

Program ImmRep meeting @ Dresden

Dynamics of Immune Repertoires: Exploration and Translation

working group “The primary B-cell immune response”

17th to 20th July 2022

<https://www.pks.mpg.de/immrep22/>

<https://docs.google.com/spreadsheets/d/1QVNY0GDuig3sH9K9nE9-knrV-oYa4hDcvJ3pvgVwQc/edit#gid=86354089>

Guidelines for presentations:

1. 5-10 slides—not more than 10 minutes (and less in more crowded sessions).
2. Put name and session in talk file title.
3. Very minimal or no background needed.
4. No acknowledgements.
5. End with take home points AND discussion questions—what do you want people to think about based on the presentation?

DAY 1

Morning: GERMINAL CENTERS

Moderators: Mark Shlomchik & David Tarlinton

I. Altered signaling and metabolism

- A. Shlomchik: "GCBC Oxidize Fatty Acids as a major metabolic energy pathway"
- B. Bannard: "Independent regulation of cyclic re-entry and B cell refuelling in GCs"
- C. Nussenzweig: "Role of BCR signaling in the light zone"
- D. Hershberg: "B cells undergo classical conditioning through calcium mediated BCR signaling and the relative activation of proliferation and death signals."

II. Positive selection

- A. Victora: "Measuring T cell help to B cells in Germinal Centers"
- B. Meyer-Herman: "Two signals are required to determine B cell selection and the number of divisions"
- C. Zarnitsyna: "Which signals control initial B cells' entry and positive selection within the Germinal Centers?"
- D. Winkler: "The role of fas/CD95 for positive selection in the germinal center"
- E. Hodgkin: "Mapping the action of molecular fate timers onto the GC selection engine"

III. Differentiation and counterselection

- A. Kurosaki: "Differentiation of GC B cells towards Memory Cell Fate"
- B. Kelsoe: "Persistence of MHCII-negative GC B cells"
- C. Shlomchik: "IL-21R and CD40 signals synergistically induce c-Myc and direct differentiation in GCBC"
- D. Zikherman: "B cell-intrinsic negative feedback loop to constrain clonal immunodominance"
- E. Meyer-Herman: "Antibody feedback to promote evolution of antibodies against hidden epitopes"
- F. Faro: "What trait(s) is(are) selected during GC B cell selection?"

Afternoon: GERMINAL CENTERS

Moderators: Garnett Kelsoe & Oliver Bannard

I. GC heterogeneity, recycling, cell movement and cellular interactions

- A. Qi: Phase transition during GC formation
- B. Bannard: Speculation 1. An unexplained link between cycling and state.
- C. Tarlinton: "IL-21 acts beyond the immunological synapse to establish and sustain germinal center dynamics"

II. What forms of antigen are B cells encountering in the GC?

- A. Kelsoe: "Dark antigen" and the generation of protective breadth to influenza virus Has.
- B. Zarnitsyna: The dual role of antibody feedback during the GC reaction
- C. Batista: "It is not soluble affinity, but rather BCR 2D affinity, that selects high affinity B cells in GCs"

III. What are the roles of FDCs, TBM and other accessory cells in the GC. How do B cells signal back to these cells?

- A. Bannard: Speculation 2. Tingible body macrophages; Normal cells performing abnormal tasks?
- B. Kelsoe: What do CD90^{neg/lo} and CD90^{hi} Tfh do in secondary responses?

IV. What role does negative selection (against self) play in GCs, and how?

- A. Faro: How do Tfr cells control the intensity and duration of germinal centers?
- B. Kelsoe: Affinity maturation in GC B cells lacking BAK and BAX.
- C. Zikherman: Negative regulation of BCR signaling and counter-selection of GC B cells.

DAY 2

Morning: B CELL MEMORY

Moderators: Gabriel Victora & Michael Cancro

I. Heterogeneity of memory B cells

- A. Shlomchik : New subsets and heterogeneity in mouse and human MBC
- B. Winkler : Transcriptional heterogeneity of human memory B cells
- C. Spencer : Human MZ B cells

II. Development of memory B cells

- A. Shlomchik : Origins of MBC subsets
- B. Meyer-Hermann : Antibody feedback as a mechanism to prevent original antigenic sin
- C. Kelsoe : sizing extra-follicular and GC B cell populations and their contributions to memory responses
- D. Nussenzweig : Human memory B cell development in the presence of pre-existing antibodies

III. Functions of memory B cells

- A. Kelsoe : location vs. commitment and Bmem re-entry into GCs (maybe a look at Tfh if it would be interesting)
- B. Victora : Labeling Pre-Germinal Center Memory
- C. Qi: Dominance of GC-derived memory B cells
- D. Cancro: Turnover and fate mapping of Tbet+ memory B cells
- E. Carsetti : In vivo response of vaccine-induced memory B cells in human

Day 2 - Afternoon: PLASMABLASTS and PLASMA CELLS

Moderators: Harinder Singh & David Allmann

I. Establishing the plasma cell fate

- A. Hodgkin : Division and time at the intersection of switching and plasma cell differentiation
- B. Shulman: Post transcriptional regulation of B cell differentiation
- C. Singh: Tracking and analyzing the genomic states of plasma cell precursors
- D. Kurosaki : Differentiation to plasma cells and their fates
- E. Allman : Can we exploit mTOR/Notch signaling to amplify early antibody titers?

II. Early plasma cells in infection and microbial symbiosis

- A. Bannard : A snapshot of plasma cell development during a viral infection
- B. Cancro: Spleen-resident Tbet+ Bmem are self-renewing plasma cell progenitors
- C. Pabst : Newly recruited gut IgA secreting cells phenotypically differ from established plasma cells

III. Plasma cell heterogeneity

- A. Qi : Plasma cell heterogeneity and long-lived subsets
- B. Winkler : Transcriptional heterogeneity of human circulating plasmablasts
- C. Tarlinton: Timestamping antibody-producing cells at homeostasis to assess lifespans and mechanisms of turnover
- D. Pabst : Clusters or gradients? Heterogeneity of intestinal IgA secreting cells
- E. Fillatreau: Characterization and Therapeutic Utilization of Regulatory Plasmocytes

DAY 3

Morning: EXTRA-FOLLICULAR RESPONSES, CYTOKINES, AND ANTIGEN PRESENTATION

Moderators: Simon Fillatreau & Nicole Baumgarth

- A. Singh : Gene regulatory network regulating the bifurcating EF and GC B cell responses
- B. Baumgarth : TLR-mediated signals drive EF responses
- C. Batista : Role of IL-4 in EF B - T cell interactions
- D. Shlomchik : Role of IL-12 in directing EF responses
- E. Tarlinton : How IL21 acts on B and T cells to influence GC commitment
- F. Fillatreau : SLPI-producing ASC in EF responses
- G. Hutloff : GC-like reactions in non-lymphoid tissues
- H. Baumgarth : Extrafollicular-derived plasmablasts in the lung after influenza infection

Afternoon: DISCUSSION ON FUNDAMENTAL MECHANISMS SEEN SO FAR

Moderators: Mark Shlomchik & Simon Fillatreau

DAY 4

Morning: MUCOSAL IMMUNITY and PATHOGENS

Moderators: Oliver Pabst & Jo Spencer

I. Functions of gut-associated lymphoid tissues

- A. Pabst : Towards fate tracking of Peyer's patch derived plasma cells
- B. Winkler : What is the origin and potential pathogenic role of circulating IgA plasmablasts in humans ?
- C. Spencer: B cell subset relationships in human GALT

II. Mucosal GC responses

- A. Ellebedy : Persisting GC in secondary lymphoid tissues after vaccination in humans
- B. Baumgarth : Antibody-mediated collapse of germinal centers following *Borrelia burgdorferi* infection
- C. Pabst: High microbiota reactivity relies on somatic mutations

III. Mucosal memory

- A. Hutloff : Memory B cells in lymphoid and non-lymphoid tissues
- B. Wardemann : *Plasmodium falciparum* surface protein CSP

IV. Immune responses to pathogens and vaccines

- A. Zarnitsyn : Durability of antibody responses to different virus and vaccine antigens
- B. Winkler : Class switch towards non-inflammatory IgG isotypes after repeated SARS-CoV-2 mRNA vaccination
- C. Wardemann : The anti-Klebsiella response

Afternoon: AUTOIMMUNITY AND ALLERGY

Moderators: Hedda Wardemann and Julie Zikherman

I. Early steps in B cell activation and tolerance

- A. Hodgkin- Variation in B cell sensing thresholds contributes to autoimmune disease
- B. Zikherman- Antigen display on viral-like particles evades B cell tolerance mechanisms

II. Regulation of B cell responses in SLE models

- A. Winkler- The role of Dnase1I3 and FcgR2b in murine lupus
- B. Zikherman-BCR isotypes and inhibitory receptors regulate self-reactive B cell entry to EF and GC responses
- C. Shlomchik- ABC in SLE mice

III. Human SLE

- A. Spencer: B cell IFN signatures
- B. Wardemann : BM PCs in SLE patients

IV. B cell depletion in SLE

- A. Cancro: “Tbet^{hi} splenic ABCs resist anti-BAFF and anti-CD20 in murine Lupus models.”
- B. Winkler: CD19 CAR-T therapy in SLE