NEUROIMMUNOLOGY

B cells on the brain

Nat. Neurosci. **21**, 506–516 (2018)

Activation or dysfunction of the immune system is associated with neurodevelopmental disorders. In *Nature Neuroscience*, Yamashita and colleagues show that IgM^{hi} B-1a cells are abundant in the brain of neonatal mice and promote the proliferation of oligodendrocyte precursor cells (OPCs). B-1a cells are recruited from neonatal blood in a manner dependent on the chemokine receptor CXCR5 and in response to the chemokine CXCL13 from the choroid plexus; their frequency peaks at day 1 after birth, and they are gone by day 10. Depletion of B-1a cells diminishes the number of oligodendrocytes in the developing brain. OPCs, but not mature oligodendrocytes, express the IgM receptor Fcα/μR, and IgM–Fcα/μR signaling regulates OPC proliferation in the neonatal brain. *IV*

https://doi.org/10.1038/s41590-018-0096-0

IMMUNOMETABOLISM

Mitochondria–ER hubs

Immunity **48**, 542–55 (2018)

Mitochondria–endoplasmic reticulum (ER) interactions are known to modulate mitochondrial respiration in non-immune cells. In *Immunity*, Bantug *et al*. show that mitochondria–ER junctions in effector memory (EM) CD8$^+$ T cells represent a signaling hub in which mTORC2–AKT–GSK3β signaling induces the oxidation of glucose to drive rapid production of the cytokine IFN-γ. More mitochondria–ER contacts are found in EM CD8$^+$ T cells than in naive CD8$^+$ T cells. Inhibition of GSK3β by mTORC2–AKT at these junctions allows recruitment of the kinase HK-I to the ion channel VDAC on the outer membrane of the mitochondria and the influx of substrates important for mitochondrial respiration. Destabilization of mitochondria–ER contracts or inhibition of the HK-1–VDAC interaction interferes with the rapid production of IFN-γ in activated EM CD8$^+$ T cells through inhibition of glycolysis and, possibly, of glycolysis-dependent histone acetylation at the *Ifng* promoter. *IV*

https://doi.org/10.1038/s41590-018-0097-z

B CELL METABOLISM

PP2A in B cells

Cell doi:10.1016/j.cell.2018.02.048 (2018)

Glycolysis generates ATP for cellular energy, whereas shunting glucose into the pentose-phosphate pathway (PPP) is needed to generate the antioxidant NADPH that is necessary for cellular redox balance. In *Cell*, Müschen and colleagues report that B cells, but not myeloid cells, critically require the phosphatase PP2A to maintain their redox balance and viability by redirecting glucose into the PPP. Loss of PP2A increases that oxidative stress of B lineage cells and, notably, B cell–derived leukemias. B cells normally have low expression of PPP enzymes due to repression of *G6pdx* and *G6pd2* by the transcription factors Pax5 and Ikaros, which makes B cells more sensitive to the activity of PP2A. Patient-derived B cell leukemias and lymphomas also show dependence on the activity of PP2A, which suggests that it might be targeted for therapeutic intervention. *LAD*

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REPRODUCIBILITY

Crisis management

Nat. Meth. doi:10.1038/nmeth.4632 (2018)

There is a well-documented reproducibility crisis in the biomedical sciences, and an important contributor to this is the widespread use of poorly validated and unstandardized monoclonal antibodies (mAbs). In *Nature Methods*, Blackshaw and colleagues describe a robust screening and validation pipeline that allows the generation of high-quality mouse mAbs to 737 human transcription factors. Full-length antigens or their domains are used to generate mAbs that are then initially screened on a human protein array. mAbs that pass the initial screen are then subjected to secondary validation via various applications, including immunoprecipitation, immunoblot analysis and, for a subset, immunohistochemistry and chromatin immunoprecipitation followed by deep sequencing. A meta-analysis of the pipeline helps to identify factors that influence the probability of generating high-quality mAbs, such as the route of immunization. *ZF*

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ATOPIC DERMATITIS

RORα in T$_{reg}$ cells

Sci. Immunol. **3**, eeao6923 (2018)

Atopic dermatitis is an inflammatory skin disease characterized by type 2 cytokines and eosinophilia. In *Science Immunology*, Malhotra et al. report that skin-resident regulatory T cells (T$_{reg}$ cells) require the transcription factor RORα to suppress skin inflammation mediated by type 2 innate lymphoid cells (ILC2s) and CD4$^+$ type 2 helper T cells (T$_H$2 cells). Transcriptomics reveals high expression of the gene encoding RORα in skin-resident T$_{reg}$ cells of mice and humans. T$_{reg}$ cell–specific loss of *Rora* increases expression of the cytokine IL-5 and chemokine CCL8 in allergen-induced skin lesions. Skin T$_{reg}$ cells express DR3, a member of the cytokine TNF receptor superfamily, sequesters the DR3 ligand TL1A and prevents potentiation of IL-33 by TL1A, thereby limiting the ability of ILC2s to express IL-5. Thus, RORα-dependent expression of DR3 in skin-resident T$_{reg}$ cells limits allergic skin inflammatory responses. *LAD*

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SYNTHETIC IMMUNOLOGY

Synthetic benefits

J. Clin. Invest. https://doi.org/10.1172/JCI91512 (2018)

The stability of vaccines can be an important consideration for both their in vivo efficacy and their use in the field, which often necessitates a cold-chain deployment. In *The Journal of Clinical Investigation*, Sewell and colleagues use a synthetic-biology approach to generate a more stable peptide vaccine against influenza A virus. Nature tends to use L-amino acids; therefore, D-amino acid–based peptides can be more resistant to enzymatic digestion. Using a combinatorial peptide library, the authors generate a vastly more stable D-amino acid nonamer peptide that binds HLA-A2, albeit somewhat weakly, yet is able to robustly stimulate a protective influenza A virus–specific response in humanized mice. The D-amino acid peptide is also stable in a simulated gastric environment and is protective in vivo after oral vaccination. *ZF*

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