■ VACCINES

Protection from Nipah

Nipah and Hendra viruses (NiV and HeV) are closely related paramyxoviruses that can infect humans and various animal species, leading to severe disease and death. Currently, no therapy or prevention method exists to combat these pathogens, but now, a recent study in nonhuman primates offers some promise toward an effective vaccine (*Sci. Transl. Med.* **4**, 146ra107).

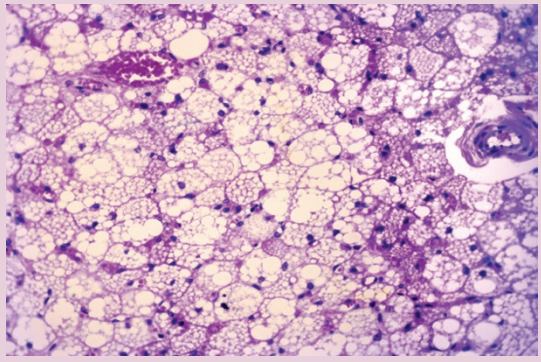
Katharine N. Bossart *et al.* tested the effects of a recombinant subunit vaccine made from the attachment (G) envelope glycoprotein of HeV (sGHeV) in an African green monkey (AGM) model of lethal NiV infection. This vaccine has previously shown efficacy in small-animal models of HeV or NiV infection. They found that vaccination led to complete protection from NiV infection, with no evidence of disease, viral replication or pathology observed in the nine vaccinated AGMs.

Bossart *et al.* suggest that the spread of NiV *in vivo* is likely to be controlled by NiV-specific neutralizing antibodies elicited by the vaccine, as there was little evidence of a primary immune response after challenge, suggesting that there were low numbers of circulating virus.

Although efficacy trials of the sGHeV vaccine remain to be completed in primates challenged with HeV, the demonstration of protection from NiV in this study is an important step on the road to licensure of a vaccine to protect against these fatal viral infections. —*MS*

OBESITY

Gaining SIRT-ainty



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The deactylase sirtuin 1 (Sirt1) seems to be a linchpin for the metabolic benefits of calorie restriction. In two new studies, more insight is gained about the importance of Sirt1 and its role in metabolic homeostasis.

In the first paper (*Cell Metab.* 16, 180–188), Chalkiadaki and Guarente show that high-fat diet–induced activation of the inflammasome in adipocytes results in caspase-1–mediated cleavage of Sirt1. They also found that genetic knockout of Sirt1 specifically in adipocytes leads to increased adiposity and whole-body insulin resistance. And transcriptome analysis showed that these knockout cells are quite similar to adipocytes from mice on a high-fat diet. These results point to a link between dietary stress and the development of obesity that involves Sirt1.

Although these findings place adipocyte-expressed Sirt1 front and center in the proper regulation of whole-body metabolism, it is still unclear how Sirt1 activity achieves this regulation. In a second study (*Cell* 150, 620–632), Li Qiang *et al.* may have uncovered at least part of this downstream mechanism. They found that in white adipocytes Sirt1 deacetylates the liganded form of the transcription factor peroxisome proliferator-activated receptor-γ (PPAR-γ), thus allowing it to interact with PRDM16 and potentiate a genetic program that leads to the 'browning' of these cells. This cellular conversion improved energy expenditure and whole-body insulin sensitivity.

Together, these results give further credence to pursuing pharmacological activators of Sirt1 as a means of improving metabolic health. They also suggest that their combined use with low concentrations of PPAR-γ agonists, such as thiazolidinediones, may be even further efficacious. —*RL*

■ CANCER

Partners in crime

Mutations in transcriptional regulators are frequently associated with hematological malignancies. For example, mutations in chromatin-bound ASXL1 occur in more than 10% of individuals with myelodysplastic syndrome (MDS) or myeloproliferative disease. In contrast, its binding partner, BAP1, with which ASXL1 forms a histone deubiquitinase, is often deleted in uveal melanoma and mesothelioma. Now, two papers report the effects of ASXL1 or BAP1 deficiency in myeloid cell transformation.

Omar Abdel-Wahab *et al.* (*Cancer Cell* **22**, 180–193) report that silencing of *ASXL1*, but not *BAP1*, in hematopoietic cells increased the expression of the homeobox genes *HOXA5–9*. They found that ASXL1 binds the transcriptional repressor EZH2, and in the absence of ASXL1, EZH2 is lost from the posterior *HOXA* locus, which probably mediates the deregulated expression of *HOXA5–9*. Furthermore, ASXL1 knockdown reduced survival and accelerated a myeloproliferative disease caused by expression of an oncogenic N-Ras allele in mouse bone marrow cells.

Anwesha Dey *et al.* (*Science*, doi:10.1126/science.1221711) confirmed that conditional deletion of BAP1 in adult hematopoietic cells did not increase *Hox* gene expression but did cause a myeloproliferative disorder similar to that seen in individuals with chronic myelomonocytic leukemia (in which ASXL1 mutations are known to occur). They identified one patient with MDS with a heterozygous mutation in *BAP1* and found reduced expression of *BAP1* mRNA in bone marrow cells from patients with MDS compared with healthy individuals. The researchers found that BAP1 associates with the epigenetic regulator HCF-1 and with O-linked *N*-acetylglucosamine transferase (OGT), both of which were reduced in amount by BAP1 deletion. The authors propose that BAP1, OGT and HCF-1 form a complex on promoters, the loss of which contributes to deregulated gene expression and myeloproliferative disease.

The findings presented in these two reports confirm the importance of chromatin modifiers in hematopoietic malignancy and suggest complementary roles for ASXL1 and BAP1 in maintaining normal hematopoiesis. —*AF*

■ CANCER

Awakening metastasis

A new study in mice uncovers a protein called Coco, a transforming growth factor-β antagonist, that induces the reactivation of dormant metastasis-initiating breast cancer cells in the lung (*Cell* **150**, 764–779).

Hua Gao *et al.* show that Coco exerts a metastatic effect by blocking bone morphogenetic protein (BMP) ligands, which they found were