patterns of GISTs from patients and found a strong divergence between SDH-deficient GISTs and GISTs that still expressed functional SDH. The SDH-deficient GISTs had greater amounts of genomic hypermethylation compared with the other tumor types, which the authors attributed to defective maintenance of epigenetic marks.

Notably, this nonrandom pattern of epigenomic changes in SDH-deficient GISTs correlated with lower genomic stability compared to SDH-proficient tumors, and it is also present in other tumor types characterized by SDH deficiency. These results provide a link between mitochondrial function and epigenomic homeostasis that may have further implications for cancer etiopathology. —*VA*

■ MICROBIOME

Microbial mediators

Research is increasingly showing the wide-ranging influence of the microbiome on immune responses and health. A collection of recent reports provide a peek into the varied molecular mediators of the microbial influence on immune responses (*Science* http://dx.doi.org/10.1126/science.1241165; *Immunity* **38**, 1187–1197; *Immunity* **38**, 1198–1210; *Immunity* **38**, 1211–1222).

Patrick Smith *et al.* asked what bacterial products can regulate colonic regulatory T (T_{reg}) cells. The researchers found that short-chain fatty acids, which are bacterial fermentation products, could trigger the proliferation of and enhance the function of interleukin-10–producing inducible T_{reg} cells in mice. These fatty acids, acting through their receptor GRP43, inhibited histone deacetylase expression, thus increasing histone acetylation in colonic T_{reg} cells, which may account for their effects.

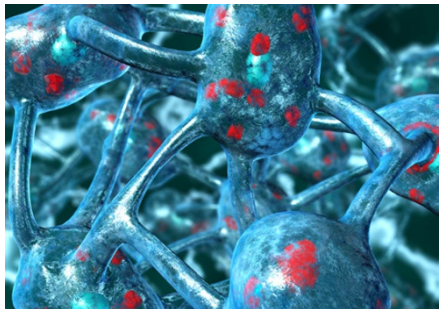
Tadaomi Kawashima *et al.* sought to understand the role of Toll-like receptors (TLRs) in the recognition of lactic acid bacteria by immune cells, as these bacteria have been shown to promote beneficial immune responses against pathogens and suppress colitis in mice. The authors found that lactic acid bacteria potently induce the production of interferon-β (IFN-β)—which is important in antiviral immunity—by bone marrow–derived dendritic cells. In contrast, pathogenic bacteria were less effective at inducing this response. Bacterial double-stranded RNA was responsible for triggering TLR3 activation and IFN-β production and mediating the anti-inflammatory effects of lactic acid bacteria in mice. The researchers found that commensal bacteria produced higher amounts of double-stranded RNA than pathogenic species, accounting for the differential induction of IFN-β.

The studies add to our understanding of how bacterial products can modulate different components of the immune system to collectively reduce inflammation and potentially facilitate responses to microbial pathogens. —*AF*

■ NEURODEGENERATION

Brain strains

Neurodegenerative diseases are characterized by the accumulation of normally soluble proteins into insoluble misfolded aggregates. Although individual proteins are associated with certain disorders, several disease-related proteins are found postmortem in the same patient. A recent study suggests that α-synuclein (α-syn) can promote aggregation of tau, an effect that depends on different strains of α-syn.



David Mack / Science Source

Virginia M.Y. Lee and her colleagues (*Cell* **154**, 103–117) found that synthetic preformed fibrils of α-syn could seed tau aggregation *in vitro* and also when injected into the brains of mice overexpressing a mutant form of human tau. This effect was dependent on the sequence of α-syn and the method of fibrillization, suggesting that distinct strains of α-syn can promote tau aggregation. These strains seem to be conformationally distinct, as they show different cleavage patterns when digested with proteinase K. Moreover, in a small subset of patients with Parkinson's disease with dementia, distinct α-syn proteinase K cleavage patterns were found. Taken together, these results suggest that different strains of α-syn may promote distinct pathology in neurodegenerative diseases. —*KDS*

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New from NPG

T_{reg} induction by a rationally selected mixture of Clostridia strains from the human microbiota
Atarashi, K. *et al. Nature* http://dx.doi.org/10.1038/nature12331 (10 July)
The authors selected 17 strains of bacteria from the human microbiota that could induce T_{reg} cells, showing that all these strains were *Clostridia*. Oral administration of a combination of the strains improved disease in mouse models of colitis.

Generation of inner ear sensory epithelia from pluripotent stem cells in 3D culture
Koehler, K.R. *et al. Nature* http://dx.doi.org/10.1038/nature12298 (10 July)
This study describes a new *in vitro* model of inner ear differentiation for investigating inner ear development and disorders that uses three-dimensional culture of mouse embryonic stem cells.

Evidence for APOBEC3B mutagenesis in multiple human cancers
Burns, M.B. *et al. Nat. Genet.* http://dx.doi.org/10.1038/ng.2701 (14 July)

An APOBEC cytidine deaminase mutagenesis pattern is widespread in human cancers
Roberts, S.A. *et al. Nat. Genet.* http://dx.doi.org/10.1038/ng.2702 (14 July)
Two new studies analyse the role of APOBEC cytidine deaminases, which are involved in RNA editing and retrovirus or retrotransponson restriction, in human cancers. The reports provide evidence that APOBEC-mediated mutagenesis is prevalent in many cancers and suggest that these mutations are functionally linked to cancer development.

Exosomes mediate the cell-to-cell transmission of IFN-α-induced antiviral activity
Li, J. *et al. Nat. Immunol.* http://dx.doi.org/10.1038/ni.2647 (7 July)
The authors report a new mechanism by which interferon-α (IFN-α) exerts an antiviral response to hepatitis B virus. IFN-α stimulates the release of exosomes containing antiviral molecules from nonpermissive liver cells to permissive hepatocytes.

The fat mass and obesity associated gene (*Fto*) regulates activity of the dopaminergic midbrain circuitry
Hess, M.E. *et al. Nat. Neurosci.* http://dx.doi.org/10.1038/nn.3449 (30 June)
The authors show that FTO affects the activity and function of midbrain dopaminergic neurons and reward-related behaviors in mice.