levels did not die, but they were pushed away from the basal layer and replaced by 'fit' cells that expressed high levels of COL17A1 (Fig. 1). Experiments using an *in vitro* model of human skin corroborated these findings. Reducing COL17A1 expression in basal epidermal cells resulted in the detachment of these cells from the basement membrane when a sufficient number of cells expressing high levels of COL17A1 were present to compete with the cells expressing low levels of COL17A1.

The authors found that high levels of COL17A1 in mice promote stem-cell maintenance by stimulating basal-cell divisions on a plane parallel to that of the basement membrane. This mechanism explains the increasingly clonal characteristics of cells that express high levels of COL17A1 during ageing. Loss of COL17A1 stimulates divisions of basal-layer cells on a plane perpendicular to that of the basement membrane. These divisions are needed to produce differentiated epidermal cells of the non-basal layers of the skin.

However, too many of these perpendicular divisions eventually cause stem-cell depletion and other ageing-associated skin defects, such as epidermal thinning and depigmentation because of the loss of skin-pigment stem cells. When Liu and colleagues restored COL17A1 expression through genetic modification, this restored the ability of epidermal stem cells to compete within the basal layer and partially mitigated skin ageing.

Collectively, these results suggest that COL17A1 is a sensor of DNA damage and ageing in epidermal stem cells. In young skin, spontaneous DNA damage in a limited number of basal-layer cells promotes COL17A1 degradation, which, in turn, impairs hemidesmosome formation, reduces the cells' adhesion to the basement membrane and triggers perpendicular cell division. Undamaged basal-layer cells with healthy, high levels of COL17A1 maintain parallel cell divisions and expand horizontally — thus effectively eliminating less fit cells from the basal layer and promoting skin youthfulness. A lifetime of damage to epidermal stem cells eventually reduces the overall level of COL17A1 to a critical threshold at which normal hemidesmosome formation is impaired. In this situation, there are fewer fit cells to compete with less-fit cells, and this leads to the depletion of skin stem cells, epidermal thinning and fragility, and skin depigmentation (Fig. 1).

The maintenance of fit stem cells through the years in which an individual is likely to reproduce probably also prevents tumour development, because these fit cells compete with (and eliminate) both damaged stem cells and tumour-prone cells[7]. Notably, cell competition has previously been shown to promote the expulsion from the epithelium of cells with tumour-causing mutations or other abnormal features[8,9].

Although cell competition has been extensively studied in fruit flies[10], Liu and colleagues' work provides evidence that healthy cells in mammals can also efficiently repopulate adult tissues, replacing unfit or damaged cells. Similar competitive interactions between fit and unfit cells can sometimes be observed in people with an inherited skin disease called junctional epidermolysis bullosa (JEB), which is caused by mutations in genes that encode COL17A1 and other components of the dermal–epidermal junction[11].

People with JEB have severe skin blistering because of structural abnormalities in their hemidesmosomes and dermal–epidermal junction[11]. Some affected individuals have reduced pigmentation at sites of healed blisters[11] and have abnormally low numbers of skin stem cells[12]. The latter observation correlates with Liu and co-workers' finding that proper adhesion of the epidermis to the basement membrane mediates the maintenance of skin stem cells. Notably, many, if not all, people with JEB caused by COL17A1 mutations have patches of normal, non-blistering skin that arise from a competitive expansion of cells in which the defect in COL17A1 has been spontaneously corrected[13,14] — a form of natural gene therapy. These patches, dubbed 'revertant skin patches', have normal pigmentation[13], which is consistent with the finding by Liu *et al.* that COL17A1 also plays a key part in the maintenance of skin-pigment stem cells.

In addition to elucidating the mechanisms of skin ageing, Liu *et al.* identify two chemicals that can induce COL17A1 expression in epidermal cells and improve the ability of skin stem cells to regenerate skin. Both chemicals improve wound healing in mouse tail skin, providing a proof-of-principle demonstration of the therapeutic potential of this new class of drug. Future studies are needed to determine the mechanisms of cell competition in other tissues, and to identify compounds capable of reversing ageing in other organs. ■

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ATMOSPHERIC SCIENCE

A closer look at lightning

Structural features have been identified on positively charged lightning channels that are not present on negatively charged ones. The discovery could explain why these two types of channel have different behaviours. SEE LETTER P.360

EARLE WILLIAMS & JOAN MONTANYÀ

Accelerated electric charge in lightning produces electromagnetic radiation over a broad range of frequencies. For more than a century, lightning has been studied using radio-frequency detection systems. And in the past few years, a radio telescope called the Low Frequency Array (LOFAR) has been trained on lightning. This telescope comprises thousands of antennas spread over multiple countries in Europe, and can observe the structure of lightning with unprecedented spatial resolution. On page 360, Hare *et al.*[1] present an analysis of LOFAR observations, and report the discovery of needles — structural features 10–100 metres in length — that extend perpendicularly from initially positively charged lightning channels (see also ref. 2). This finding could lead to a better understanding of lightning and explain why lightning flickers.

A lightning flash is a giant electrical discharge. An analogue in the laboratory is the discharge of an electronic device called a capacitor through a resistor — a process that can be extremely efficient, because the charge on the capacitor decays exponentially with time. The discharge of a thunderstorm by lightning is markedly less efficient, in part because the charge resides on particles that are

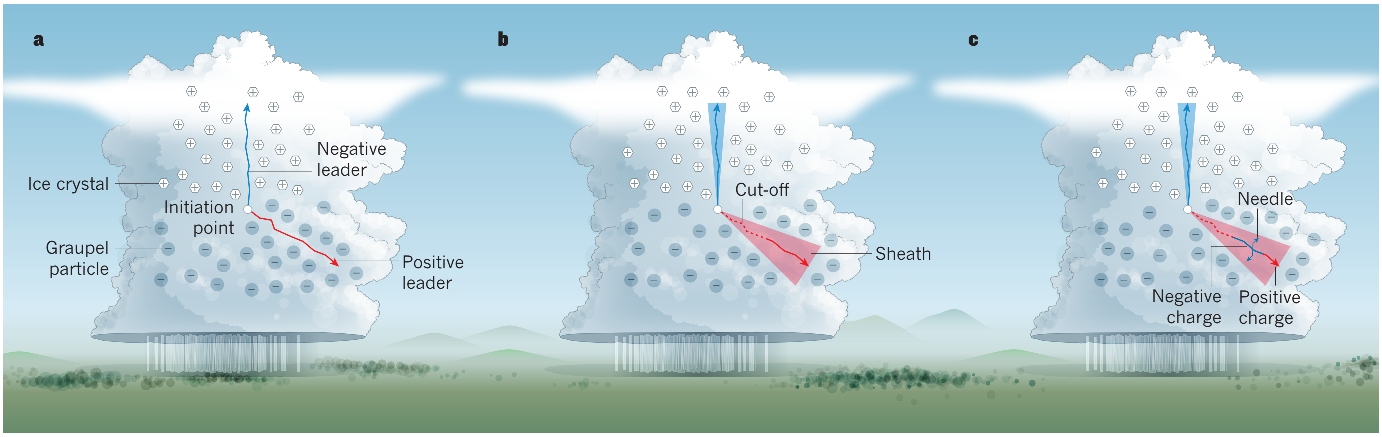

Figure 1 | Progression of a lightning flash. **a**, In a simple intracloud lightning flash, lightning forms a channel of ionized air that propagates away from the initiation point with negatively and positively charged ends, respectively called negative and positive leaders. The negative leader extends upwards into a region of positively charged ice crystals, whereas the positive leader extends downwards into an area of negatively charged graupel (soft hail) particles. **b**, During the flash, charge is pushed away from the leaders, forming conical structures called corona sheaths. In addition, current cut-off — a large reduction in current flow — occurs in the positive leader. **c**, Hare *et al.*[1] report that positive charge accumulates at the end of the positive leader and that negative charge piles up near the end of the leader. Small negative leaders (10–100 metres in length), known as needles, are launched perpendicularly from the negatively charged section of the positive leader.

spatially distributed. An efficient discharge would require the establishment of a conductive path to every charged particle in the storm. Given that air must be ionized to provide all of these paths, such a process would require an unfeasible amount of energy.

Instead, lightning forms a bidirectional channel of ionized air that propagates away from the initiation point with positively and negatively charged ends — known respectively as positive and negative leaders (Fig. 1a). The positive leader extends downwards into a region of negatively charged graupel (soft hail) particles, whereas the negative leader extends upwards into an area of positively charged ice crystals. The discharge of a thunderstorm is therefore much more intricate than that of a capacitor.

A lightning discharge differs from an idealized capacitor discharge in one other key aspect that is highly relevant to needles: the electrical resistance of lightning channels is not constant, and increases strongly with decreasing current. For example, the resistance per unit length of a channel carrying a current of 1 ampere is about 300 times that of a channel carrying 100 A (ref. 3). Hare and colleagues emphasize the role of this 'negative differential resistance' in provoking current cut-off — a dramatic reduction in current flow — in the positive leader.

The term 'polarity asymmetry' refers to differences in the macroscopic behaviour of objects that have opposite attributes, such as positive and negative charge. Polarity asymmetry in lightning leaders is conspicuous, and is ultimately attributable to the marked polarity asymmetry in the charge carriers in ionized air[4]: free electrons are highly mobile, whereas heavier positive ions are not. Lightning channels are fed by free electrons, with electron convergence at the head of the positive leader and divergence from the negative leader. As a result, the negative leader is fast and energetic, emits copious radio-frequency radiation and produces many free electrons. By contrast, the positive leader is slow and smoothly progressing, emits little radio-frequency radiation and generates few free electrons. The latter characteristics could make the positive leader more fragile, more prone to current cut-off and more likely to exhibit needles than the negative leader.

The needles identified by Hare *et al.* can now be depicted in the context of polarity-asymmetrical leaders that span positively and negatively charged regions of a thundercloud in a simple intracloud lightning flash (Fig. 1a). During the flash, charge deposited along a leader produces a large radial electric field that pushes charge away from the leader. This discharge forms a conical structure called a corona sheath that expands outwards until the radial electric field becomes smaller than a particular threshold. Smaller sheath radii are therefore associated with larger thresholds. Polarity asymmetry in these thresholds allows the volume of the sheath around the positive leader to be about 10 times greater than that around the negative leader[5] (Fig. 1b).

Negative charge carried by graupel particles is mobilized by the volume-filling discharge[6] in the corona sheath of the positive leader. This charge moves towards the positively charged region of the thundercloud, but piles up near the tip of the positive leader (Fig. 1c). Compared with the rest of the leader, this region is least prone to current cut-off because its free-electron population is the most recently formed. Therefore, whereas the lightning on large scales depletes the overall electrostatic energy, the local concentration of negative charge (and electrostatic energy) is enhanced. Small negative leaders — needles — are then launched perpendicularly from the positive leader, and the LOFAR measurements can resolve the speed of their radial progression to verify their negative charge.

Hare *et al.* emphasize that the diminished flow of negative charge towards the positive end of the thundercloud represents a diminished current in the lightning channel. Diminished current is a prerequisite for runaway instability leading to current cut-off[4,7,8] that is not readily accounted for in conceptual models of lightning structure[9]. In future work, it will be valuable to establish the connection between the formation of needles and the development of recoils and discharges called K changes in the positive leader. Such effects are recognized signatures of current cut-off and the formation of further strokes in the lightning flash. It will also be important to establish the role of the lightning corona sheath in the occurrence of other bidirectional leader developments observed in proximity to positive leaders[10,11]. ■

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