immune cells feedback to regulate VAT MSCs.

Artis and colleagues also set out to reveal the source of IL-33 in adipose tissue and, specifically, its role in regulating ILC2s. Similarly to Mathis and colleagues, they identified fat-resident PDGFRα^{+}SCA1^{+} stromal cells as the main IL-33 producers in all white adipose tissues, characterizing them as adipose stem and progenitor cells (ASPCs). Using IL-33–enhanced green fluorescent protein reporter mice, Artis and colleagues also distinguished IL-33-producing mesothelial cells, which encase visceral fat depots but not subcutaneous fat depots.

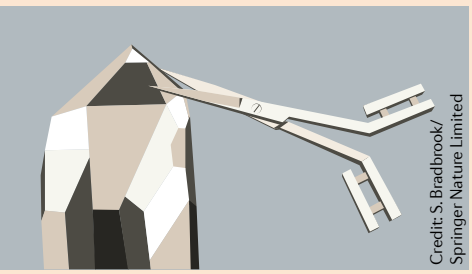
They showed that in IL-33-deficient mice, ILC2 numbers in VAT are unchanged but their function is compromised; they produce less IL-5, which is known to maintain eosinophils. Consistent with a key role in supporting ILC2s, transfer of wild-type ASPCs into IL-33-deficient mice rescued the defective ILC2 and eosinophil responses in adipose tissue. In the context of HFD-induced obesity, they showed that after only 3 days of feeding mice a HFD, there was a sharp decrease in *Il33* transcript in ASPCs but not in mesothelial cells, and this was associated with increased adipose tissue mass due to the generation of new adipocytes and with the induction of pro-inflammatory chemokines.

Finally, the presence of IL-33 in the mesothelial membrane that lines visceral cavities suggested it may function as an alarmin in this setting. Indeed, intraperitoneal challenge with the helminth *Nippostrongylus brasiliensis* induced rapid secretion of IL-33 in mesothelial cells and IL-5 secretion by peritoneal ILC2s.

With previous studies having identified various sources of IL-33 in different tissues, the current studies further highlight the importance of non-haematopoietic progenitors in immunological and physiological mechanisms that sustain normal tissue homeostasis.

Lucy Bird

ORIGINAL ARTICLES Spallanzani, R. G. et al. Distinct immunocyte-promoting and adipocyte-generating stromal components coordinate adipose tissue immune and metabolic tenors. *Sci. Immunol.* **4**, eaaw3658 (2019) | Mahlakõiv, T. et al. Stromal cells maintain immune cell homeostasis in adipose tissue via production of interleukin-33. *Sci. Immunol.* **4**, eaax0416 (2019)



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crystals (but not GAL10^{mut}) were able to promote sensitization to OVA and type 2 airway inflammation in a model of allergic airway inflammation.

Previous studies have shown that inorganic and organic crystals can promote inflammation via the NLRP3 inflammasome. However, the GAL10 crystals were able to promote type 2 immunity in mice lacking various inflammasome components. Furthermore, although crystals have been shown to promote inflammation by inducing necroptosis, the authors did not see reduced inflammation when GAL10 crystals were administered to *Ripk3*$^{-/-}$ mice, which have defective necroptosis.

These findings indicated that targeting inflammasomes or necroptosis is likely to be ineffective in preventing GAL10 crystal-driven inflammation; therefore, the authors adopted a novel approach. They generated several antibodies against the crystal-packing interfaces of GAL10 that were able to block GAL10 autocrystallization in vitro as well as to dissolve preformed GAL10 crystals. Remarkably, the antibodies could dissolve CLCs in fresh mucus samples from patients with CRSwNP and were also protective in a humanized mouse model of CLC-mediated airway inflammation.

These findings indicate that CLCs are not simply a biomarker of tissue eosinophilia in many diseases but are an actual driver of type 2 tissue inflammation and pathology. The authors suggest that their dissolving antibodies targeting GAL10 could be of benefit for relieving mucus plugging and tissue inflammation in asthma and in other severe inflammatory airway diseases.

Yvonne Bordon

ORIGINAL ARTICLE Persson, E. K. et al. Protein crystallization promotes type 2 immunity and is reversible by antibody treatment. *Science* **364**, eaaw4295 (2019)

Journal club

COMPLEX FUNGUS–HOST INTERACTIONS

β-glucan is one of the most abundant cell wall components of fungi. In the early 2000s, dectin 1 was identified as being an innate immune receptor that recognizes β-glucan. Blocking antibodies to dectin 1 abrogated killing of nonopsonized *Pneumocystis carinii* by alveolar macrophages in vitro and decreased cytokine production in response to pulmonary infection with *Aspergillus fumigatus*. However, the ultimate proof of a role for dectin 1 in defence against fungi awaited the generation of dectin 1-deficient mice. Two back-to-back publications in 2007 reported opposite results on the role of dectin 1 in clearing systemic *Candida albicans* infection. Taylor et al. showed that dectin 1-deficient mice (on the 129/Sv background) had reduced inflammatory cell recruitment and increased fungal burden. By contrast, Saijo et al. showed that although dectin 1-deficient mice (on the C57BL/6 background) are more susceptible to *P. carinii* infection, they are no more susceptible than wild-type mice to *C. albicans* infection. The mystery of the discrepancy between these results was not solved until 2013 by Marakalala et al.

> “the dependency of fungal clearance on dectin 1 is *C. albicans* strain specific”

This study compared the *C. albicans* strains and the dectin 1-deficient mice that were used by both groups in the 2007 papers. They discovered that the dependency of fungal clearance on dectin 1 is *C. albicans* strain specific. Surprisingly, dectin 1 dependency is not related to the level of β-glucan exposure. Rather, it correlates with the chitin levels in the cell wall of the fungus. Fungi with high levels of chitin were less dependent on dectin 1 for clearance.

These reports had broad implications for the study of fungus–host interactions. Fungal cell wall architecture is complex and adaptable, such that the cell wall architecture of the same fungus may be different in vivo and in vitro. Fungi grown in different culture conditions may differ in their cell wall composition. Fungi having the same name but of different strains may differ in their cell wall composition. In addition, other work has shown that the same cell may use different receptors for different responses to the same fungus. It is not difficult, therefore, to appreciate that the relationship between host and fungus is very complex.

Betty A. Wu-Hsieh
National Taiwan University, Taipei, Taiwan
e-mail: bwh@ntu.edu.tw

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ORIGINAL ARTICLE Marakalala, M. J. et al. Differential adaptation of *Candida albicans* in vivo modulates immune recognition by dectin-1. *PLoS Pathog.* **9**, e1003315 (2013)
FURTHER READING Taylor, P. R. et al. Dectin-1 is required for β-glucan recognition and control of fungal infection. *Nat. Immunol.* **8**, 31–38 (2007) | Saijo, S. et al. Dectin-1 is required for host defense against *Pneumocystis carinii* but not against *Candida albicans*. *Nat. Immunol.* **8**, 39–46 (2007)