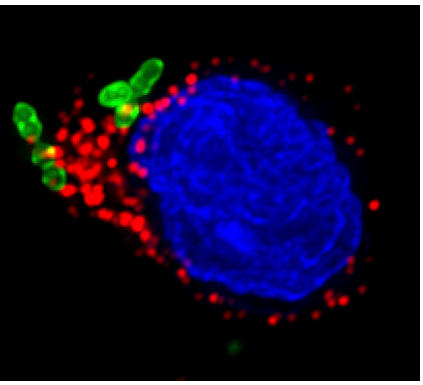


β protein helps GBS (green) bind to Siglec-5 (red) on human leukocytes.

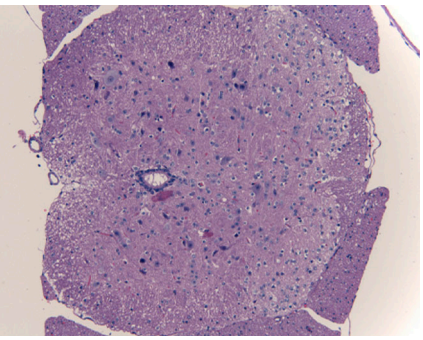
Proteins are the new carbs

On page 1691, Carlin et al. uncover a new tool of bacterial deception.

Bacteria wear camouflage to creep through our bodies undetected. Some adorn their surfaces with sugary structures tipped with sialic acids that engage inhibitory receptors on white blood cells. Normally, these receptors, called Siglecs (Sia-recognizing Ig superfamily lectins), help the body recognize itself. Because sialic acids decorate our own cells, the receptors may help prevent inflammatory self-attack. Some bacteria have tapped into this pathway, impairing phagocytosis and cytokine production by immune cells, and thus helping to ensure their own survival.

Now, Carlin and colleagues show that the cell wall β protein from group B *Streptococcus* (GBS) can do what sialic acid does—making this the first known protein to bind Siglecs. β protein engaged Siglec-5 on human monocytes and neutrophils, triggering an inhibitory cascade that shut off immune cell defenses and promoted bacterial survival.

But why would the bacteria turn to proteins with sialic acids already in hand? As certain Siglecs evolve quickly—particularly in sialic acid-binding sites—a protein-based trigger that targets other parts of the Siglec molecule might provide bacteria with longer lasting protection. β protein is already used for protection in other ways, one of which is to inhibit the complement cascade. The protein's skill for multitasking may explain why strains expressing high levels of β protein are the most virulent. **AM**



IL-9R deficiency ameliorates the severity of EAE.

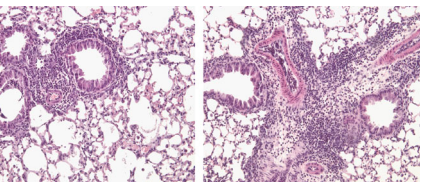
IL-9 gets around

Some cytokines refuse to be pigeonholed. On page 1653, Nowak et al. show that interleukin (IL) 9 can derive from a number of $CD4^+$ T cell types. And when produced in an autoimmune setting, IL-9 contributed to disease.

Many types of $CD4^+$ T cells, including Th2 and regulatory T cells, produce IL-9 in response to TGF-β. And despite earlier reports to the contrary, Nowak and colleagues now find that this also holds true for Th17 cells. In fact, Th17 cells produced more IL-9 in culture in response to TGF-β than did other types of $CD4^+$ T cells.

In the absence of IL-9 signals, mice were partially protected against EAE, a Th17-driven autoimmune disease that models multiple sclerosis. These mice had fewer IL-17– and IL-6–producing cells in the CNS and fewer mast cells in draining lymph nodes. IL-9 is known to enhance mast cell recruitment, and mast cells have been shown to contribute to EAE. However, in other contexts, the cytokine appears to suppress, rather than exacerbate, inflammation.

As for recent claims regarding which lineages can or cannot secrete IL-9, the authors suggest that diet may influence cytokine secretion, perhaps accounting for conflicting results. Diets high in vitamin A raise retinoic acid levels, and the authors have initial evidence that retinoic acid inhibits IL-9 secretion. **AM**



Inflammation narrowed a mouse's airways when activin-A was blocked (right).

Activin eases asthma

A mysterious cytokine quells asthma by triggering regulatory T (T reg) cells that prevent dendritic cells from growing up, Semitekolou et al. reveal (page 1769).

Like many cytokines, activin-A triggers different effects in different situations. In some studies, it incited inflammation, but in others it had the opposite effect. The abundance of activin-A in the blood of patients with asthma and in the lungs of mice with inflamed airways suggests a role for the protein in allergy and asthma. But whether the cytokine exerts pro- or anti-inflammatory effects during these reactions remains unclear.

Semitekolou et al. addressed the issue by dosing asthmatic mice with an activin-blocking antibody shortly before the animals inhaled an allergen. Asthma symptoms were more severe in treated rodents than in controls. And injections of activin-A helped mice breathe easier.

Activin-A exerted its effects in part by boosting the number of T reg cells. In vitro, these T reg cells squelched Th2 responses and when transferred into mice, they alleviated asthma symptoms. The T reg cells worked by releasing the soothing cytokines interleukin-10 and TGF-β1 and by blocking maturation of dendritic cells, which are essential for Th2 specialization. **ML**

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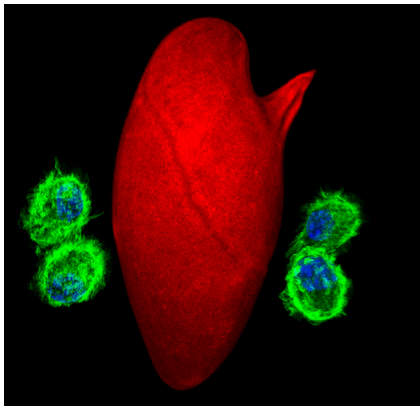
Cracking the schistosome egg

Schistosoma worms are experts at concealment, but now researchers have revealed one of their biggest secrets. Two groups have nabbed a long-sought protein in the worms' eggs that polarizes helper T cells.

The eggs that female schistosome worms pump out at a rate of 300 per day can spark a Th2 response. This immune reaction appears to be a lifesaver for the host, as parasitized mice that can't activate Th2 die from excessive inflammation. However, pinning down the polarization trigger has been tricky because an egg secretes several hundred proteins.

Using different techniques, the two groups homed in on an RNA-slicing enzyme called omega-1. After pinpointing the size of the Th2 trigger, Steinfelder et al. (page 1681) purified the protein from the supernatant of worm egg cultures, which was easier to sift through because it contains fewer kinds of proteins than whole egg extracts. Everts et al. (page 1673) simply went after the most abundant egg secretions, omega-1 and another protein called IPSE/α-1. In cultures of human dendritic and helper T cells, omega-1 was a Th2 polarizer, whereas IPSE/α-1 wasn't.

The studies also offer some clues about how omega-1 works. Steinfelder et al. found that the protein inhibits interactions between dendritic cells and T cells, perhaps mimicking the antigen-scarce situation that favors the Th2 shift. Still uncertain, however, is whether omega-1 exerts its effects through a receptor, through its enzymatic activity, or through both routes. And the protein probably doesn't act alone. Everts et al. showed that egg extracts lacking omega-1 could still trigger polarization if injected into mice. **ML**



Omega-1 from schistosome eggs (red) drives Th2 responses in part by acting on dendritic cells (green).

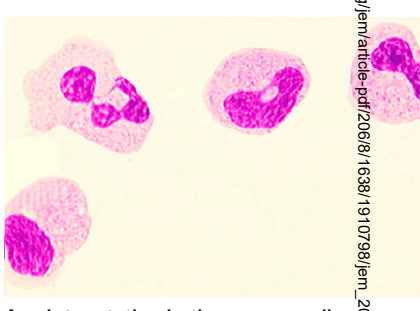
Neutrophils gone wild

Plo et al. have identified the first inherited condition that boosts the number of neutrophils (page 1701).

The patient with the condition was an 18-year-old man suffering from systemic inflammation that triggered fever, rapid heartbeat, difficulty breathing, and other symptoms. Tests revealed that his blood teemed with neutrophils—around three times the normal number. Eleven other members of the patient's family also harbored an excess of circulating neutrophils (neutrophilia) but apparently suffered no ill effects from the copious cells. Why only one family member became ill is unclear.

The overabundance of neutrophils pointed to faulty signaling by granulocyte colony stimulating factor (G-CSF), which spurs neutrophil precursors to differentiate and divide. Although G-CSF levels weren't elevated, all 12 family members carried a mutation in the gene encoding the G-CSF receptor (G-CSF-R) that produced a single amino acid swap. To confirm that the mutation in G-CSF-R leads to excess neutrophils, Plo et al. engineered mouse bone marrow cells to produce the mutant G-CSF-R and transferred them into irradiated mice. Indeed, the animals developed neutrophilia.

The researchers found that the mutant receptors remain stuck together as dimers, rendering them permanently switched on. As a result, neutrophil precursors continually receive orders to proliferate and differentiate. **ML**



A point mutation in the gene encoding the G-CSF receptor boosts numbers of circulating neutrophils.