ImmunoTools IT-Box-Cy55M-Award 2013

Ella Levit

PhD Supervisor: Dr. Elias Hobeika

Max-Planck-Institut, Immunbiologie,
Stübeweg 51, 79108 Freiburg, Germany

Survival of mature B cells deficient in BCR signalling molecules

A main focus of our research in the last years are the role of BCR expression as well as BCR signaling in the maintenance of mature murine B cells. The BCR is composed of the heavy chain (HC), light chain (LC) and the signaling molecules Ig-α and Ig-β.

With the help of B-cell specific tamoxifen-inducible Cre mice we are able to delete individual components of the BCR as well as molecules involved in signaling downstream of the BCR *in vivo*. Current studies in our laboratory include the deletion of Ig-α or the Syk kinase as well as the heavy chain (HC) in mature B cells.

Switching-off Ig-α expression in mature B cells results in loss of the BCR. To delete Ig-α we are using the *cmb-1* mouse model, in which the tamoxifen-inducible Cre (*mb1*-CreER^{T2}) as well as an Ig-α/GFP^{inv} cassette are expressed under the control of the *mb-1* locus promoter encoding for Ig-α. Treatment of these mice with tamoxifen results in the inversion of the Ig-α/GFP^{inv} cassette thus leading to the expression of GFP instead of Ig-α and consequently giving rise to BCR-deficient B cells. The fate of these GFP-positive B cells is then easily traced by flow cytometry. Unexpectedly, Ig-α knockout (Ig-α KO) B cells were detected for up to 200 days in tamoxifen-treated mice. Whilst spleen tyrosine kinase (Syk)'s central role in signal transduction from the BCR is well documented for B cell activation, less is known about its contribution to the survival of mature B cells. In the same context, experiments done with the help of

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mb1-CreER^{T2};Syk$^{fl/fl}$ mice revealed that although more than 60 % of mature B cells require Syk for their maintenance, a large number of mature B cells persisted without Syk. In accordance with the literature and in contrast to *mb-1* and *Syk* deletion, the conditional deletion of the *HC* gene with the *mb1*-CreER^{T2} mouse strain led to rapid elimination of mature B cells within 20 days. This might be due not only to the lack of the B-cell survival signal but also to the induction of apoptosis via the unfolded protein response (UPR) detecting unassembled BCR components in the endoplasmic reticulum (ER).

We would like to incubate mature B cells derived from the different mutant mice with different cytokines from the *IT-Box-Cy55M* in the purpose to extend the survival or accelerate the elimination of these cells in culture.

ImmunoTools *IT-Box-Cy55M* for **Ella Levit**
includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS

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