disease-causing bacteria,*Vibrio cholerae* and *Streptococcus pneumoniae*, were detected by shotgun metagenomics and matched strains of bacteria that had previously been sequenced on the same apparatus. The detection of these bacteria is therefore most probably the result of cross-contamination of the authors' sequencing machine. The ability of modern sequencing methods to detect low numbers of bacteria is thus a problem in some experiments, because even tiny levels of contaminants can result in a false-positive detection. Greater contamination of the authors' samples occurred during the earlier stages of sample preparation than in later stages. The authors confirmed previous reports[14] stating that a relatively rich microbiota was present in commercial DNA-extraction kits, and identified company-specific communities of bacteria from the genetic material extracted from the blank control samples.

Overall, the complex procedures used by de Goffau and colleagues to identify contaminants allowed them to reach a clear conclusion: only one type of bacterium was convincingly found in the placental samples in their study, and it was in only about 5% of those samples. This finding provides strong evidence that there is no functional microbiota in the placenta and suggests that it is highly unlikely that infants acquire microbes from the placenta in normal physiological conditions.

The bacterium occasionally detected in the placenta was *Streptococcus agalactiae*. If present in the mother during childbirth, *S. agalactiae* can be transmitted to the newborn and cause pneumonia, septicaemia and meningitis; several clinical practices are used to prevent such transmission[18]. The identification of *S. agalactiae* in some of the placenta samples in the study does not conflict with the dogma that the womb is microbe-free in healthy pregnancies, because this bacterium is associated with disease. Indeed, the finding that *S. agalactiae* is the only bacterium to be found on the placenta, and in a low number of samples, mirrors the expectation that a small fraction of pregnant mothers are infected with it, and that it can undergo intrauterine transmission — therefore adding credibility to the experimental findings.

De Goffau and colleagues' carefully controlled, large-scale study was needed to provide strong evidence for the absence of bacteria in the placenta. As such, the study also sets a benchmark for investigations dealing with other human organs or tissues that, at most, carry a small number of bacteria, such as the lungs or blood. Nevertheless, negative results are hard to prove conclusively, so the dogma that the womb is free of microbes should be further investigated. Bacteria can overcome many host barriers under certain conditions, and just one bacterial cell that reaches the gut of the fetus could potentially start *in utero* colonization. How the symbiosis of a human host with their microbiota is established remains an intriguing, fundamental question, but we can now be confident that the placenta is not a microbial reservoir and therefore is not a major direct stream of diverse microbes to the fetus under healthy conditions. ■

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CELL BIOLOGY

How plants perceive salt

High salt levels in the soil harm plant growth and limit crop yields. A salt–binding membrane lipid has been identified as being essential for salt perception and for triggering calcium signals that lead to salt tolerance. SEE ARTICLE P.341

LEONIE STEINHORST & JÖRG KUDLA

Salt as a nutrient for humans is a double-edged sword, being tasty in small amounts but generating an adverse response as the concentration rises. Distinct protein receptors have been shown to mediate these opposing reactions in animals. Excessive uptake of salt is not only unhealthy for humans but also detrimental for plants, because high levels of salt in the soil limit plant growth and crop yields. This is of concern, given that such conditions affect approximately 7% of land globally, including areas used for agriculture, and high salinity affects about 30% of irrigated crops[1]. On page 341, Jiang *et al.*[2] shed light on how plants recognize salt in their surroundings.

The salt sodium chloride (NaCl) is the main cause of salt stress in plants. It is toxic to cells because at high intracellular concentrations, Na^+ ions compete with other ions for involvement in biological reactions. It also has a negative effect on cellular functions by perturbing the balance of ions and thus of water — generating what is called an osmotic perturbation. It was not known how plants perceive stress generated by high salt and whether they can distinguish between ionic and osmotic perturbations.

The exposure of plants to salt stress triggers an immediate temporally and spatially defined rise in the concentration of cytoplasmic calcium ions (Ca^{2+}). It is thought that a calcium channel, of as yet unknown identity, provides a route for Ca^{2+} to enter cells during such calcium signalling. This Ca^{2+} signal leads to cellular adaption to salt stress in plant roots, and the subsequent formation of Ca^{2+} waves that spread over long distances and mediate adaptation responses throughout the entire plant[3,4]. Central to salt tolerance is the evolutionarily conserved SOS pathway. In this pathway, proteins such as SOS3, which can bind Ca^{2+} ions, decode the Ca^{2+} signal and activate[5] a protein kinase enzyme called SOS2. This enzyme, in turn, activates a protein in the cell membrane called SOS1, which is a type of protein known as an antiporter that can transport Na^+ ions out of the cell. SOS2 also promotes the sequestration of Na^+ from the cytoplasm into an organelle called a vacuole[6]. However, the components and mechanisms governing the perception of extracellular Na^+ and driving salt-induced Ca^{2+} signalling were unknown.

"It was not known how plants perceive stress generated by high salt."

Jiang and colleagues performed a genetic screen using the model plant *Arabidopsis thaliana* to identify mutant plants that had an abnormally low Ca^{2+}-signalling response to high Na^+ exposure, but that could still generate Ca^{2+} signals when challenged with other types of stress. Taking this approach, they identified a plant that had a mutation

in the gene encoding the protein IPUT1. IPUT1 acts at a central step required for the synthesis of a type of lipid called a sphingolipid. This is surprising because, in animals, Na^+ ions are sensed by protein receptors rather than through the involvement of lipids.

IPUT1 catalyses the formation of the lipid glycosyl inositol phosphorylceramide (GIPC). GIPCs are major constituents of the outer layer of the lipid bilayer in the plasma membranes of plants, accounting for up to 40% of plasma-membrane lipids, and they can be considered equivalent in function to lipids called sphingomyelins that are found in animals[7].

Other mutations previously identified[8] in the gene for IPUT1 severely affect plant development; the mutation studied by the authors did not impair development, however, which enabled the role of this protein in the response to salt to be investigated. Emphasizing the importance of Ca^{2+} signalling for plant tolerance to high salt levels, the authors report that the abnormal Ca^{2+} signals and long-distance Ca^{2+} waves in these mutant plants were associated with the plants' high sensitivity to salt stress. Remarkably, these mutants showed no alterations in their resilience to comparably severe osmotic stress that was induced experimentally in ways that did not require the manipulation of Na^+ levels.

Jiang and colleagues report that salt-stress-triggered changes in membrane polarization (the difference in electrical charges between the interior and exterior of the cell) and activation of the SOS pathway were impaired in the mutant plants, compared with wild-type plants. The authors carried out biochemical tests revealing that GIPCs can bind Na^+ ions and other ions that have a single positive charge, such as potassium (K^+) and lithium (Li^+). This observation is interesting because there is evidence for an inverse relationship between the concentrations of K^+ and Na^+ in plant cells during salt stress[5]. It would be worth investigating whether and, if so, how K^+ binding GIPCs modulates the ability of GIPC to bind Na^+, and vice versa. Taken together, the authors' evidence supports their conclusion that direct binding of Na^+ by GIPCs is an essential step in sodium sensing in plants that then triggers the calcium signals that lead to salt-tolerance responses.

The authors propose that plant GIPCs function in the same way as a type of lipid called a ganglioside that is found in animal cells. In neuronal cells, gangliosides directly or indirectly regulate important properties of receptors and ion channels in specific regions of the plasma membrane known as microdomains, which have a distinctive lipid composition[9]. The authors suggest that, like ganglioside function in animals, GIPCs in plants interact directly with Ca^{2+} channels. Na^+ binding to GIPCs might modulate channel activity, leading to the generation of Ca^{2+} signals in the cell (Fig. 1a).

However, the evidence currently available also supports a different model, in which GIPCs stimulate Ca^{2+} signals through an indirect and more complex mechanism (Fig. 1b). There is growing evidence that microdomains in lipid membranes, and specifically GIPCs in these microdomains, aid the regulation of signalling in plants.

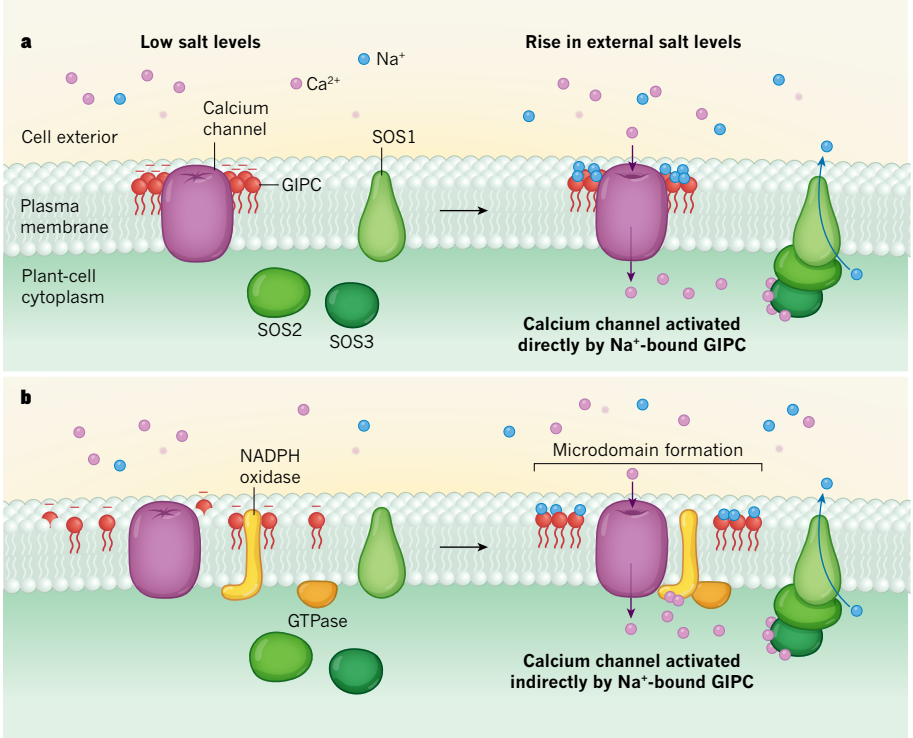

Figure 1 | How plants sense salt and activate calcium channels. **a**, When the sodium ions (Na^+) of salt are sensed outside a plant cell, an unknown calcium channel is activated and calcium ions (Ca^{2+}) enter the cell. Jiang *et al.*[2] reveal that a type of negatively charged membrane lipid called glycosyl inositol phosphorylceramide (GIPC) directly binds external Na^+ ions. The authors propose that a direct interaction between sodium-bound GIPC and the calcium channel leads to channel activation. The subsequent influx of Ca^{2+}drives an adaptive response to high salt levels in which the Ca^2-binding protein SOS3 activates the protein SOS2, which, in turn, activates the protein SOS1 to pump Na^+ out of the cell. **b**, An alternative model for the calcium-channel activation is that Na^+ binding to GIPCs drives the formation of a microdomain — a region of distinctive lipid composition — in the plasma membrane. This microdomain would alter the dynamics of signalling proteins (such as NADPH oxidases or GTPases) in the microdomain, which can affect Ca^{2+} signalling. By an unknown mechanism, Na^+ binding to GIPCs might alter the assembly and activity of proteins in the microdomain, indirectly activating the calcium channel.

Salt stress also triggers the generation of molecules called reactive oxygen species (ROS)[4,10], which can induce Ca^{2+} signalling in plants[11]. Moreover, salt stress affects the formation and dynamics of microdomains in the plasma membrane, consequently affecting the activity and lateral mobility (the speed and range of movements) of enzymes called NADPH oxidases that act in the production of ROS signals[12]. Such stress also affects the lateral mobility of enzymes called GTPases that regulate NADPH oxidases[12]. These changes in microdomain arrangement in response to salt stress depend on the GIPC composition of the plasma membrane[12,13].

It is therefore tempting to speculate that the binding of Na^+ ions or other positively charged ions to GIPCs modulates the dynamics and assembly of protein complexes in microdomains. Thus, Na^+ binding to GIPCs might lead to the assembly of signalling complexes in a microdomain that enables a Ca^{2+} signal to be generated in response to salt-induced stress. In this way, Ca^{2+}-ion-channel activation might be an indirect consequence of Na^+ binding to GIPCs, and might involve the dynamic assembly and activation of other signalling proteins (such as NADPH oxidases) in these microdomains. It would be interesting to investigate whether SOS1 might be incorporated into such a microdomain.

There is evidence in plants that another type of membrane lipid called phosphatidylserine can also affect the formation of microdomains that mediate the regulation of GTPases, Ca^{2+} or ROS signalling[13]. It has been reported[14] that phosphatidylserine can regulate GTPase-mediated signalling in plants and enable the formation of hormone-induced (rather than salt-stress mediated) clustering of GTPases in lipid membranes. Moreover, GIPCs can contribute to the generation of other signalling events in plants. For example, they act as receptors for specific toxins that cause plant disease, and plants with altered GIPC composition are more resistant to such toxins than are plants with a normal GIPC composition[15]. These observations, together with those reported

50 Years Ago

With the growth of telecommunications based on geostationary orbits, there is growing concern that satellites may become so closely crowded together that they interfere with each other … An article in the current issue of the *Proceedings of the Institution of Electrical Engineers* … consists of a calculation of the capacity of the equatorial orbit to accumulate geostationary communications satellites. Their chief conclusion is that the capacity of the equatorial orbit, with present arrangements, is probably limited to about 2,000 telephone circuits for each degree of the orbit. For practical purposes, this amounts to roughly one satellite in each four degrees of the orbit, which in turn implies that it may take very little further development before parts of the equatorial orbit — over the Atlantic and America, for example — may be overcrowded.
From *Nature* 16 August 1969

100 Years Ago

The war has been responsible for great developments in many branches of science … [C]lose attention has been given to the subject of marine physics … especially … submarine acoustics … The singular property which distinguishes a submarine from other ships is its capacity of rendering itself invisible when pursued or when seeking and attacking its prey. Robbed of this power, it is an extremely vulnerable craft … The acoustic method of detecting a submerged submarine … was found to be far more sensitive and to give a much longer range than all other methods. Instruments used for this purpose are called hydrophones. … [T]he improved hydrophones developed for war service should greatly reduce the dangers of collisions and shipwreck.
From *Nature* 14 August 1919

by Jiang and colleagues, indicate that GIPCs fulfil versatile sensing and signalling functions in plants. This work also points to a crucial role for membrane-lipid composition in organizing functionally important signalling domains for many key processes in plants. ■

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ASTROPHYSICS

X marks the spot for fast radio bursts

Fast radio bursts are enigmatic astronomical signals that originate from deep in extragalactic space. Observations using an array of radio telescopes have identified a likely host galaxy for one of these signals. SEE LETTER P.352

JASON HESSELS

In 2007, astronomers detected a flash of radio waves that was much shorter in duration than the blink of an eye[1]. Such signals, now called fast radio bursts (FRBs), are thought to have been produced billions of years ago in distant galaxies[2]. If so, the sources of FRBs must be spectacularly energetic and, quite possibly, unlike anything that has ever been observed in our Galaxy. Pinpointing the galaxies that host FRBs is the key to unlocking the mysterious origins of these signals. On page 352, Ravi *et al.*[3] report the discovery of the likely host galaxy of an FRB that travelled for 6 billion years before reaching Earth. The properties of this galaxy suggest that active star formation is not essential for making an FRB source.

The maxim 'location, location, location' applies to FRBs: knowing where these signals originate is crucial to understanding what generates them. Although astronomers have detected almost 100 FRB sources so far[2], the measured positions of these sources on the sky have typically been too inaccurate to identify their host galaxies. One exception is the first FRB source observed to produce repeat bursts[4]. This source was localized to a region of active star formation in a puny 'dwarf' galaxy[5]. The finding supported theories that ascribe the origin of FRBs to the extremely condensed remnants of powerful stellar explosions called supernovae. For example, the repeating FRBs could originate from young and hyper-magnetized neutron stars — the collapsed remnants of massive stars[6].

However, most FRB sources have not been seen to produce repeat bursts. Astronomers have therefore questioned whether these apparently one-off events have a different origin from that of the repeating FRBs[2]. From a practical point of view, one-off FRBs are much more challenging to study than repeaters. In the case of a repeating FRB, a patient observer can wait for further bursts and refine the measured position of the source. But for a one-off FRB, the position needs to be pinpointed by capturing the necessary high-resolution data at the same time as the burst is discovered.

Ravi and colleagues achieved this feat using an array of ten relatively small (4.5-metre-diameter) radio dishes spread across an area of roughly one square kilometre in Owens Valley, California. This distributed telescope network, known as the Deep Synoptic Array 10-antenna prototype (DSA-10), can scan a broad swathe of sky for FRBs (Fig. 1a). It can also provide enough spatial resolution to determine the position of a burst on the sky with high precision[7]. This precision must indeed be extremely high: unless the position is known to 1,000th of a degree, robustly associating an FRB with a specific host galaxy is impossible[8]. Even though Ravi *et al.* determined the position of their FRB to this level of precision (Fig. 1b), there is still some uncertainty as to whether or not the identified galaxy is the true host.

The authors demonstrate that this likely