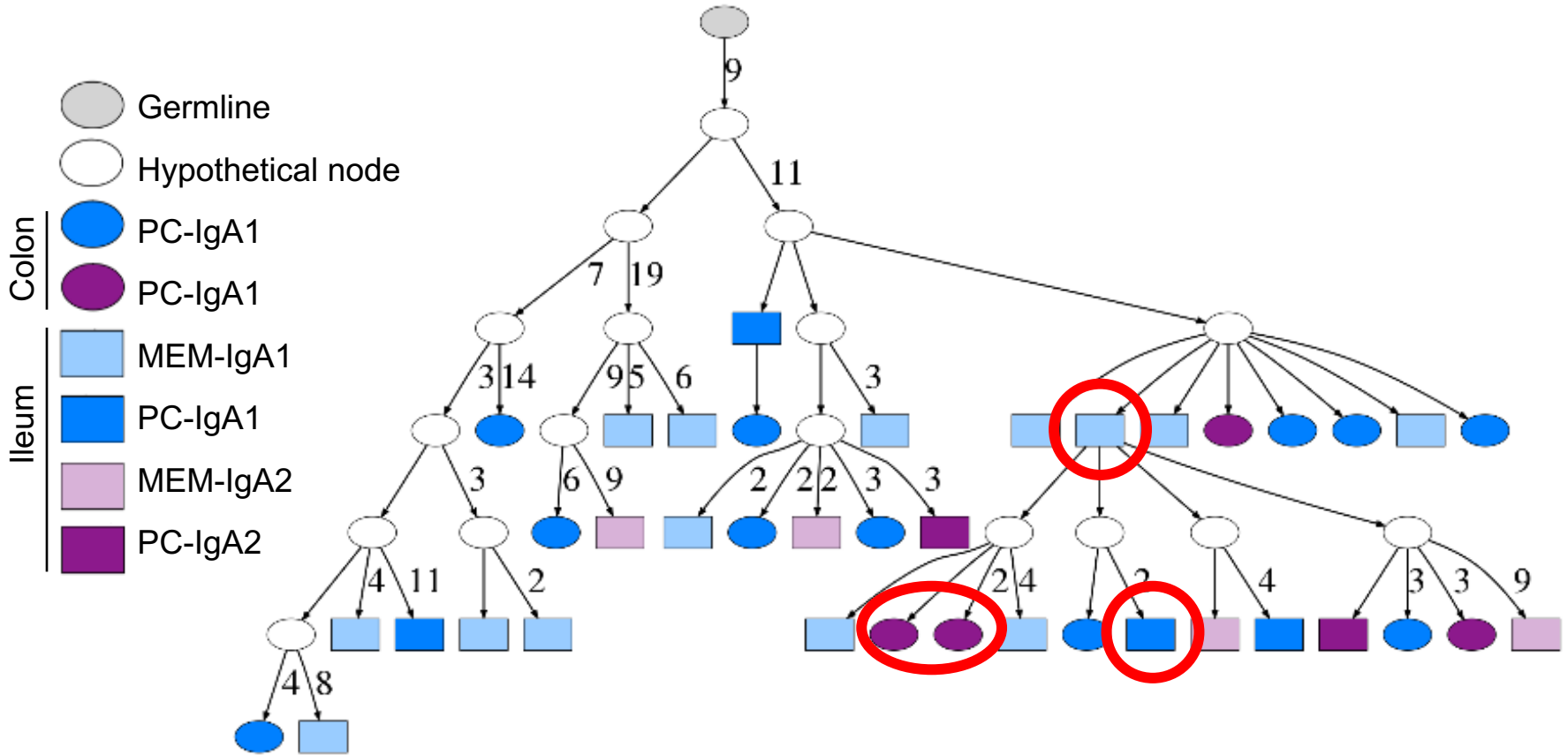
---

Donor 1:  
(Results were  
similar in all  
Donors)



However, this  
does not say  
much about  
the actual order  
of switching

# Ig Lineage Trees As Molecular Archeology

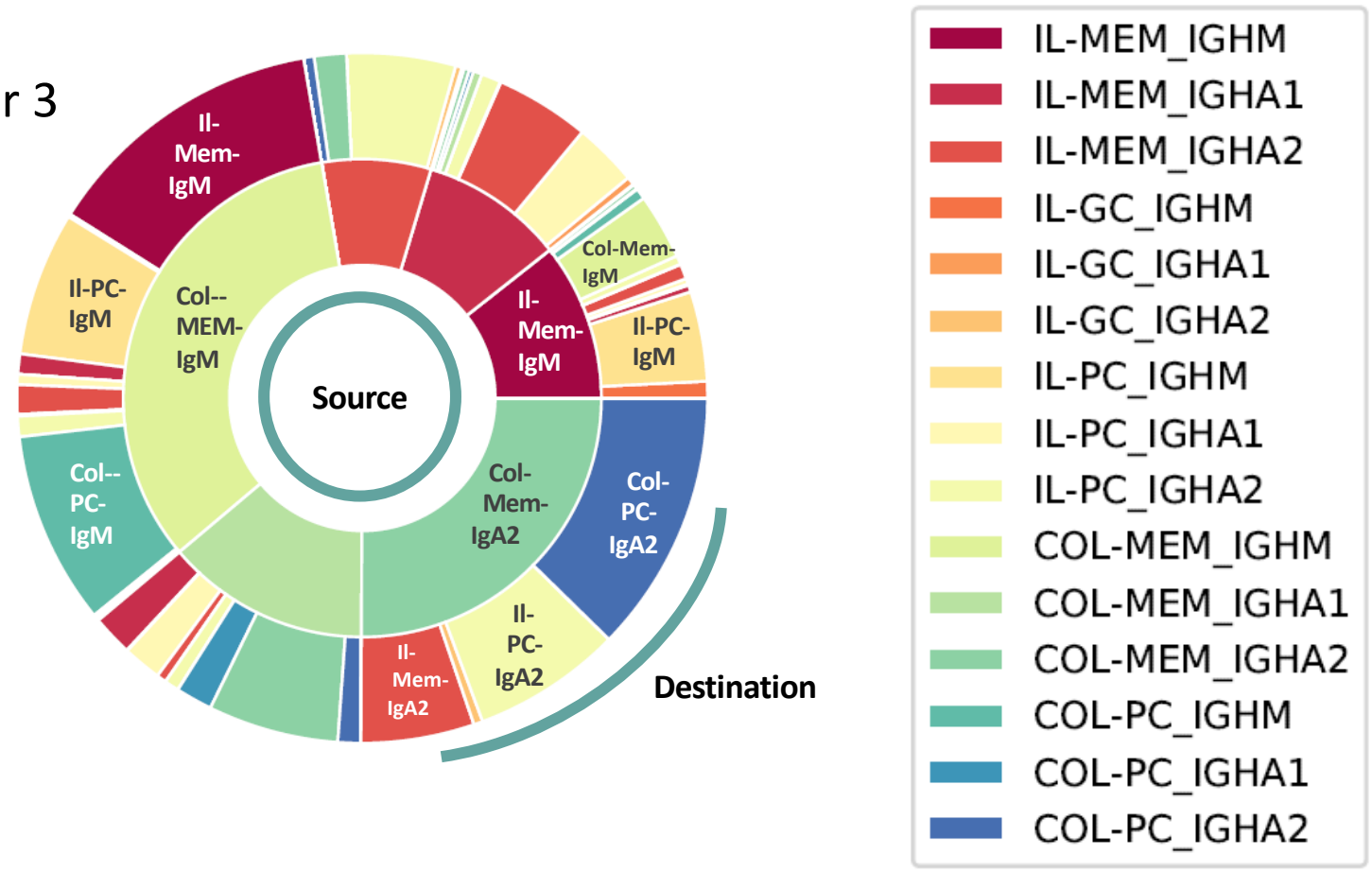


Summarize each repertoire transitions



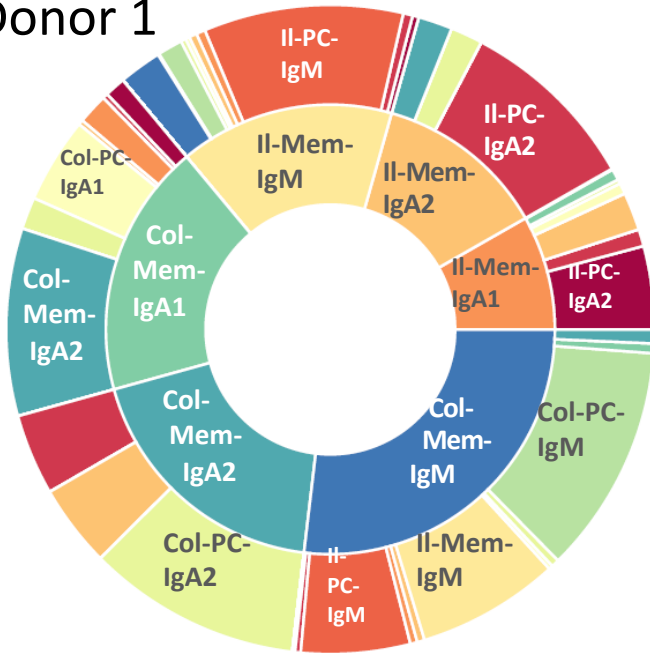
# IgM cells tend to change location or population rather than switching

Donor 3

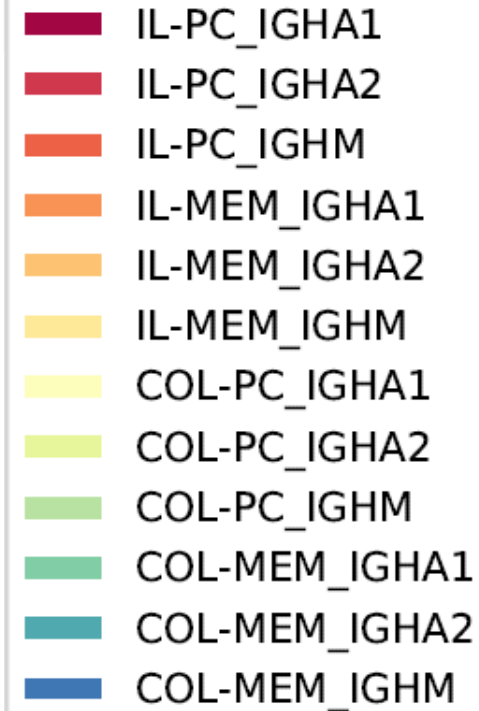
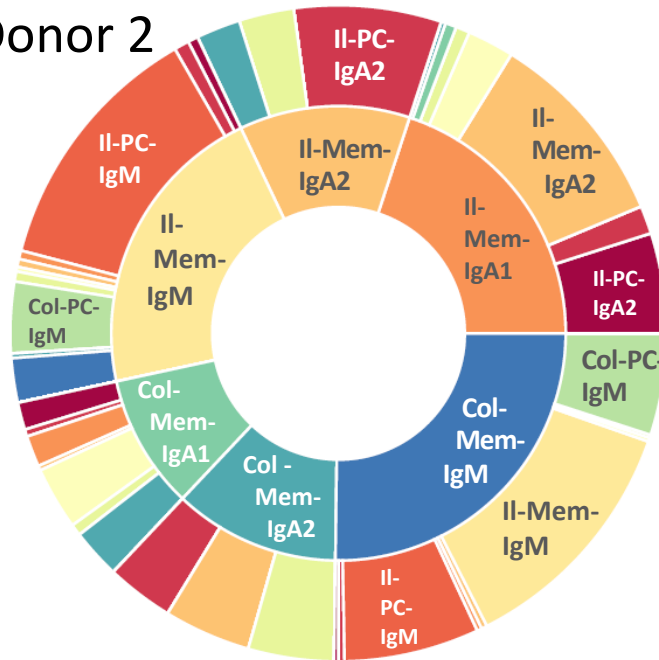


# Most abundant class switching in the ileum and colon is from IgA1 to IgA2

Donor 1

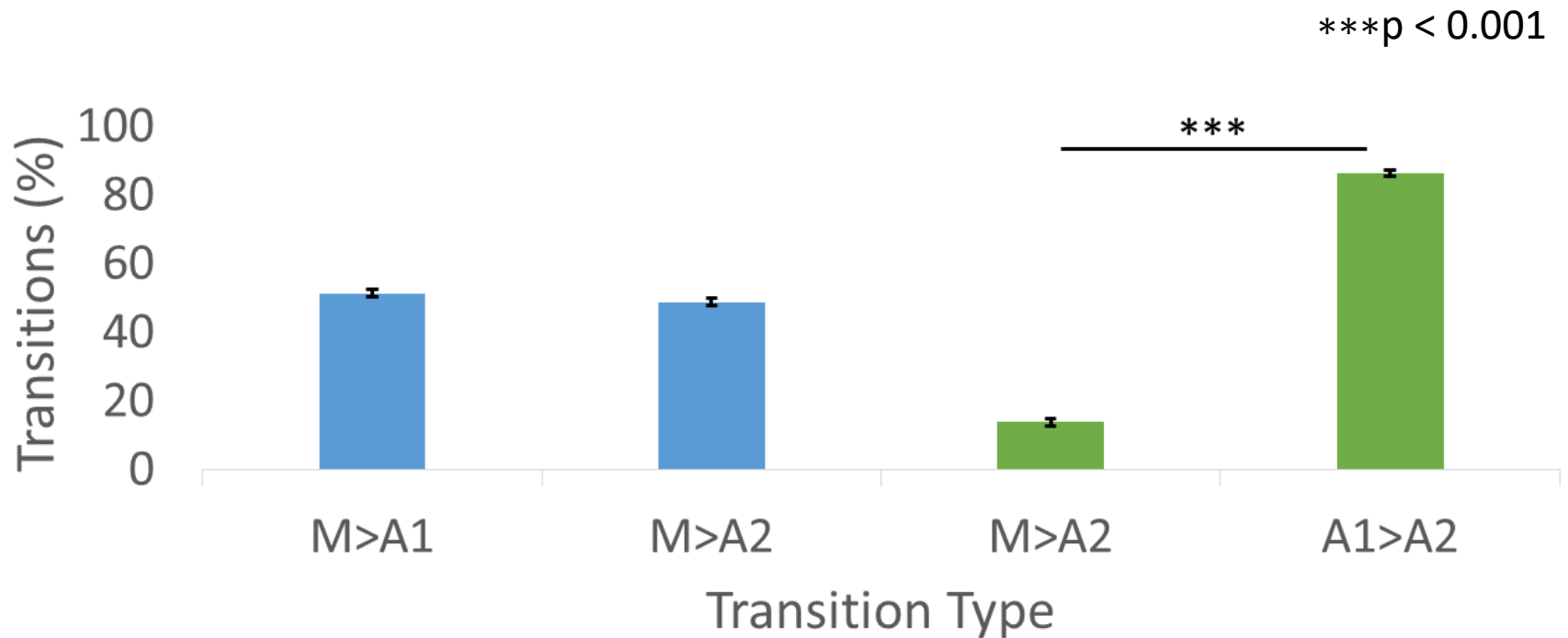


Donor 2

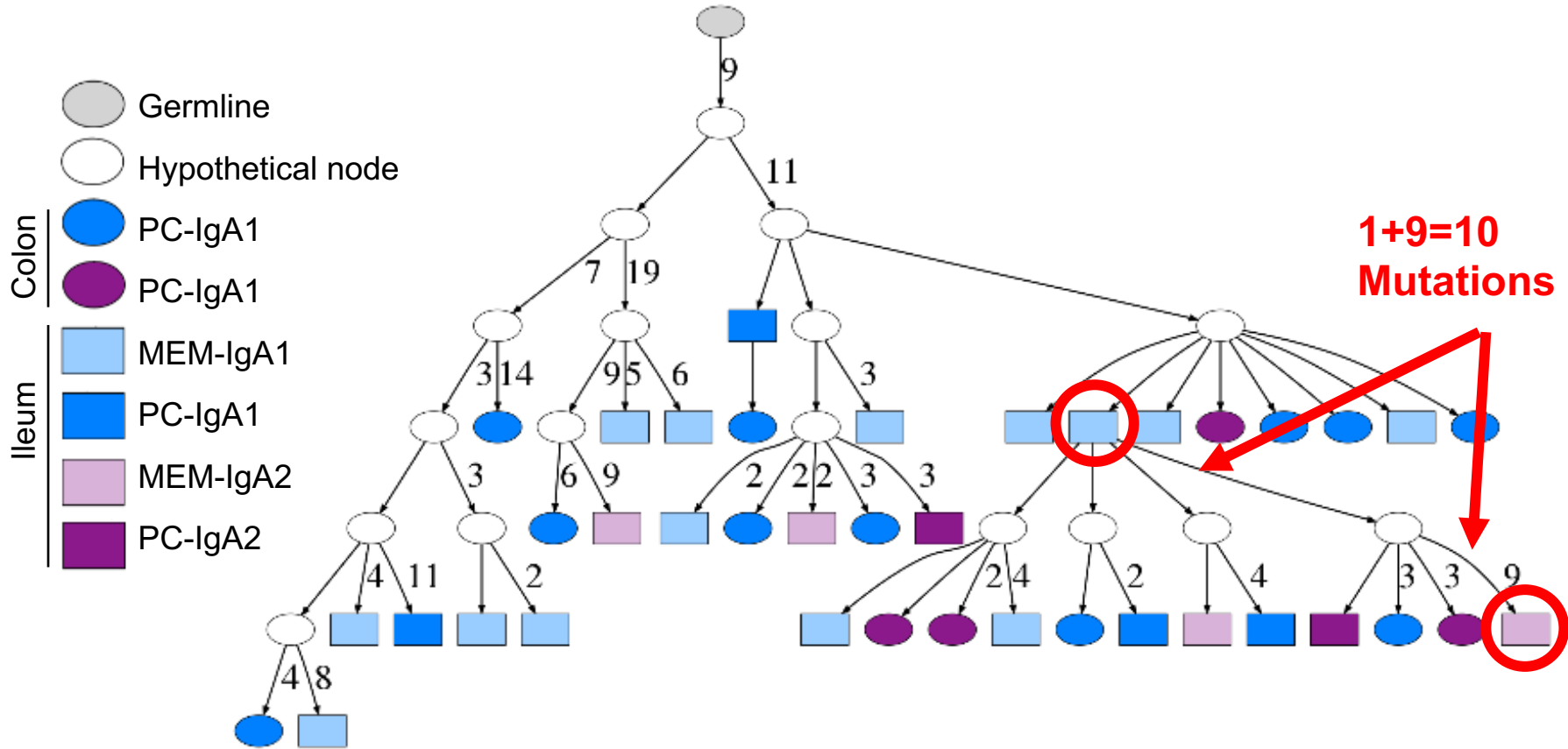


IgA1 to IgA2 switching was significantly more abundant than IgM to IgA2

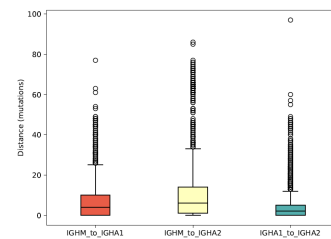
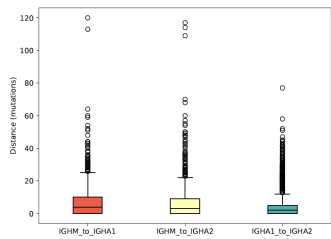
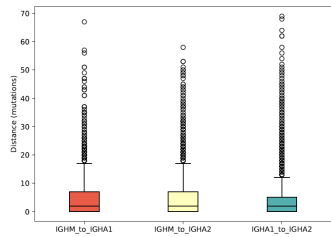
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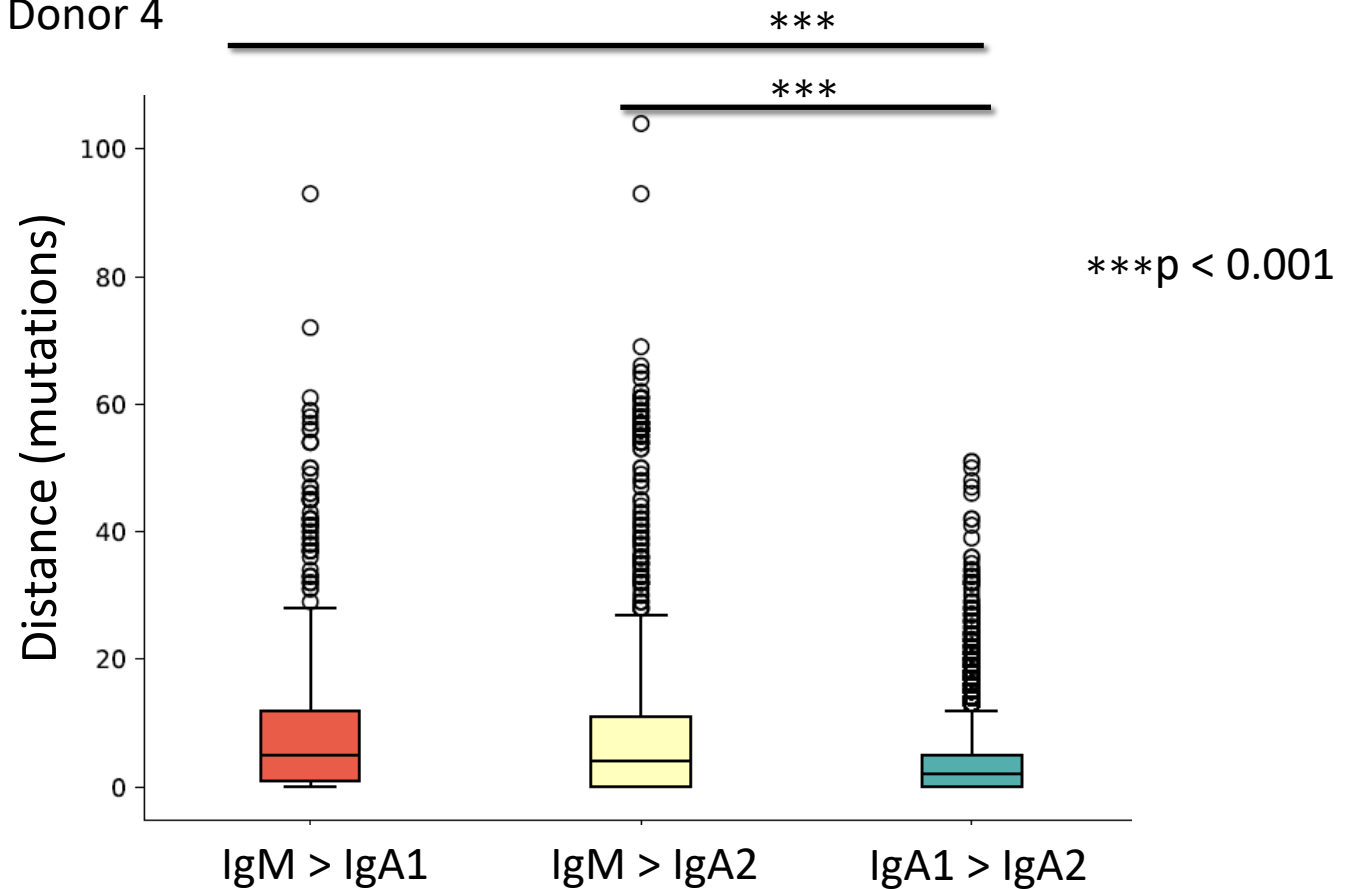
# Ig Lineage Trees As Molecular Archeology



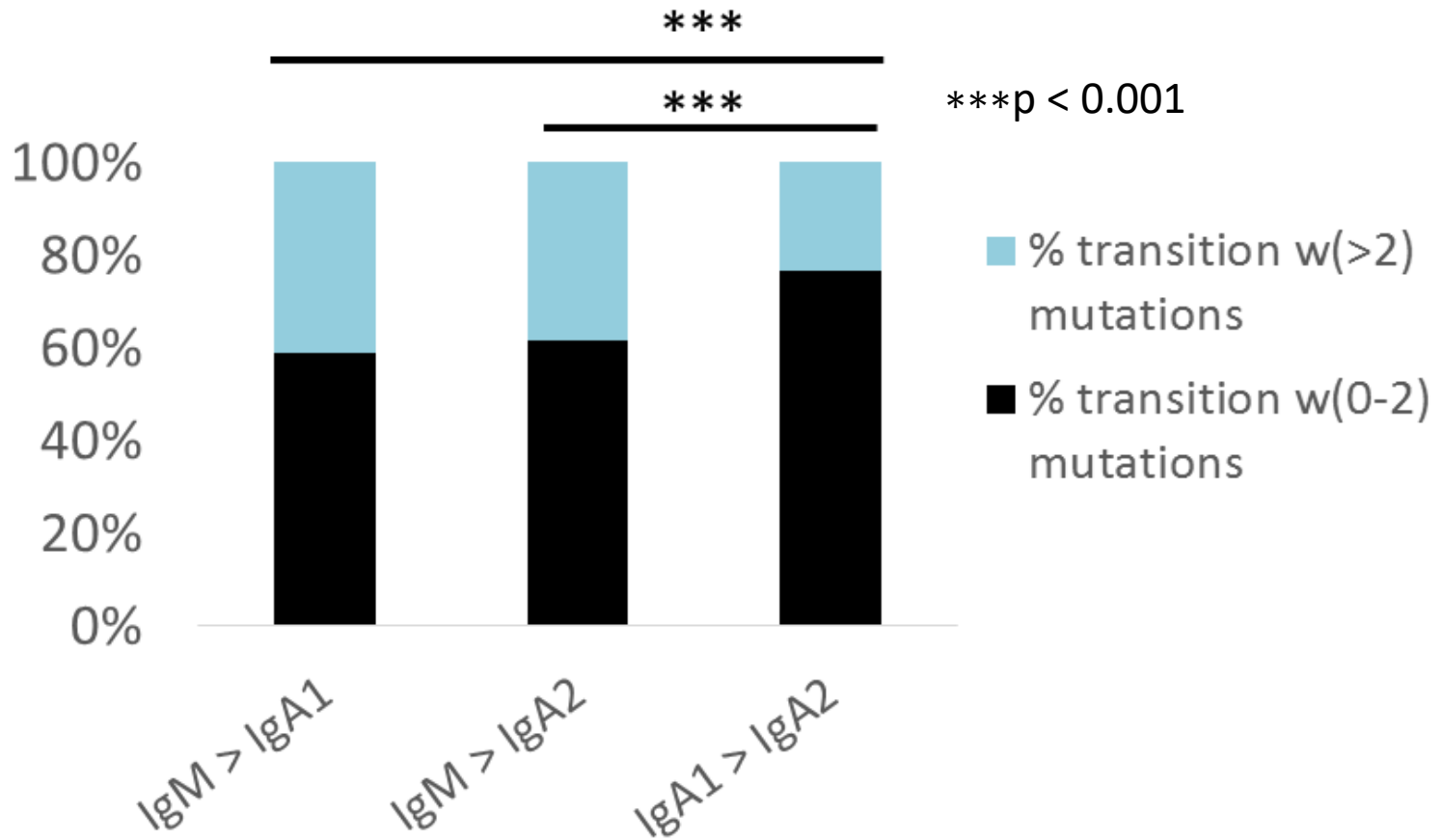
# IgA1-to-IgA2 switches were associated with significantly fewer mutations than switches from IgM



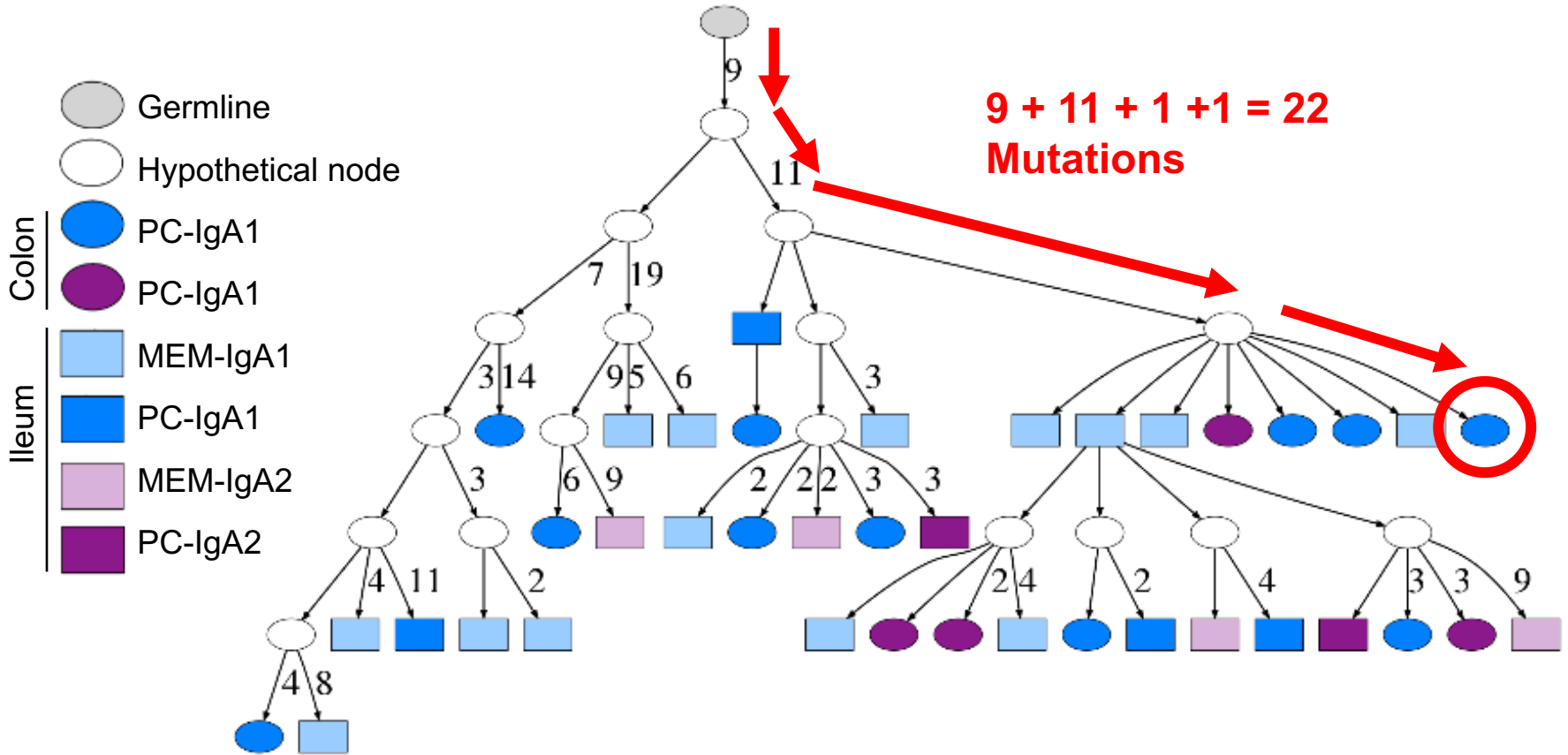
Donor 4



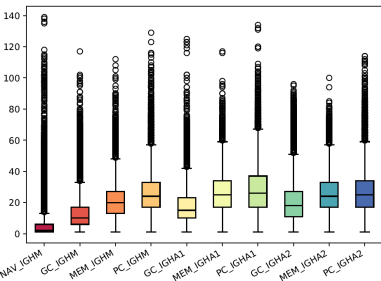
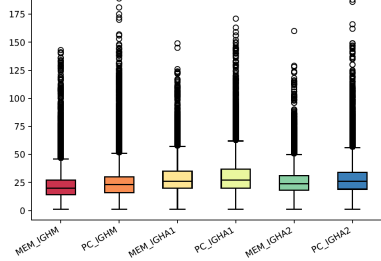
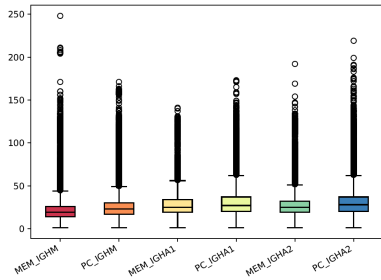
# Most IgA1-to-IgA2 switches were associated with at most two mutations



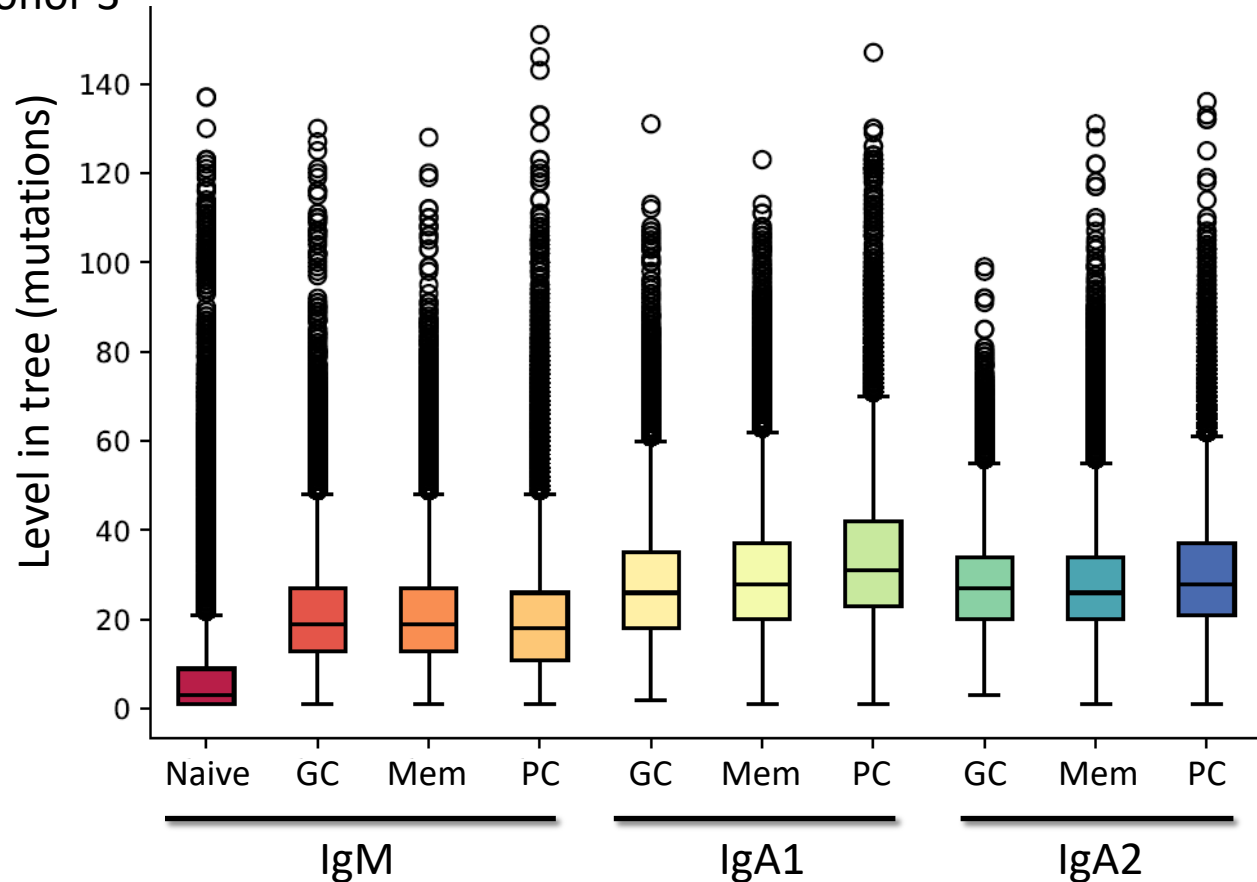
# Ig Lineage Trees As Molecular Archeology



# IgM cells appeared in significantly higher levels than IgA1 and IgA2

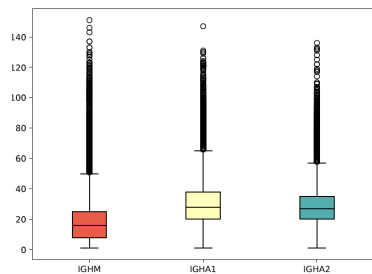
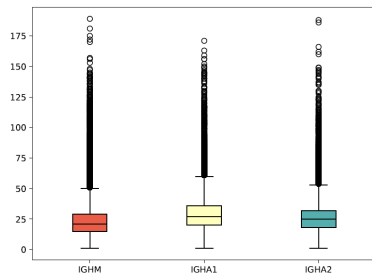
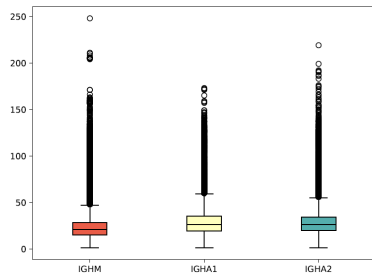


Donor 3

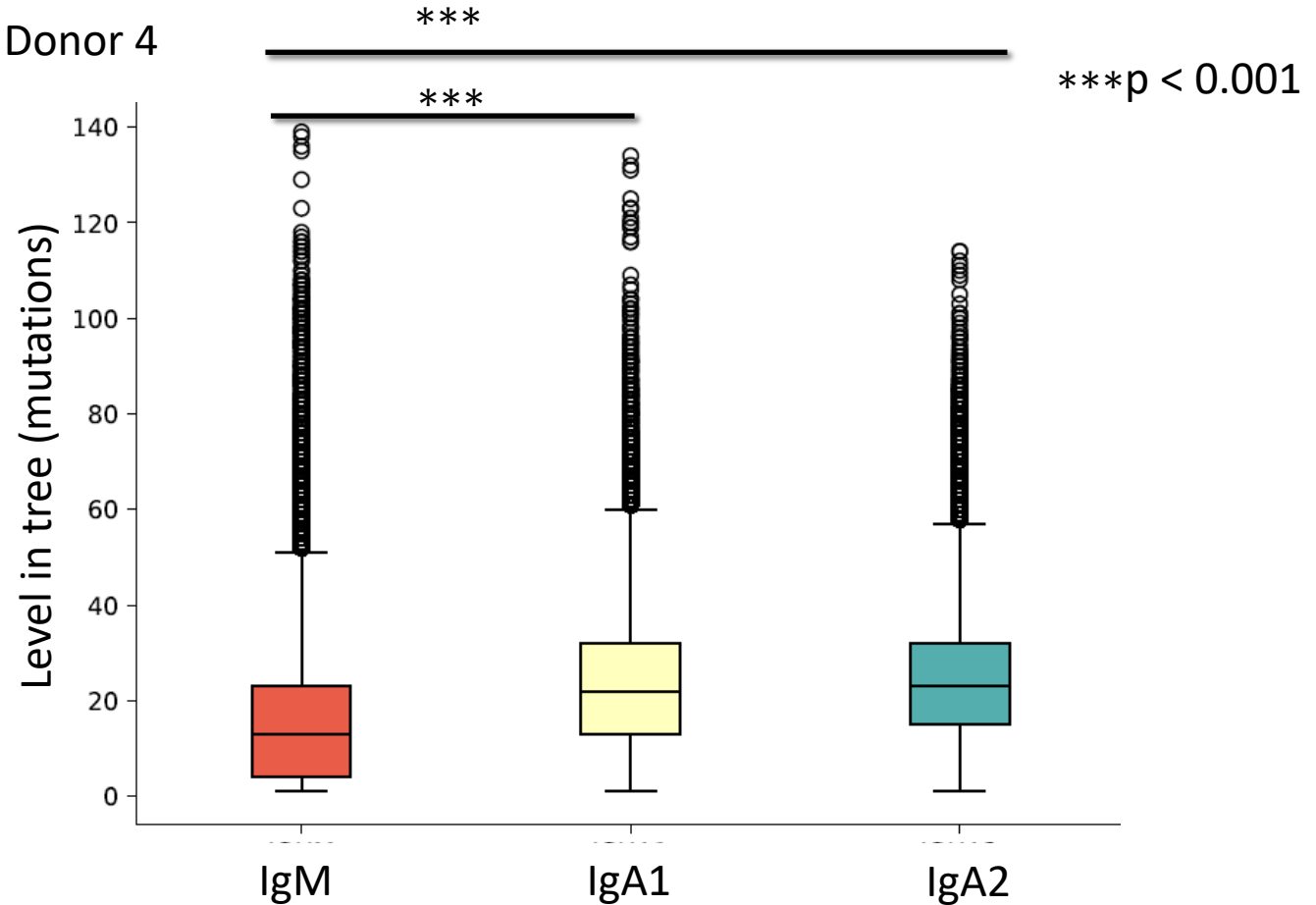




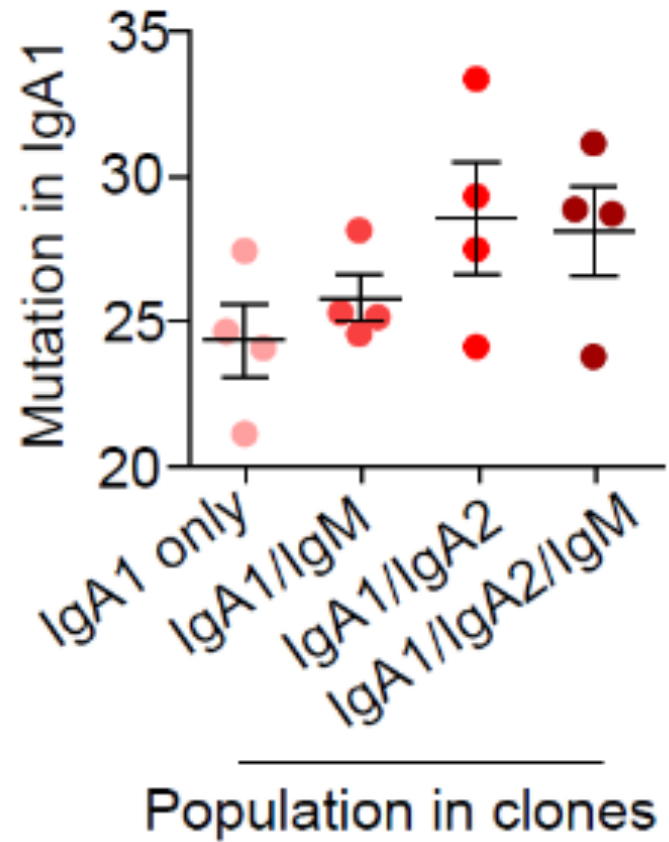
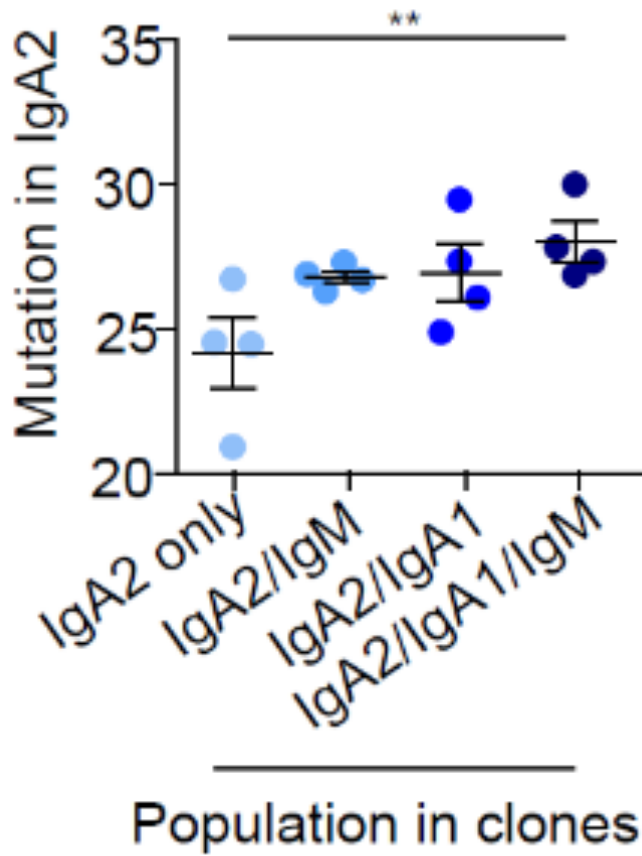
# IgM cells appeared in significantly higher levels than IgA1 and IgA2



Donor 4



The average number of mutations in mixed IgA2<sup>+</sup> clones was significantly larger



# Conclusions

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Overall, these results show that sequential IgM-to-IgA1-to-IgA2 switching is a much more common pathway than direct IgM-to-IgA2 switching.

The large number of transitions involving fewer than two mutation indicates the dominance of the T cell-independent IgA synthesis.

# Acknowledgment

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