IN BRIEF

VIRAL INFECTION

The next SARS?

Human-infecting coronaviruses (CoVs), such as SARS-CoV and MERS-CoV, are thought to emerge from circulating bat CoVs. To test the emergence potential of SARS-like CoVs currently present in bats, Menachery *et al.* selected the bat CoV SHC014 (which metagenomics studies identified as a close relative to the epidemic SARS strains) and cloned its spike protein (which mediates viral attachment to host cells) into a mouse-adapted SARS-CoV backbone. The chimeric virus could replicate inside human cell lines and was capable of replicating in mouse lungs. Importantly, currently available therapeutics (monoclonal antibodies and vaccines) failed to protect the mice from viral infection. Finally, the authors synthesized a full-length SHC014 CoV, which was capable of replicating in human cells. These data suggest that CoVs currently circulating in bats have the potential for human emergence.

ORIGINAL ARTICLE Menachery, V. D. *et al.* A SARS-like cluster of circulating bat coronaviruses shows potential for human emergence. *Nat. Med.* <u>http://dx.doi.org/10.1038/</u>nm.3985 (2015)

MICROBIOME

Commensals promote anticancer immunotherapy

Immunotherapy has shown recent success against cancer by potentiating the antitumour responses of immune cells, but how such responses are regulated is unknown. Now, two studies reveal that the gut microbiota is a key contributor to successful immunotherapy using antibodies against cytotoxic T lymphocyte protein 4 (CTLA4) and programmed cell death protein 1 ligand 1 (PDL1). Vétizou et al. compared specific pathogen-free (SPF) and germ-free (GF) mice and observed that CTLA4 blockade controlled sarcoma progression in SPF but not in GF mice. The authors linked the abundance of specific bacterial taxa to immunotherapy success, and tested these links by carrying out monocolonization experiments. Notably, monocolonization of GF mice with Bacteroides thetaiotaomicron, Bacteroides fragilis, Bacteroides uniformis or Burkholderia cepacia resulted in the recovery of antitumour responses. Sivan, Corralles et al. compared tumour growth in mice from Taconic Farms (TAC) or Jackson Laboratory (JAX) and found that melanomas grew faster in TAC mice than in JAX mice. Notably, faecal transfer from JAX mice to TAC mice was sufficient to delay melanoma growth, and tumour control provided by faecal transfer was comparable to that provided by anti-PDL1 therapy. Furthermore, combining faecal transfer with immunotherapy further improved tumour control. The authors identified a positive correlation between Bifidobacterium abundance and antitumour responses, and mice treated with a cocktail of Bifidobacterium species (including Bifidobacterium breve and Bifidobacterium longum) were better at controlling tumour growth and responded better to anti-PDL1 therapy than untreated mice. Although the mechanisms by which the gut microbiota influences antitumour immunity are unknown, both studies suggest that commensal bacteria modulate the function of dendritic cells, which in turn results in enhanced antitumour T cell function.

ORIGINAL ARTICLES Vétizou, M. et al. Anticancer immunotherapy by CTLA-4 blockade relies on the gut microbiota. *Science* **350**, 1079–1084 (2015) | Sivan, A., Corrales, L. et al. Commensal *Bifidobacterium* promotes antitumor immunity and facilitates anti–PD-L1 efficacy. *Science* **350**, 1084–1089 (2015)