symmetries. (The structure of a material with n-fold rotational symmetry remains unchanged under rotation by an angle of $360°/n$ around the symmetry axis.) Other rotational symmetries are possible in quasicrystals. By far the most commonly found quasicrystals in alloys are icosahedral, or axial with decagonal (10-fold) symmetry. Other, more rarely observed quasicrystals are octagonal (8-fold) and dodecagonal (12-fold). Interestingly, until now, all reported soft-matter quasicrystals had 12-fold symmetry. Computer simulations show how dodecagonal symmetries are preferred in micellar systems because of entropy[8]. Indeed, one of the two quasicrystal phases discovered by Fischer and colleagues is 12-fold symmetric (Q12; Fig. 1b).

Much more surprising is their report of an additional phase with 18-fold symmetry (Q18; Fig. 1c) from the analysis of the quasicrystals' X-ray and neutron diffraction patterns, which Fischer *et al.*[1] classified as an enneagonal (9-fold) quasicrystal. Because diffraction patterns are always inversion symmetric, it is an open question whether their quasicrystal has 9-fold or 18-fold symmetry in real space. Although not prohibited, 18-fold (or 9-fold) rotational symmetry has never before been reported.

The preference for certain symmetries may be understood by recognizing that quasicrystals can be embedded into higher-dimensional periodic lattices. The minimal embedding dimension of an n-fold symmetric structure is four for $n = 5$, 8, 10 and 12, and six for $n = 7$, 9, 14 and 18. All known quasicrystals have a low minimal embedding dimension of four. Perhaps, then, quasicrystals with $n = 5$, 8, 10 and 12 are easier to form than other quasicrystals[9]. Indeed, Fischer and colleagues' 18-fold structure is the first report of a quasicrystal with a novel rotational symmetry in more than 20 years.

Proper identification of soft-matter quasicrystals is challenging because they tend to be more thermally disordered than atomic crystals. This has important implications for the interpretation of diffraction patterns. As previously shown[10], the scattering conditions responsible for the appearance of the Bragg diffraction peaks that characterize order in a material are highly sensitive to structural imperfections. These imperfections can lead to the appearance of secondary peaks. Fischer *et al.*[1] find an f.c.c. phase, at higher temperatures than for either Q12 or Q18, that has pronounced secondary peaks and thus many structural defects. The transition to the quasicrystal on cooling involves a change of the layer stacking in f.c.c., which would be signified by a transformation of the secondary peaks into primary peaks. With the authors' currently available diffraction data, however, one cannot definitively confirm this transformation scenario.

Quasicrystal identification from diffraction experiments also suffers from the fact that if a system contains two orientations of a crystal, then the diffraction pattern is the superposition of the two respective diffraction patterns. In many cases, the constituent crystals can share a very specific orientational relationship. For example, an f.c.c. twin can seem to have 12-fold symmetry. Fischer *et al.* ruled out twinning by comparing the experimental diffraction patterns with simulated diffraction patterns of an f.c.c. twin and a quasicrystal model. In future work, real-space images of the quasicrystals, captured by cryo-scanning electron microscopy and transmission electron microscopy, will allow even more definitive quasicrystal identification. That the observed structures are quasicrystals, and not twinned structures, is further supported by the observed phase transitions: from f.c.c. (at temperatures above 25 °C) to Q12 (at 20–15 °C) to Q18 (at less than 10 °C). Such a sequence is not expected from a system that undergoes twinning.

The discovery of Q18 constitutes the first account of a novel quasicrystalline structure on the nanoscale with no equivalent known for atomic crystals. It has the highest order of diffraction symmetry recorded so far in any single-domain crystal. Such an order of symmetry may be relevant for photonic (quasi-)crystals[11]. Photonic crystals affect the propagation of light in the same way as the potential in a semiconductor crystal affects electron motion by defining a region of forbidden electronic energies, the bandgap. In photonics, a high degree of rotational symmetry is desirable for uniform bandgaps. The discovery of this new quasicrystal is even more remarkable — the system is a chemically well known, aqueous solution of simple block copolymers common in industrial applications as wetting, dispersing and foaming agents. The finding should spur a closer look at micelle-forming systems and inspire, in an interesting twist, the search for atomic analogues of soft-matter structures. ■

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1. Fischer, S. *et al. Proc. Natl Acad. Sci. USA* **108,** 1810–1814 (2011).
2. Ziherl, P. & Kamien, R. D. *Phys. Rev. Lett.* **85,** 3528–3531 (2000).
3. Zeng, X. *et al. Nature* **428,** 157–160 (2004).
4. Talapin, D. V. *et al. Nature* **461,** 964–967 (2009).
5. Haji-Akbari, A. *et al. Nature* **462,** 773–777 (2009).
6. Hayashida, K., Dotera, T., Takano, A. & Matsushita, Y. *Phys. Rev. Lett.* **98,** 195502 (2007).
7. Lee, S., Bluemle, M. J. & Bates, F. S. *Science* **330,** 349–353 (2010).
8. Iacovella, C. R., Keys, A. S. & Glotzer, S. C. Preprint at http://arxiv.org/abs/1102.5589 (2011).
9. Mikhael, J. *et al. Proc. Natl Acad. Sci. USA* **107,** 7214–7218 (2010).
10. Förster, S. *et al. Nature Mater.* **6,** 888–893 (2007).
11. Man, W., Megens, M., Steinhardt, P. J. & Chaikin, P. M. *Nature* **436,** 993–996 (2005).

PROGRAMMED CELL DEATH

Apoptosis meets necrosis

Apoptotic cell death is essential for the development of multicellular organisms. Paradoxically, three proteins instrumental in apoptosis also collaborate to preserve life by preventing necrotic cell death. SEE LETTERS P.363, P.368 & P.373

MARCUS E. PETER

Apoptotic cell death can be induced by two distinct pathways: one intrinsic to cells and one extrinsic. Among the main players in the extrinsic pathway in both mice and humans are the adapter protein FADD, the death-executing protease enzyme caspase-8, and a regulator of caspase-8 activity, FLIP. These death-promoting proteins are also involved in embryonic development. How can such apparently opposing functions coexist? Three papers in this issue[1–3] provide evidence that the proteins act together to suppress another type of programmed cell death — necrosis.

The extrinsic pathway of apoptosis begins with the binding of an appropriate ligand to members of the death-receptor family, which lie in the cell membrane. These then recruit and activate the death-inducing signalling complex (DISC). FADD, caspase-8 and FLIP are all essential components of DISC.

Deletion of the genes encoding each of these DISC proteins causes mice to die *in utero* at mid-gestation as a result of vascular, cardiac and blood-cell-formation defects. Also, *in vitro* proliferation of immune cells called T cells is impaired if any of the three genes is deleted. What's more, tissue-specific deletions of caspase-8 unveiled immunity-related functions of this enzyme: the prevention of

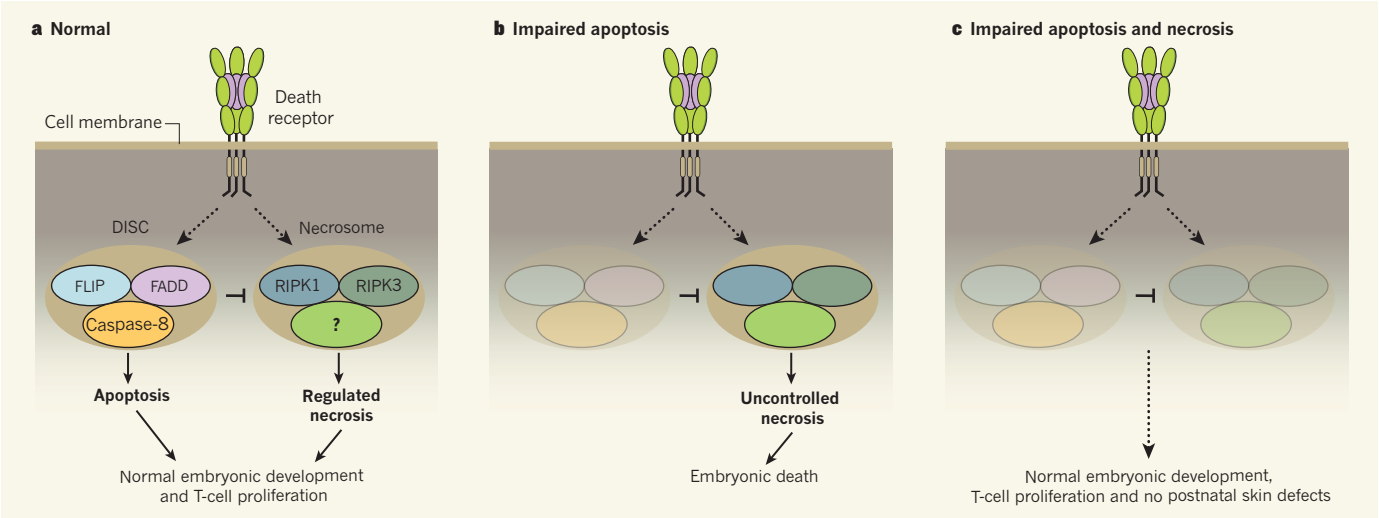

Figure 1 | Programmed-cell-death pathways are intertwined. **a**, In normal mice, death-receptor-mediated apoptosis and necrosis exist in a balance that is in part accomplished by cleavage of the necrosome components RIPK1 and RIPK3 by components of the apoptotic DISC complex. **b**, In mice deficient in any of the DISC proteins FADD, caspase-8 and FLIP, uncontrolled necrosis causes cell death and defects in various tissues, leading to embryonic death. **c**, New work[1–3] shows that, in mice lacking any of the three DISC proteins and either RIPK1 or RIPK3, neither apoptosis nor necrosis seems to occur, preventing the defects described in **b**. Nonetheless, mice deficient in both FADD and RIPK1 die shortly after birth, and those lacking both caspase-8 and RIPK3 develop a lymphoaccumulation disease due to the absence of death-receptor-mediated apoptosis.

skin inflammation, generation of myeloid and lymphoid cells, and differentiation of macrophages. The question remained whether these various defects were due to loss of one or several functions of the DISC components. The new reports[1–3] suggest that almost all defects seen in any of the DISC-gene mutant mice can be traced back to one activity: the suppression of necrosis.

But how does necrosis relate to apoptosis? Although apoptosis has been synonymous with programmed cell death for many years, there are at least three main forms of programmed cell death: autophagy, necrosis and apoptosis. Autophagy allows a cell to survive — for instance, under conditions of limited nutrient availability — by digesting its own components; if carried to exhaustion, this results in cell death. Necrosis, in contrast to apoptosis, has been viewed as a form of accidental cell death brought about by injury to the cell by pathogens or toxins.

Although several studies have suggested that certain forms of necrosis are programmed, the big breakthrough in the study of programmed necrosis (also called necroptosis[4]) came from the discovery that the enzymatic activity of the protein RIPK1 is instrumental in the execution of necrosis[5]. Intriguingly, RIPK1 was originally cloned through its interaction with CD95, a death receptor that induces apoptosis.

More recently, RIPK3 — another member of the RIPK family — was found[6,7] to function with RIPK1 in a complex called the necrosome. Caspase-8 can cleave both RIPK1 and RIPK3, inhibiting their role in caspase-independent cell death[8,9]. This finding suggested crosstalk between DISC and the necrosome.

To generate mice lacking both a DISC and a necrosome component (double-knockout mice), Oberst *et al.* (page 363)[1] and Kaiser *et al.* (page 368)[2] crossed caspase-8-deficient mice with RIPK3-deficient mice; Zhang and colleagues (page 373)[3] crossed FADD-deficient mice with RIPK1-deficient mice. Strikingly, in all cases, the embryonic lethality observed in the absence of either FADD or caspase-8 was completely corrected. This observation alone confirms that FADD and caspase-8 on one side, and RIPK1 and RIPK3 on the other, are components of two opposing death mechanisms; the former seem to suppress the latter during embryonic development (Fig. 1).

Oberst *et al.*[1] and Kaiser *et al.*[2] also report that T-cell proliferation in their double-knockout mice was normal. This suggests that, in the absence of a gene encoding any DISC protein, uncontrolled necrosis inhibits T-cell proliferation. Moreover, none of the double-knockout mice showed chronic skin inflammation, and the development of various immune cells was also normal.

Why are genes of the necrosome expressed, only to be inhibited during embryonic development? After all, without a functional necrosome, mice make it through embryonic development just fine[10]. Part of the answer probably lies in an additional activity of RIPK1 — to activate the transcription factor NF-κB. In Zhang and colleagues' study[3], RIPK1-deficient mice died shortly after birth, and this neonatal mortality could not be corrected by additional deletion of FADD. Moreover, Oberst *et al.*[1] and Kaiser *et al.*[2] find that, with age, mice lacking both RIPK3 and caspase-8 suffered from a disorder of the immune system called progressive lymphoaccumulation, which also occurs in CD95-deficient mice[11].

Apoptosis and necrosis seem to be regulated by different forms of caspase-8. The induction of apoptosis requires a fully processed, heterotetrameric form of caspase-8. However, mice carrying a mutant caspase-8 that prevents release of the mature enzyme, and so renders it inactive for mediating apoptosis, develop normally, showing no defects in T-cell proliferation[12]; this hints at suppression of the necrosome.

Although none of the teams[1–3] generated mice deficient in both FLIP and RIPK1 or FLIP and RIPK3, Oberst *et al.*[1] tackled this question *in vitro*. They demonstrate that FLIP, independently of its activity in regulating caspase-8, is required for the protective function of the DISC genes during embryonic development. The caspase-8–FLIP complex seems to participate in preventing the formation of a FADD–RIPK1–RIPK3-containing complex in response to TNF — a factor that induces necrosis. These data suggest that mice lacking FLIP and either RIPK1 or RIPK3 also may not show defects in development or T-cell proliferation.

On the basis of these data[1–3], it is tempting to conclude that all of the non-apoptotic effects of caspase-8 are due to its role in cleaving the necrosome. Let's not forget, however, that caspase-8 has various non-apoptotic activities, ranging from growth promotion, cell motility and invasiveness, to tumour metastasis. Investigation is needed into whether all of these activities can be traced back to suppression of the necrosome. The simple view that caspase-8 controls the necrosome through proteolytic cleavage of RIPK1 and/or RIPK3 is not fully supported by the available data[13]. And Zhang and colleagues' study suggests that FADD-deficient embryos show greatly increased levels of RIPK1 as well as signs of RIPK3 aggregation, which may not be solely

caused by a lack of cleavage by caspase-8.

Little is known about pathways downstream of the necrosome. Either reactive oxygen species or activation of autophagy through deregulated metabolism might be essential for the completion of programmed necrosis[14]. It has become clear, however, that the various death pathways are more closely intertwined than was previously thought. The crosstalk between the components regulating autophagy[15], apoptosis and necrosis[1–3] amply demonstrate that. ■

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1. Oberst, A. *et al. Nature* **471,** 363–367 (2011).
2. Kaiser, W. J. *et al. Nature* **471,** 368–372 (2011).
3. Zhang, J. *et al. Nature* **471,** 373–376 (2011).
4. Degterev, A. *et al. Nature Chem. Biol.* **4,** 313–321 (2008).
5. Holler, N. *et al. Nature Immunol.* **1,** 489–495 (2000).
6. He, S. *et al. Cell* **137,** 1100–1111 (2009).
7. Cho, Y. *et al. Cell* **137,** 1112–1123 (2009).
8. Lin, Y., Devin, A., Rodriguez, Y. & Liu, Z. *Genes Dev.* **13,** 2514–2526 (1999).
9. Feng, S. *et al. Cell Signal.* **19,** 2056–2067 (2007).
10. Newton, K., Sun, X. & Dixit, V. M. *Mol. Cell Biol.* **24,** 1464–1469 (2004).
11. Adachi, M. *et al. Nature Genet.* **11,** 294–300 (1995).
12. Kang, T.-B. *et al. J. Immunol.* **181,** 2522–2532 (2008).
13. Osborn, S. L. *et al. Proc. Natl Acad. Sci. USA* **107,** 13034–13039 (2010).
14. Zhang, D.-W. *et al. Science* **325,** 332–336 (2009).
15. Maiuri, M. C. *et al. Nature Rev. Mol. Cell Biol.* **8,** 741–752 (2007).

EARTH SCIENCE

Continental jelly

An approach integrating different data sets has been used to map out seismic-velocity ratios in the crust of western North America. High inferred quartz content correlates with tectonic deformation zones. SEE LETTER P.353

ROLAND BÜRGMANN & PASCAL AUDET

Ever since the recognition of plate tectonics on Earth, with its jigsaw puzzle of shifting plates, geoscientists have wondered why otherwise strong and rigid continents repeatedly break up and collide along the same zones of apparent weakness. On page 353 of this issue, Lowry and Pérez-Gussinyé[1] propose that the inherent weakness of these persistent deformation zones may be caused by the low strength of quartz, and its relative abundance in such zones in the continental crust — Earth's outermost layer, which is generally 30–50 kilometres thick in continental regions.

The authors' data were drawn from the EarthScope Transportable Array of seismic stations in western North America, with additional constraints coming from gravity and heat-flow measurements. They used a new approach to develop a map of the ratio between pressure-wave (v_P) and shear-wave (v_S) propagation velocities in the crust from distant earthquakes (see Fig. 3 on page 355). On the basis of experimental data[2], Lowry and Pérez-Gussinyé argue that low values of this ratio (v_P/v_S of about 1.8 or lower) are uniquely associated with high concentrations of quartz in the crust, a mineral that flows much more readily than other crustal constituents at the high temperatures found at depth[3].

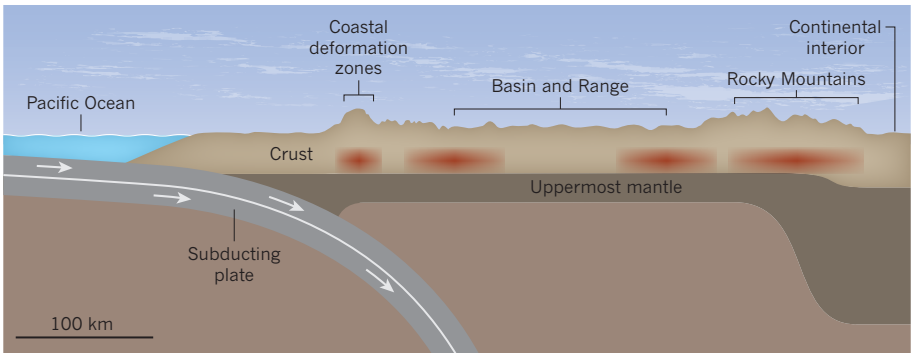

Figure 1 | Cross-section through zones of active deformation in western North America and the stable continental interior. At the left (west) is the subduction zone; at right, the stable continental interior. Lowry and Pérez-Gussinyé[1] find that regions of high inferred quartz content in the lower crust (red) correlate well with zones of recent tectonism exemplified by the coastal deformation zones, parts of the Basin and Range province and the Rocky Mountains. The thickness of the North American plate (crust and rigid uppermost mantle) decreases from more than 200 km in the interior to about 50 km in the west as a result of thermal thinning and hydration caused by past and present subduction.

The study region is the western Cordillera, reaching from the San Andreas fault system in California to the Rocky Mountains in Wyoming and Colorado. The apparent association of low v_P/v_S with zones of recently active plate-boundary deformation in this region suggests that high abundance of quartz-rich rocks in the lower crust, often described as a weak zone of jelly in the continental sandwich of crust and mantle[4], is a key ingredient for initiating deformation (Fig. 1). Once a deformation zone has been initiated, further weakening by rising temperatures and addition of fluids may sustain a permanently weak zone over many plate-tectonic cycles. Such inherited weakness may isolate continental interiors from deformation and force the repeated reactivation of plate-boundary faults during alternating cycles of plate divergence and convergence[5].

The method developed by Lowry and Pérez-Gussinyé relies on an automated data-analysis product[6], which calculates bulk crustal properties (v_P/v_S and crustal thickness, H) at several hundreds of seismic stations using converted pressure-to-shear-wave arrivals resolved on the radial component of motion. Those parameters are notoriously difficult to estimate accurately because of a well-known trade-off between H and v_P/v_S. To improve the resolution of the estimates, the authors use two additional constraints from statistical inference: optimal spatial interpolation and gravity modelling. The model uses gravity anomalies to obtain an optimal density structure that fits variations in v_P/v_S, H and additional contributions from heat-flow data. The technique thus cleverly combines disconnected data sets with statistical modelling to significantly improve the accuracy of the solution.

Nevertheless, the method is limited by the initial automated solution, which is obtained assuming a single-layer, isotropic crust with a flat crust–mantle boundary. Any deviation from this simple model, produced by non-horizontal structure, anisotropy or multiple layering, may produce complicated patterns of shear-wave arrivals on both radial and transverse components of motion; when inverted for the single-layer crust, interference patterns result that can bias the solution. One possible improvement to the method would be to use transverse-component shear-wave arrivals both to evaluate the validity of the single-layer crustal model and to help refine it.

There is some debate on where the strength of tectonic plates resides. In the traditional jelly-sandwich model of continental plate strength, a weak lower crust underlies a strong and brittle upper crust and overlies a strong uppermost mantle layer[4]. An alternative view is that the uppermost mantle contributes little to continental strength in many regions, leaving the brittle crust alone to support tectonic stresses[7].

Studies that model geodetically measured