EUROPEAN SCIENCE FOUNDATION
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EMBO European Molecular Biology Organization

RESEARCH CONFERENCES

ESF-EMBO Research Conference

B Cells and Protection: Back to Basics

Hotel Eden Roc, Sant Feliu de Guixols (Costa Brava) • Spain
18-23 April 2010

Chair: **Rita Carsetti,** Bambino Gesu Children's Hospital, Rome, IT
Co-Chair: **Deborah K. Dunn-Walters,** King's College London School of Medicine, UK

www.esf.org/conferences/10323

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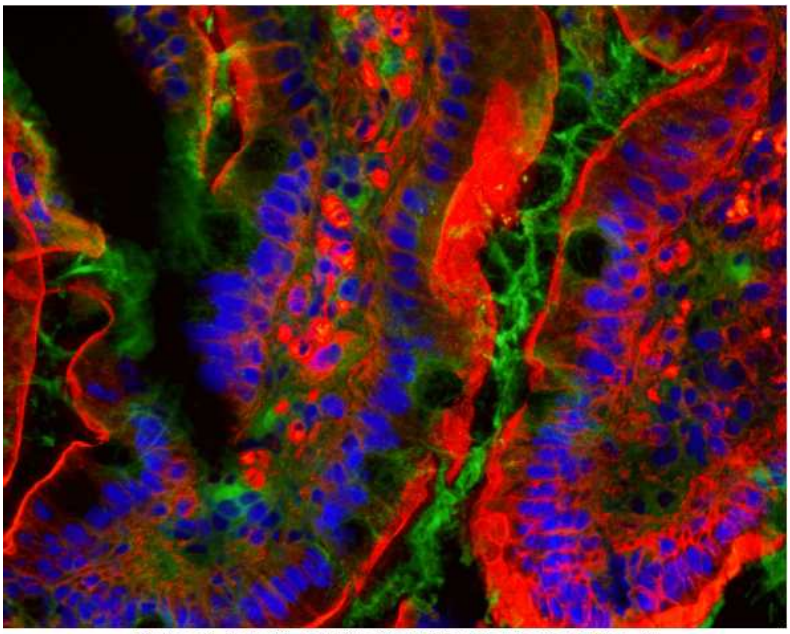
Highlights & Scientific Report



Source: R. Carsetti, Bambino Gesu Children Hospital, Rome, IT

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Conference Highlights

Please provide a brief summary of the conference and its highlights in non-specialist terms (especially for highly technical subjects) for communication and publicity purposes. (ca. 400-500 words)

The 2010 ESF/EMBO meeting on 'B Cells and Protection: Back to Basics' was scheduled to take place in idyllic San Filieu de Guíxols on the coast of Catalonia with a globally representative cast of speakers and session organizers.
However, due the eruption of the volcano, Eyjafjallajokull, most participants and speakers were unable to reach the venue.
Some attending from faraway places, including the USA, Brazil and Israel, boarded planes the previous evening and arrived safely in Barcelona. Fewer than 20 of the expected attendees made it.

However, rather than give up, this small group transformed the get-together into a workshop of sorts.

Executive Summary

(2 pages max)

The meeting thus began with brief overviews of B-cell differentiation and activation, after which the group settled into a full day of thought-provoking talks from all invited speakers and poster presenters in attendance. Within this quickly fashioned but well-constructed framework, a series of timely and conceptually related themes emerged. Judging from the entirety of abstracts submitted
for the originally planned meeting, these represented a solid cross-section of the blueprint originally envisaged by the chairs.
Several talks revolved around understanding the role of commensal microbiota in B-cell development and regulation,
as well as how the immune system manages to avoid eliminating these beneficial microbes. Many of these suggested that normal microbiota could influence the balance of inflammatory responsiveness in a variety of scenarios, including tolerance
and allergy models. Jenny Hansson (Nestlé Center, Lausanne) presented work suggesting that the establishment of normal
peripheral
B-lymphocyte numbers and subsets is independent of neonatal commensal colonization. Nonetheless, work described in the abstracts of several registrants who were unable to attend suggests that splenic architecture and B-cell subsets, as well as the species composition of gut microbiota, can influence one another. In a related presentation, François Leulier (IBDML, CNRS, Marseille) explored the basic principles of this balance by studying how mutualism is maintained in the nuclear factor-κB (NF‑κB) system of Drosophila spp. His findings suggest molecular mechanisms for tuning NF‑κB-mediated signals on the basis of intervening molecular circuits. These prompt speculation that common molecular paradigms might be at work in tuning the adaptive and innate receptor systems of vertebrates. Together, the take-home message

seems to be that setting this balance involves autonomously driven developmental and homeostatic programmes combined
with cross-talk between the commensal niche, innate immunocytes and the adaptive immune repertoire.

A second cluster of talks centred on molecular and cellular aspects of B-lineage differentiation. Yehudit Bergman (The Hebrew U. Medical School, Jerusalem) presented an elegant series of studies showing that in haematopoietic stem cells (HSCs) the asynchronous replication
time mode for each allele is not maintained in a clonal manner. Choosing one allele becomes fixed in pro‑B cells. Once a clonal replication decision is established it acts as the basis for initially choosing one allele to rearrange. She also showed that both alleles are packaged in differential chromatin states, with the open conformation allele being the preferred target for rearrangement. As for the Vκ genes, she has shown that they are opened in a mono-allelic way on both chromosomes. Yehudit suggests that this might afford a means for ensuring that different Vκ genes are used on either allele during receptor editing. This intriguing observation also raises the question as to whether this is exemplary of a general differentiative mechanism, through which epigenetic marks can be preserved at selected loci once lineage specification ensues. Representing the Nóbrega laboratory at the Federal University of Rio de Janeiro, Elize Hayashi and Alessandra Granato showed that Toll-like receptor 4 (TLR4) ligands afford both phenotypic and functional B-cell maturation from B-cell progenitors in vitro. Interestingly, this TLR4-mediated process involved the classical NF‑κB pathway and was BAFF (from the TNF family) independent. Moreover, when added together, BAFF and lipopolysaccharide (LPS) showed synergistic effects on the number of mature B cells generated. It is tempting to speculate that the classical NF‑κB-dependent, LPS-driven signals replace the role of B cell receptor signals in this differentiative scheme, and can be further augmented through the survival-promoting effects of BAFF. These observations underscore the suspicion that we have not yet fully unravelled the tangled web of cross-talk of the signalling systems downstream from innate, adaptive and BAFF receptor families.
final area of interest centred on the dynamics of T cell-dependent immune responses, particularly on events involved in the formation and evolution of germinal centres (GCs). few of these talks occurred on the day after the main meeting, due to late arrivals that had made their way by a combination of boat, automobile and train across Europe. Among these, Yang Zhang—a PhD student from Kai-Michael Toellner's group at U. Birmingham—showed a series of cleverly designed experiments to assess the role of GC‑associated antibody in affinity maturation. With a combination of careful in vivo histological studies and subsequent in silico analyses, she demonstrated that the immunoglobulin within GCs is in equilibrium with antibody outside, and that the replacement rate of GC associated antibody relies on relative affinities. In related studies, work from Radhika Goenka (Pennsylvania, Philadelphia) suggested that BAFF receptor TACI is downmodulated on GC B cells, thereby dramatically lowering levels of bound BAFF in the and making T_{FH} the primary source of BAFF in these regions. Considered together, these findings indicate
that many layers of competition—for antigen, cognate interactions and survival factors—might underlie the process of affinity maturation within GCs.

Forward Look

(1 page min.)

- *Assessment of the results*
- *Contribution to the future direction of the field – identification of issues in the 5-10 years & timeframe*
- *Identification of emerging topics*

The conference was rescheduled for June 2011