■ INNATE IMMUNITY

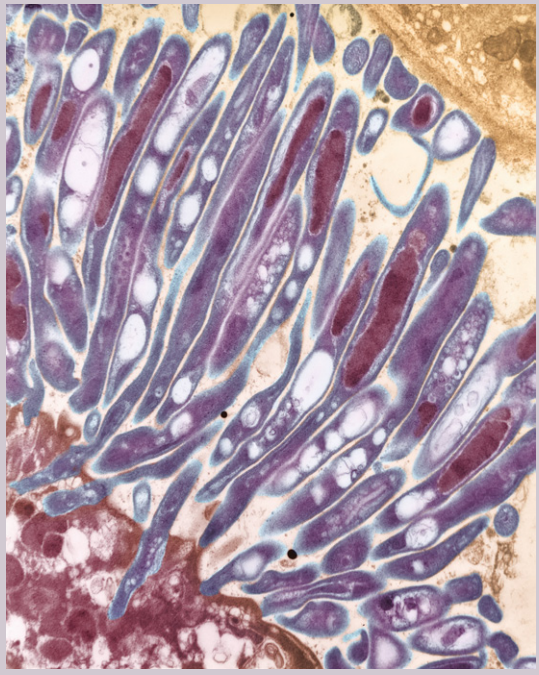
Innate sensing of retroviruses

Retroviruses are adept at evading recognition by the host immune system. However, recent studies have shown that these viruses can induce innate immune responses. The cellular sensor that recognizes retroviruses has nevertheless been unclear. Daxing Gao *et al*. now report that the cyclic GMP-AMP synthase (cGAS) that they previously found senses DNA viruses, such as vaccinia virus, is also capable of triggering an interferon (IFN) response to retroviral DNA (*Science*, http://dx.doi.org/10.1126/science.1241800).

The authors found that infection of a monocytic cell line with a modified HIV-1 virus induced IFN-β production, which was blocked by inhibiting reverse transcription of the retroviral genome. Cytosolic DNA can bind and activate cGAS, resulting in the formation of cGAMP from ATP and GTP. cGAMP, in turn, activates stimulator of interferon genes (STING), eventually leading to the induction of cytokines and interferons. The authors showed that cGAS and STING were also required for sensing retroviral cDNA and that the retroviral cDNA was required for induction of cGAMP production by cGAS, which triggered the subsequent IFN response pathway. The authors extended their findings to primary human monocyte-derived macrophages and monocyte-derived dendritic cells that were rendered permissible to HIV-1 infection, and they further showed that the same pathway was active in sensing SIV and murine leukemia virus. These findings lend support to the idea that retroviruses are not invisible to the immune system, and they suggest a pathway for possible intervention to enhance their immune recognition.—*AF*

MALARIA

Total protection from malaria



London School of Hygiene & Tropical Medicine / Science Source

Finding a malaria vaccine that can confer full protection has been elusive until now. Intravenous injection of irradiated *Plasmodium falciparum* sporozoites, the infective stage of the malaria parasite, protected adults from malaria infection in a phase 1 trial. (*Science* http://dx.doi.org/10.1126/science.1241800)

Robert Seder and his colleagues showed that the sporozoite vaccine was safe when given 4–6 times intravenously, but full protection was only achieved in adults who received five doses, whereas three out of nine people who received four doses and five out of six nonvaccinated subjects developed malaria. It is unclear whether the different dosage schedule or the total number of parasites administered dictates the partial versus total level of protection. The vaccine elicited both sporozoite-specific antibody and cellular responses (of various types of lymphocytes) in a dose-dependent manner. However, the numbers of $CD8^+$ T cells (which are thought to be required for protection from malaria infection) were low in the blood from some of the protected adults, and it is unclear whether antibodies contribute to protection.

This vaccine provides proof of concept that protective immunity against malaria infection can be achieved through the intravenous administration of irradiated sporozoites, which could prevent infection in the liver and transmission of the malaria parasite. Future work should address how to implement this vaccination route in endemic areas (or how to find more feasible routes while maintaining efficacy) and how long this protection will last. This study also underscores the urgent need to define which immune responses and antigens confer protection in order to assess the efficacy of future malaria vaccines.—*CP*

■ CANCER EPIGENETICS

Unraveling chromatin checkpoints

A new report provides an interesting mechanistic link between alterations in chromatin modifiers and gross chromosomal aberrations in cancer (*Cell* **154**, 541–555).

Chromatin regulators have recently jumped to the forefront of cancer biology as genomic studies have shown that they are frequently altered in cancer. However, their specific functional contribution to tumorigenesis remains to be unraveled. Joshua C. Black and his colleagues now show that aberrant expression of KDM4A, a histone-modifying enzyme, induces one of the key features of many types of tumors, copy number gains in specific chromosomal regions.

Consistent with earlier studies, the authors found that KDM4A was genomically amplified in several tumor types. As previous work had shown that increased dosage of this enzyme could alter replication dynamics at heterochromatic regions, which are regions of densely packed chromatin generally associated with gene repression, the authors studied the effects of KDM4A on genomic stability. Elevated demethylation of histones by the enzyme caused specific copy gains in the 1q12h region. Mechanistically, the copy gains are a result of re-replication during each cell cycle, and the observed site specificity is probably determined by the chromatin microenvironment surrounding KDM4A-binding sites.

The fact that human tumors also show concomitant KDM4A deregulation and 1q12h gain supports the notion that this mechanism may underlie human tumorigenesis. This study opens up several interesting questions that may shed light on the elusive mechanisms that drive genomic instability in cancer.—*VA*

■ ADDICTION

A bad combination

Nicotine may promote alcohol intake by decreasing the dopamine-mediated response to ethanol by the brain's reward system, according to new research published in *Neuron* (**79**, 530–540).