■ HIV INFECTIONS

Restricting HIV from macrophages

In addition to HIV-1–infected CD4+ T cells, macrophages may also be a key source of the viral reservoir in HIV-1–infected people. A recent study reveals details of how HIV-1 is restricted from macrophages, which might inform the design of new strategies for eradicating the HIV reservoir (*J. Exp. Med.* **210**, 517–534).

The Imamichi laboratory previously showed that interleukin-27 (IL-27) inhibits HIV-1 replication in monocyte-derived macrophages. In their new study, this group sought to identify how IL-27 exerts its anti–HIV-1 effects. They found no evidence that IL-27 blocks entry of HIV-1 into macrophages but showed that macrophages induced with IL-27 produced less proviral cDNA of late HIV-1 gene products than control macrophages, suggesting that IL-27 interferes with HIV-1 replication between viral entry and reverse transcription.

Dai *et al.* then found that spectrin β nonerythrocyte 1 (SPTBN1) was downregulated in IL-27–treated macrophages compared with control macrophages. Knockdown of SPTBN1 in control macrophages prevented their infection by HIV-1, and overexpression of SPTBN1 in IL-27–induced macrophages rendered them susceptible to HIV-1 infection. The authors found that SPTBN1 associates with HIV-1 Gag proteins in macrophages and suggest that this interaction may be important for reverse transcription of the HIV-1 genome, but the functional relevance of the SPTBN1-Gag association still remains to be investigated in more detail. In addition, the effects of IL-27 need to be assessed in an *in vivo* model of HIV-1 infection. —*MS*

■ INFECTIOUS DISEASES

Clash of the interferons

Interferon-β (IFN-β) is well known for its antiviral effect, but a new study shows that it may counteract protective immune responses in the context of *Mycobacterium leprae* infections (*Science* http://dx.doi.org/10.1126/science.1233665)

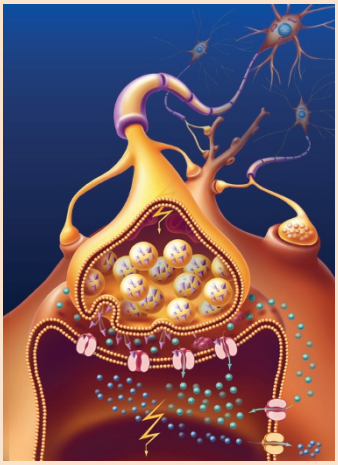
Studying IFN responses in human lepromatous lesions, Rosane Teles *et al.* found an inverse correlation between the gene-expression programs induced by IFN-β and IFN-γ. Healing lepromatous lesions preferentially expressed IFN-γ and its downstream genes, consistent with their known antimicrobial activity. In contrast, disseminated lesions expressed IFN-β and its downstream genes, particularly interleukin-10 (IL-10). Crucially, IFN-β and IL-10 inhibited the IFN-γ–induced antimicrobial response in macrophages *in vitro*, suggesting that the balance in the production of IFNs may help determine the outcome of infections by *M. leprae* and perhaps by other pathogens.

The lack of an established animal model of leprosy makes it hard to determine the *in vivo* relevance of these findings. However, it would be interesting to study whether strategies that block IFN-β and augment IFN-γ–mediated responses promote protection against other mycobacteria. —*JCL*

NEURODEVELOPMENTAL DISORDERS

Synaptic supervision

Loss of expression of the fragile X mental retardation protein (FMRP) leads to the neurodevelopmental cognitive disorder fragile X syndrome (FXS). FMRP is known to modulate protein synthesis at the postsynaptic portion of synapses in the brain. Now, Pan-Yue Deng *et al.* identify a key role of FMRP in the presynaptic side of the synapse in regulating the duration of action potentials (*Neuron* 77, 696–711).



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The researchers found that loss of FMRP could increase action potential duration within neurons in the hippocampus and cortex, two brain regions that modulate learning and memory. Reintroducing FMRP back into only the presynaptic neuron could restore normal action potentials, suggesting that FMRP is acting on the presynaptic side of the synapse.

Potassium channels are known to regulate action potential duration. Deng *et al.* found that neurons treated with blockers of BK potassium channels showed similar broadening of action potentials as neurons lacking FMRP. They showed that FMRP binds the regulatory subunit of BK channels to control the sensitivity of the channels to calcium. Neurons from mice lacking this regulatory subunit did not broaden their action potentials upon FMRP blockade.

Although the direct relevance of the findings to behavioral abnormalities in FXS still needs to be determined, these data suggest that activating BK channels could be beneficial in normalizing synaptic dysfunction in this disease. —*EC*

■ INFLUENZA VIRUS

Endogenous lipids halt influenza

Lipid mediators derived from omega-3 polyunsaturated fatty acids (PUFAs), found in the diet, have anti-inflammatory properties. One of these lipid mediators, protectin D1, is now shown to improve disease in mice infected with influenza by inhibiting viral replication through a mechanism that blocks export of viral transcripts (*Cell* http://dx.doi.org/10.1016/j.cell.2013.02.027).

Masayuki Morita *et al.* screened human lung epithelial cells infected with the influenza virus H1N1 to find PUFA-derived lipids that block virus replication. Protectin D1 showed the largest blocking effect, even in cells infected with other human pathogenic influenza strains. In mice, protectin D1 protected from infection with H1N1 and was also therapeutic when given with the antiviral peramivir, even at late time points in infection, when other antiviral drugs are ineffective.

The amounts of endogenous protectin D1 were reduced in infected mice; a reduction that correlated with the pathogenicity of the strain. The authors also found that its production was dependent on a specific enzyme expressed mostly in epithelial cells and leukocytes.

The findings identify a new innate suppressor of influenza virus replication that may be further investigated as a potential antiviral drug and biomarker to protect from and treat severe influenza infections. —*CP*

■ AUTOIMMUNE DISEASES

Salt spurs autoimmunity

Several environmental factors are thought to contribute to the increasing incidence of autoimmune disease; however, it remains to