antiviral IFN γ -secreting CD8 $^{+}$ T-cell response, and decreased expression of programmed death 1 (PD1) on T cells, which has recently been identified as having a key role in sustaining suppression of CD8 $^{+}$ T cells during persistent infection.

Elevated levels of IL-10 are observed during human HIV, HBV and HCV infections, and correlate with reduced T-cell activity and failure to control viral replication. Therefore, these two papers raise the possibility that IL-10 blockade might enhance the treatment of these persistent infections. And importantly, given that such a strategy is targeting a host factor that does not directly interact with the virus, it is unlikely that resistance owing to viral mutation would emerge, which is a cause of many treatment failures with current drugs.

Charlotte Harrison

ORIGINAL RESEARCH PAPERS Brooks, D. G. *et al.* Interleukin-10 determines viral clearance or persistence *in vivo*. *Nature Med.* **12**, 1301–1309 (2006) | Ejrnaes, M. *et al.* Resolution of chronic viral infection after interleukin-10 blockade. *J. Exp. Med.* **203**, 2461–2472 (2006)

FURTHER READING Klenerman, P. & Ludewig, B. Virus scores a perfect 10. *Nature Med.* **12**, 1246–1248 (2006)

directly inhibited the capacity of these cells to activate and polarize antigen-specific T cells. However, the maturation status of the DCs was not affected. The authors showed that the capacity of DCs to form stable and long-lasting interactions with T cells was abolished in the presence of FTY720, which might account for the inability of FTY720-treated DCs to stimulate T cells.

Therefore, FTY720 suppresses experimental asthma by blocking the migration of DCs from the lung to the draining lymph node without inducing peripheral lymphopenia and by reducing the capacity of DCs to activate naive and effector T $_{H2}$ cells. This study indicates that targeting lung DCs might be an effective strategy in the treatment of asthma.

Olive Leavy, *Nature Reviews Immunology*

ORIGINAL RESEARCH PAPER Idzko, M. *et al.* Local application of FTY720 to the lung abrogates experimental asthma by altering dendritic cell function. *J. Clin. Invest.* **116**, 2935–2944 (2006)

LEUKAEMIA

Getting to the root of relapse

Patients with acute myeloid leukaemia (AML) currently face a bleak prognosis. Although chemotherapeutics targeting rapidly dividing tumour cells usually induce temporary remission, a small number of quiescent or slowly dividing leukaemic stem cells (LSCs) provide the seeds for relapse. Now, a study by Liquing Jin *et al.* raises hope that a tool targeting these elusive cells could be on the horizon. Reporting in *Nature Medicine*, the authors show that a new antibody treatment can interfere with the anchoring of LSCs in their hiding places and prompt them to differentiate, causing them to lose their cancer-repopulating capacity.

The concept of cancer stem cells has fundamentally changed the understanding of cancer development. Although cancer stem cells have only been identified for certain types of cancer, considerable research efforts are presently focusing on targeting these cells in the hope of achieving curative treatment for cancers that are prone to relapse.

In their study, Jin and colleagues discovered that the stem cells of AML can be manipulated with the activating monoclonal antibody H90, directed at the adhesion molecule CD44. In a murine model system of human AML, non-obese diabetic/severe combined immunodeficiency (NOD/SCID) mice were transplanted with human AML blast cells. The rare sub-population of LSCs in the human AML samples is characterized by the surface molecule signature CD34 $^{+}$ CD38 $^{-}$, and is further defined by their capacity to initiate AML upon 'serial transplantation' of leukaemic cells from mouse to mouse. When NOD/SCID

mice were treated with H90 a few weeks after AML transplantation, the leukaemic cell population was markedly reduced, and serially transplanted mice did not develop leukaemia. Closer analysis demonstrated that H90 directly targets CD34 $^{+}$ CD38 $^{-}$ LSCs, and interrupts their transport to stem-cell supportive micro-environmental niches in the bone marrow and spleen by reducing trans-endothelial cell migration, the last step in stem-cell homing. Moreover, CD44 ligation with the H90 antibody also directly enhanced the differentiation of LSCs into granulocytes and monocytes.

These findings identify CD44 as a key regulator of leukaemogenesis (indeed, the expression of certain CD44 isoforms on AML cells is indicative of a poor prognosis), and demonstrates the dependence of LSCs on a micro-environmental niche, a finding which might provide an 'Achilles heel' that can be targeted to eradicate these cells. Furthermore, it has been shown that certain types of solid tumours are also maintained by a small number of cancer stem cells, and the authors speculate that CD44 might be involved here as well. So, their study provides hope for a potential generalized therapeutic strategy to eradicate cancer stem cells through interrupting their interaction with supportive micro-environments, and closer analysis could uncover further drug targets involved in this interaction.

Alexandra Flemming

ORIGINAL RESEARCH PAPER Jin, L. *et al.* Targeting of CD44 eradicates acute myeloid leukemic stem cells. *Nature Med.* **12**, 1167–1174 (2006)