methylation. Mohamed X. Ibrahim *et al.* investigated the role of ICMT in the disease phenotype of a mouse model of progeria caused by knockout of the gene *Zmpste24*. Taking advantage of a hypomorphic allele of *Icmt* (*Icmt*^{hm}), they found that *Zmpste24*$^{-/-}$;*Icmt*$^{hm/hm}$ mice showed improvement in several symptoms associated with progeria compared with *Zmpste24*$^{-/-}$ mice that had normal expression of *Icmt*.

In fibroblasts from the *Zmpste24*$^{-/-}$;*Icmt*$^{hm/hm}$ mice, prelamin A was relocalized away from the nuclear rim, although the nuclei were still misshapen. In contrast to *Zmpste24*$^{-/-}$ fibroblasts, which proliferate slowly and enter senescence prematurely, *Zmpste24*$^{-/-}$;*Icmt*$^{hm/hm}$ fibroblasts showed wild-type rates of proliferation. Mechanistically, these effects seem to be mediated by upregulation of AKT1–mTOR signaling in conditions of *Icmt* deficiency. The authors then extended these findings to the human situation by inhibiting ICMT in cells from people with Hutchinson-Gilford progeria syndrome (HGPS) using either shRNAs or a pharmacological inhibitor, showing that, as in the mouse cells, ICMT inhibition resulted in increased proliferation and delayed senescence. —*MS*

■ MALARIA

Malaria network using vesicles

Plasmodium, the parasite responsible for malaria, must differentiate once in its life cycle to the sexual stage form, called the gametocyte, to ensure transmission to other hosts. Two new studies show that malaria-infected red blood cells communicate with each other by vesicles, which induces gametocyte production and host immunomodulation (*Cell* http://dx.doi.org/10.1016/j.cell.2013.04.029; *Cell Host Microbe* **13**, 521–534, 2013).

The two groups provided insights into how blood-stage *Plasmodium falciparum* communicates in the host. Neta Regev-Rudzki *et al.* showed that the release of exosome-like vesicles from infected red blood cells before parasite egress enables transfer of genes between parasites. This not only allows parasites to exchange drug resistance genes to promote their survival but also signaling that allows the parasites to differentiate into their sexual forms. Pierre-Yves Mantel *et al.* found that a larger type of vesicle, microvesicles, caused an increase in gametocyte numbers and also activated innate immune cells to release proinflammatory cytokines, which might contribute to disease. These vesicles contained red blood cell–derived proteins and parasite antigens, but it is unknown what other cargo may be inside and what proteins are responsible for triggering differentiation into the sexual stage.

The studies also show that *P. falciparum*–infected red blood cells can internalize exosomes and microvesicles and that this uptake increases in conditions of stress and when the blood concentration of vesicles increases. This suggests that parasite crosstalk may lead to optimized gametocyte production and transmission to mosquitoes. This vesicle-mediated transport could be targeted to block parasite transmission and reduce disease progression. —*CP*

■ IMMUNOLOGY

Restraining natural killer cells

Regulatory T cells (T_{reg} cells) suppress the activity of several immune cell types; however, the direct mechanism whereby they control natural killer (NK) cell function remains unclear. Three studies suggest T_{reg} cells may attenuate NK cell activity by limiting the amount of interleukin-2 (IL-2) available.

In a mouse model of type 1 diabetes, Jonathan Sitrin *et al.* (*J. Exp. Med.* http://dx.doi.org/10.1084/jem.20122248) show that ablation of T_{reg} cells induces the accumulation and activation of NK cells in the pancreas, leading to diabetes. Inhibition of IL-2, a cytokine previously shown to promote NK cell proliferation and interferon-γ (IFN-γ) production, reduced NK cell infiltration into the pancreas and their production of IFN-γ.

Georg Gasteiger *et al.* (*J. Exp. Med.* http://dx.doi.org/10.1084/jem.20122462; *J. Exp. Med.* http://dx.doi.org/10.1084/jem.20122571) report that T_{reg} cell depletion induces systemic autoimmunity, leading to increased NK cell cytotoxicity toward missing self targets. This activity was dependent on IL-2, as inhibition of IL-2 or depletion of $CD4^+$ cells, a dominant source of IL-2, reduced NK cell activity. Ablation of T_{reg} cells also resulted in IL-2–dependent expansion of an immature subset of $CD127^+$ NK cells. Taken together, these findings highlight how adaptive immune responses can control innate immune cell homeostasis and activation in the steady state and in disease. —*KDS*

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New from NPG

Hypothalamic programming of systemic ageing involving IKK-β, NF-κB and GnRH
Zhang, G. *et al. Nature* http://dx.doi.org/10.1038/nature12143 (1 May)
The authors show that aging in mice is regulated by hypothalamic nuclear factor-κB (NF-κB) signaling. This pathway leads to decreased amounts of gonadotropin-releasing hormone (GnRH) and reduced neurogenesis. Administration of GnRH stimulated neurogenesis in adult mice and slowed aging.

The collagen receptor discoidin domain receptor 2 stabilizes SNAIL1 to facilitate breast cancer metastasis
Zhang, K. *et al. Nat. Cell Biol.* http://dx.doi.org/10.1038/ncb2743 (5 May)
This study shows that stabilization of SNAIL1 by discoidin domain receptor 2 (DDR2) promotes breast cancer metastasis. DDR2 expression associated with nuclear SNAIL1 was found in a number of human invasive ductal breast carcinomas.

Multiple populations of artemisinin-resistant *Plasmodium falciparum* in Cambodia
Miotto, O. *et al. Nat. Genet.* http://dx.doi.org/10.1038/ng.2624 (28 April)
By sequencing whole genomes of *P. falciparum* isolated from 825 malaria cases, the authors were able to characterize patterns of genetic variation and drug resistance, as well as genetic markers that can identify resistant strains.

T cells maintain an exhausted phenotype after antigen withdrawal and population reexpansion
Utzschneider, D.T. *et al. Nat. Immunol.* http://dx.doi.org/10.1038/ni.2606 (5 May)
The authors find that 'exhausted' $CD8^+$ T cells transferred from chronically lymphochoriomeningitis virus (LCMV)-infected mice to naive mice could proliferate and control a viral infection. The progeny of the transferred cells still expressed exhaustion markers in the absence of chronic infection, suggesting that the exhausted phenotype may represent a stable differentiation state.

GABA progenitors grafted into the adult epileptic brain control seizures and abnormal behavior
Hunt, R.F. *et al. Nat. Neurosci.* http://dx.doi.org/10.1038/ni.3392 (5 May)
Grafting the precursors of GABA-producing inhibitory neurons into the hippocampus of adult epileptic mice reduced seizures and ameliorated behavioral deficits.