field, resulting in a phenomenon similar to the Hall effect in magnetic materials. The authors' calculations suggest that the curious Hall effect they observed can be explained by magnetic-field-induced changes to the resistivity of VS_2–VS, which, in turn, result from the peculiar mixture of 1D and 2D components in the system.

Zhou *et al.* found that the distinctive Hall effect could be detected even at room temperature, unlike many other quantum phenomena, which occur only at much lower, cryogenic temperatures. This feature has potential in future devices. It is to be hoped that the authors' observations will launch more-detailed experimental and theoretical investigations to shed light on the origin and implications of this peculiar effect in VS_2–VS, and whether it can be reproduced in other heterodimensional structures. In a case of the whole being greater than the sum of its parts, the result indicates that such heterodimensional compounds could offer a route to maximizing the benefits of multiple classes of material. They might even be used to make materials with properties that are not possible in known 'homodimensional' structures.

Zhou and colleagues' work also offers an exciting blueprint for producing quantum materials with mixed dimensionality. Previous efforts to build heterostructures have focused largely on combining materials that have the same dimensionality. But some have succeeded in integrating 2D and 3D materials through arduous processes such as mechanical construction[5] or precise, layer-by-layer synthesis methods[6,7].

By comparison, the authors' method produces mesoscale crystals through a relatively rapid process called chemical-vapour deposition, which involves reacting vaporized precursor materials. This technique is a staple of the semiconductor industry, meaning that materials grown in this way might one day be scaled up for industrial applications with relative ease. If the approach (or methods like it) can be extended to other chemical compounds, it could provide a fruitful playground for enhancing the properties of a wide new family of materials.

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Immunology

Immune cells use hunger hormones to aid healing

Vishwa Deep Dixit

Immune cells called monocytes have long been implicated in the killing of invading bacteria. However, a closer look reveals a surprising role for them: monocytes partner with a hormone to improve skin healing after bacterial infection. **See p.166**

Production of the hormone ghrelin from stomach cells stimulates hunger[1], whereas the hormone leptin, which is released from fat cells called adipocytes, acts on the hypothalamus in the brain to inhibit food intake[2]. A loss of appetite is the most common symptom associated with the fever and inflammation that are induced by infection[3]. To coordinate a successful response to infection and to ultimately restore normal function, the body's immune, metabolic and nervous systems need to communicate by means of receptors, signalling molecules called cytokines, and hormones[4]. What are the specific restorative signals that dictate tissue healing and repair after infection? Kratofil *et al.*[5] report on page 166 a previously unsuspected connection between hormones and immune cells during healing.

"This study chimes with current ideas that immune and metabolic systems are not completely independent."

The eradication of bacterial infection by immune cells requires a strong inflammatory response. This is followed by the production of factors that promote healing and the repair of tissue damage. Research in this area has long focused on the production of pro- or anti-inflammatory cytokines, which can govern the action of infection-fighting immune cells and induce wound healing by activating stromal cells. A new research trend is to investigate how the ending (resolution) of inflammation is influenced by a variety of other molecules such as metabolites, hormones and neurotransmitters[6]. The identification of such tissue-reparative factors might enable better management of infection and repair responses in at-risk individuals, such as older people or those with obesity-associated metabolic diseases.

A major hurdle for endeavours to identify factors needed for healing is the scarcity of suitable experimental systems to mimic disease and recovery. What is needed is a clinically relevant animal model of infectious disease, in which the immune cells in question can be tracked and investigated during repair processes. To try to overcome this problem, Kratofil and colleagues developed a model system in which beads were coated with *Staphylococcus aureus* bacteria to mimic bacterial entry on a foreign body such as a splinter. These beads were inserted into the skin of mice to imitate the typical entry route of skin-penetrating bacteria during infection. This method revealed that neutrophils, immune-cell first responders to infection, infiltrated the skin and ingested (engulfed) the bacteria, whereas immune cells of another type, called monocytes, moved in from blood vessels to envelop the infection site.

The authors used live-cell imaging and determined that monocytes surround this bacterial invasion zone (Fig. 1) to orchestrate healing and tissue repair, but do not directly kill the bacteria inside the wound. This result was unexpected because, in several previous studies of models of infection, monocytes were implicated in killing the harmful bacteria[3]. By studying mice that lack the gene *Ccr2*, which is crucial for recruitment of monocytes into the skin after infection, the authors found that there was delayed wound healing in the absence of monocytes, and that overgrowth and leakage of newly formed blood vessels increased swelling in the area — a characteristic reminiscent of non-resolving persistent inflammation.

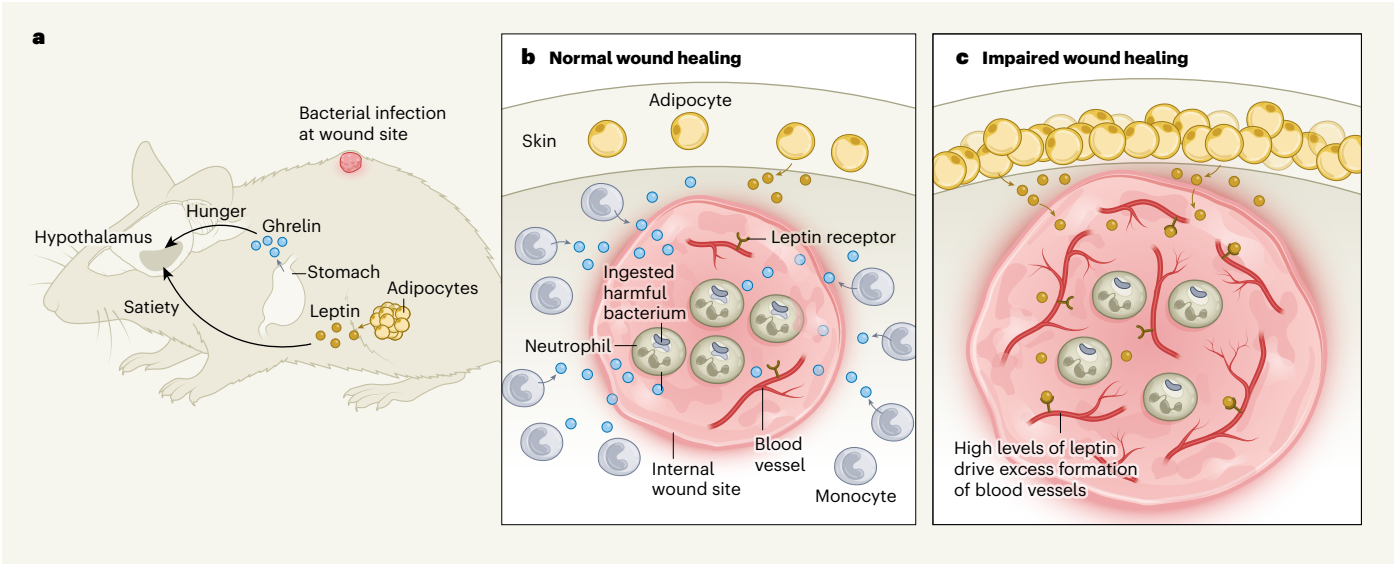

Figure 1 | Hormonal control of healing after bacterial infection. a, The hypothalamus region of the brain controls behavioural responses related to food intake. These responses are modulated by the opposing actions of the hormones ghrelin and leptin. Ghrelin, which is produced at sites such as the stomach, drives hunger. The cessation of hunger after food intake (satiety) is moderated by leptin, which is made by fat cells called adipocytes found beneath the skin. Kratofil *et al.*[5] discovered a role for these hormones when mice tackle a bacterial infection introduced at a wound under the skin. **b**, In a normal wound-healing response, immune cells called neutrophils ingest the infection-causing bacteria and new blood vessels form. Immune cells called monocytes surround the wound site and produce ghrelin, which aids healing. In this context, little leptin is produced by adipocytes in the skin. **c**, Kratofil *et al.* report that mice engineered to lack monocytes had abnormal, delayed wound healing. A large number of adipocytes were present in the skin and produced high levels of leptin. Binding of leptin to receptors on blood vessels drove excessive formation of blood vessels.

The absence of monocytes in the invasion zone was accompanied by an unexpected observation: impaired tissue healing was associated with a rise in the number of adipocytes found in the skin layer called the dermis. Such dermal adipocytes are known to participate in host defence and to control bacterial infections of the skin through the production of antimicrobial peptides[7]. Moreover, the adipocyte-derived hormone leptin is implicated in promoting wound healing and in the growth of blood vessels[8]. Kratofil and colleagues' experimental results raised the question of whether these gathering adipocytes secrete factors that contribute to tissue injury when monocytes are absent.

To investigate this, Kratofil *et al.* assessed multiple secreted proteins in skin that are known to regulate wound healing and the formation of blood vessels (vascularization). Out of the regulators tested, the authors found that only the level of leptin was elevated in the non-healing wounds of mice that lacked monocytes in infected skin. The authors report that blocking leptin at the site of infection in mice lacking *Ccr2* reduced the excessive vascular growth, whereas elevating leptin levels through the use of intradermal injections mimicked the increased blood-vessel growth observed in non-healing wounds. Mice lacking receptors for leptin on blood vessels escaped vascular defects in the infection model in which monocytes were absent in skin, suggesting that leptin acts on the endothelial cells that line the blood vessels. This, in turn, suggests that monocytes secrete a factor that acts on skin adipocytes to regulate leptin production and action.

The authors went on to identify a role for ghrelin, which is produced by monocytes in the skin of infected mice. Ghrelin counters the effects of leptin by stimulating hunger. Can immune cells harness such molecules to fine-tune tissue repair instead? Previous studies indicate that ghrelin is expressed in immune cells, and that a rise in ghrelin protects against inflammation and an inflammation-associated condition called sepsis[9]. Consistent with this, the authors report that giving ghrelin to monocyte-deficient mice blocks leptin's harmful effects of blood-vessel overgrowth.

Ghrelin treatment improved wound healing in mice that retain monocytes in the skin after infection. Notably, the authors showed that infected animals that lack ghrelin in immune cells had delayed wound repair. These findings suggest that leptin and ghrelin function like opposing inflammatory regulators in this mouse model of skin infection.

In future studies, it would be interesting to determine how monocytes unleash this tissue-reparative program in infected skin. A multi-pronged mechanism might underlie how ghrelin's repair response counterbalances leptin's effects in skin. Whether ghrelin acts on dermal adipocytes to regulate leptin or whether it activates receptors for ghrelin on blood-vessel cells to dampen leptin signalling is unknown. Also unknown is whether fasting, which increases ghrelin and lowers the concentration of leptin in the blood[1,2], can enhance the regenerative properties of immune cells.

Kratofil and colleagues' discovery that the local production of ghrelin from monocytes is a reparative signal is a valuable contribution to the field. These findings are especially relevant to obesity, in which higher-than-normal levels of leptin (hyperleptinaemia) correlate with a higher risk of infection and of impaired immune surveillance and tissue repair[6]. This study by Kratofil *et al.* chimes with current ideas that immune and metabolic systems are not completely independent, but can instead co-opt and deploy common immunometabolic mediators — once thought to be system-specific factors — to aid tissue repair and regeneration.

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