depth—>7% over a limited depth range—ruling out temperature as the cause of the wave speed variations.

This globally present, rapid wave speed decrease is coincident with the intersection of the temperature-depth profile and the carbon-bearing, mantle solidus (*9*), suggesting that it is caused by 1% partial melt. The deeper thermal layer also likely contains partial melt and may interact chemically and physically with the underlying mantle. Moreover, this layer of melt at the base of the cratonic plate may aid in isolating the overlying strong, buoyant mantle from the convecting mantle beneath, giving increased importance to driving forces at plate edges.

Imaging techniques over the past decades that have focused on secondary seismic arrivals (also referred to as reflectivity analysis, receiver functions, or converted arrivals) suggest that the bases of the tectonic plates are not controlled by temperature but by secondary factors, including water content, presence of melt, or composition (*10*). The results presented by Tharimena *et al.*, implicating a carbon-associated melt, add to a growing set of findings suggesting that plates are controlled by secondary features that have a first-order effect on rheology, the defining characteristic of plates.

Recent work highlights that the cratonic lithosphere is not as simple as once thought. Although it may be dry and chemically distinct, relative to the convecting mantle, internal structures such as mid-lithosphere discontinuities (*11*), dipping reflectors (*12*), possible strong layering (*8*), and the xenolith constraints demonstrate strong internal variation. The length scales and details of these variations may play a decisive role in advancing our understanding of the craton's origin, longevity, and deformation.

What was the process that chemically strengthened the cratonic lithosphere? What is the role of the cratonic lithosphere's thermal boundary? How do the geochemical, seismological, and geodynamic properties vary within cratons, and over what scales? Solving these questions will require detailed examination of the cratons, but doing so within a global context. The results of Tharimena *et al.* do just that, by proposing a stronger role for chemical changes than for thermal history in defining tectonic plates, by explicitly requiring the presence of in situ melt, globally. In the context of recent seismic and xenolith data, these results demonstrate that the cratonic lithosphere is much richer and more complex than a massive, homogeneous, impenetrable body. New and striking complexities within the cratonic lithosphere are crucial to unraveling the question of how the continents were made. ■

REFERENCES

1. S. Tharimena, C. Rychert, N. Harmon, *Science* **357**, 580 (2017).
2. P. Tackley, *Science* **288**, 2002 (2000).
3. A. Lenardic, L.-N. Moresi, H. Mühlhaus, *J. Geophys. Res.* **108**, 2303 (2003).
4. G. Hirth, D. Kohlstedt, *Earth Planet. Sci. Lett.* **144**, 93 (1996).
5. T. H. Jordan, *Nature* **274**, 544 (1978).
6. H. Zhu, E. Bozdağ, D. Peter, J. Tromp, *Nat. Geosci.* **5**, 493 (2012).
7. B. Savage, B. M. Covellone, Y. Shen, *Earth Planet. Sci. Lett.* **459**, 394 (2017).
8. H. Yuan, B. Romanowicz, *Nature* **466**, 1063 (2010).
9. R. Dasgupta, M. Hirschmann, *Nature* **440**, 659 (2006).
10. K. M. Fischer, H. A. Ford, D. L. Abt, C. A. Rychert, *Annu. Rev. Earth Planet. Sci.* **38**, 551 (2010).
11. E. Rader *et al.*, *Geochem. Geophys. Geosyst.* **16**, 3484 (2015).
12. M. S. Miller, D. W. Eaton, *Geophys. Res. Lett.* **37**, 18 (2010).

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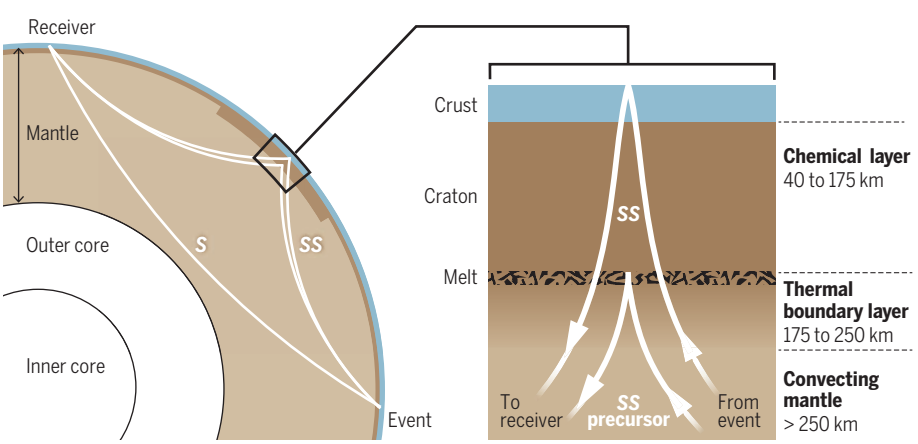
Cross sections of Earth

The full path of the *SS* and *SS* precursors along with details at the surface bounce point where the craton and its melt layer at the base of the chemical craton is identified globally. The *S* wave is direct, the fastest or minimum time, shear wave speed arrival, whereas the *SS* wave includes a single, surface bounce. *SS* precursors propagate along with *SS* but reflect, or bounce, off of Earth's strong contrast, internal boundaries, and arrive just before *SS*.



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MICROBIOLOGY

Intracellular signaling in CRISPR-Cas defense

New molecular communication in type III CRISPR-Cas systems has been identified

By **Gil Amitai** *and* **Rotem Sorek**

The CRISPR-Cas (clustered regularly interspaced short palindromic repeats–CRISPR-associated protein) system is known to protect bacteria against foreign invading DNA, usually from phages (viruses that infect bacteria) or plasmids (circular DNA found in the cytoplasm of bacteria). Since the first demonstration of CRISPR-Cas functionality a decade ago (*1*), mechanistic understanding of CRISPR-Cas has not only enabled genome editing but also revolutionized our appreciation of bacterial defense against their viruses. CRISPR-Cas systems show a high degree of sophistication in providing immunity against phages, including elaborate mechanisms to accurately identify the invading DNA, safety checks to prevent self-targeting (*2*), and high diversity of target destruction mechanisms among different types of CRISPR-Cas systems (*3*). Kazlauskiene *et al.* (*4*), on page 605 of this issue, and a study by Niewoehner *et al.* (*5*) report the discovery of an unexpected aspect of CRISPR-Cas immunity: intracellular signaling.

Kazlauskiene *et al.* and Niewoehner *et al.* show that in type III CRISPR-Cas systems, identification of phage nucleic acids by the CRISPR-Cas effector complex leads to the generation of a small molecule called cyclic-oligoadenylate (cOA). This molecule then activates a CRISPR-associated ribonuclease (RNase), the function of which was previously unclear. Both papers demonstrate that the RNase, once activated, cleaves cellular RNA nonspecifically, probably leading to dormancy or death of the infected bacterium.

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CRISPR-Cas systems typically encode an array of phage- or plasmid-derived pieces of DNA (known as the CRISPR array) that forms the bacterial immune memory. The CRISPR array is transcribed and processed into short RNA sequences, CRISPR-RNAs (crRNAs), that bind Cas proteins to form the effector RNA-protein (RNP) complex. The effector complex recognizes the nucleic acids of the foreign genetic material via base-pairing with the crRNA, eventually leading to cleavage of the foreign genetic material by endonuclease domains of one or more of the Cas proteins.

CRISPR-Cas systems are grouped into six types, each of which uses a different set of Cas proteins (*6*). Whereas most CRISPR-Cas types target foreign DNA, the kind of nucleic acids targeted by type III systems was subject for debate. Early on, it was reported that type III systems target DNA (*7*); but seemingly contradictory reports indicated that RNA was targeted (*8*). Eventually, it was realized that the type III effector RNP complex base-pairs with messenger RNA (mRNA) derived from the transcription of the invading DNA. Upon binding, the effector complex cleaves the mRNA and also cleaves the DNA from which it is transcribed (*9*–*11*).

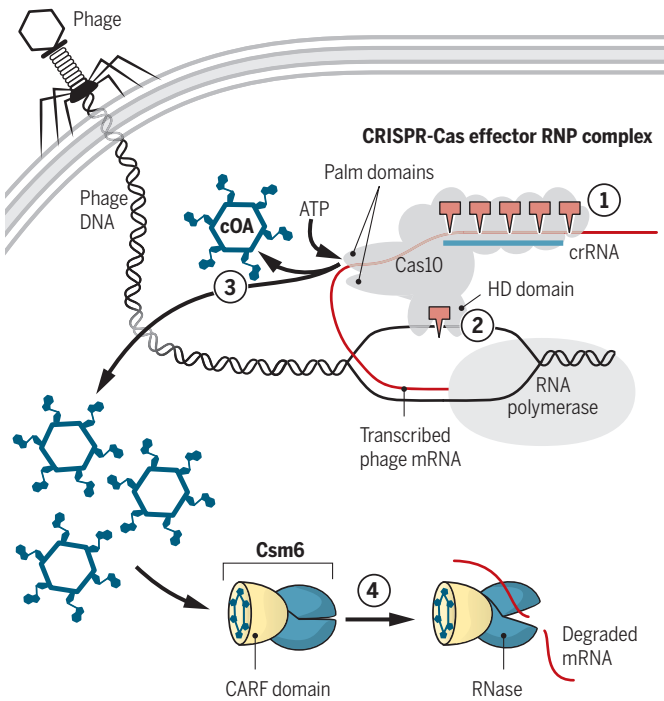
The multiprotein effector RNP complex of type III CRISPR-Cas systems includes a large protein called Cas10. Cas10 typically encodes an HD nuclease domain, which degrades the foreign DNA, and two Palm (polymerase/nucleotide cyclase-like) domains that had no known roles in the activity of CRISPR-Cas until now. Kazlauskiene *et al.* and Niewoehner *et al.* discovered that the Cas10 Palm domains are responsible for synthesizing cOA, which is a short, cyclic oligomer composed of multiple adenosine monophosphate (AMP) molecules that are derived from adenosine triphosphate (ATP). The production of cOA by Cas10 is triggered by base-pairing between the effector complex and the foreign mRNA. Once produced, cOA molecules probably disperse through the cell and activate another Cas protein, Csm6, which is a single-strand endoribonuclease that nonspecifically cleaves cellular RNA, likely degrading both bacterial and phage mRNAs.

The exact role of Csm6 in CRISPR-Cas immunity was unclear. This protein is not associated with the CRISPR-Cas effector RNP complex and was shown to be essential for immunity only when phage mRNA was part of the late-expressed phage genes or when phage mRNA sequence was mutated (*12*). The two studies now offer a plausible unified model for the mode of action of type III systems. Other types of CRISPR-Cas system, such as type I or type II, form the "first line of defense" and attempt to cleave and destroy foreign DNA. If this fails and the infection process proceeds with the transcription of phage DNA, the type III system goes into action, senses the foreign mRNA, and attempts to terminate the phage infection by cleaving both the mRNA and its DNA template. During the course of this targeting, the Cas10 protein in the type III effector RNP complex generates a measured amount of cOA. Possibly, a small amount of cOA will not suffice to induce fully fledged RNase activity of Csm6 in a manner substantial enough to damage the cell; but if multiple type III complexes identify phage mRNAs, the cumulative amount of cOA will fully activate Csm6, leading to massive degradation of cellular RNA and possibly to cell dormancy or death. This suggested mode of action ensures that if the last line of defense has failed and transcription of phage RNA is sensed from multiple loci (meaning that multiple phage infections co-occur, or that phage DNA has been replicated), then the cell commits "suicide" to prevent production of new phage particles and protect nearby bacteria from the spread of the infection.

Kazlauskiene *et al.* and Niewoehner *et al.* report the discovery of cOA as an intracellular signaling molecule involved in antiphage immune defense. This molecule binds Csm6 proteins at the CARF (CRISPR-associated Rossmann fold) domain, and this binding allosterically triggers RNase activity of Csm6. Interestingly, additional Cas proteins are also known to have CARF domains, and even non-CRISPR proteins associated with immunity against foreign DNA were reported to encode CARF domains (*13*). It is therefore plausible that this immunity-associated intracellular signaling represents just one aspect of a larger network of signaling, to be revealed by future studies, that takes place in bacterial and archaeal cells as part of their overall defense against phages. ■

CRISPR-Cas intracellular signaling

Binding of the type III CRISPR-Cas effector RNP complex to transcribed phage mRNA initiates production of cOA molecules that activate the Csm6 RNase, which degrades phage and cellular mRNA.



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REFERENCES

1. R. Barrangou *et al.*, *Science* **315**, 1709 (2007).
2. G. Amitai, R. Sorek, *Nat. Rev. Microbiol.* **14**, 67 (2016).
3. L. A. Marraffini, *Nature* **526**, 55 (2015).
4. M. Kazlauskiene *et al.*, *Science* **357**, 605 (2017).
5. O. Niewoehner *et al.*, *Nature* 10.1038/nature23467 (2017).
6. E. V. Koonin, K. S. Makarova, F. Zhang, *Curr. Opin. Microbiol.* **37**, 67 (2017).
7. L. A. Marraffini, E. J. Sontheimer, *Science* **322**, 1843 (2008).
8. C. R. Hale *et al.*, *Cell* **139**, 945 (2009).
9. J. R. Elmore *et al.*, *Genes Dev.* **30**, 447 (2016).
10. M. A. Estrella, F. T. Kuo, S. Bailey, *Genes Dev.* **30**, 460 (2016).
11. M. Kazlauskiene *et al.*, *Mol. Cell* **62**, 295 (2016).
12. W. Jiang, P. Samai, L. A. Marraffini, *Cell* **164**, 710 (2016).
13. K. S. Makarova *et al.*, *Front. Genet.* **5**, 102 (2014).

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