molecule. Human Dicer (hDicer) is specialized for pre-miRNAs and is thus non-processive. Although structures of Dicer enzymes from various organisms are available, the new studies of hDicer clarify the catalytic cleavage step (also known as 'dicing'), as well as revealing evolutionarily conserved pre-miRNA features that are important for efficient RNA processing.

The multidomain protein hDicer (Fig. 1) includes two RNase III domains, a helicase domain, a dsRNA-binding domain (dsRBD) and a PAZ domain, which, together with the platform domain, accommodates the two ends of the pre-miRNA hairpin[4]. Dicer not only cleaves the pre-miRNA but also functions as a 'molecular ruler' by essentially measuring the distance between the end of the RNA stem and the catalytic centres of the enzyme to produce a dsRNA that is 20–23 nucleotides in length. The sequences of pre-miRNAs are highly diverse, but besides the common RNA features of the hairpin structure, a two-nucleotide 3′ overhang on one side of the RNA (its 3′ end) and a phosphate group on the other side of the RNA (its 5′ end), no specific sequences or extra local structural motifs that might guide cleavage had been found previously.

To find such features, the first study by Lee *et al.*[1] used a pre-miRNA-processing approach in which RNAs were engineered to randomize the sequence of the upper stem of the pre-miRNA. Then the authors tested RNA-processing efficiency by sequencing the small RNA products produced after cleavage by Dicer. They thereby found an evolutionarily conserved sequence of nucleotides that they term GYM. This nucleotide motif, located around the cleavage site, consists of a paired guanine (G, one of the four main bases found in RNA), a paired pyrimidine (Y, which can be either one of the bases cytosine and uracil) and a mismatched (M) nucleotide pair. When this motif is engineered onto a random short hairpin RNA, Dicer processing of the RNA is markedly increased compared with the case for RNAs lacking the motif.

In their second study, Lee *et al.*[2] used hDicer and a pre-miRNA with a GYM motif as the material for generating structural data by means of cryo-electron microscopy. Strikingly, the authors found complexes with hDicer in the dicing state, which had not been seen so far.

Compared with structures in the pre-dicing state, in which the helicase domain binds to the pre-miRNA loop and keeps the pre-miRNA away from the catalytic centre, the helicase domain is not visible in the dicing-state structure. This observation indicates that the helicase domain becomes very flexible in the dicing state (Fig. 1). It might no longer bind to the pre-miRNA, enabling the pre-miRNA to move into a cleavage-competent position. Furthermore, in this position, the dsRBD of Dicer recognizes the GYM motif and stabilizes the interaction between the RNA and Dicer for a more efficient cleavage reaction. This molecular interaction explains the evolutionary conservation of the GYM motif.

Although several Dicer structures are available from different organisms and in different states[5–9], there are still many unknowns about this fascinating molecular machine. First, and most intriguingly, how is the cleavage product released in a post-dicing state? A RISC-loading complex has been postulated [10], consisting of Dicer, its partner protein TRBP and an Argonaute protein that takes over handling the miRNA from Dicer after cleavage. Major structural rearrangements and long-distance movements of the cleavage product are obviously required for this step. The helicase domain might become more static in such a complex, and TRBP might also contribute to structural rearrangements. Another question is how a correctly loaded RISC might be released from this complex.

Furthermore, we have not even begun to understand the role of alterations (termed post-translational modifications) of Dicer, such as the addition of phosphate groups (phosphorylation), in this process. Many such modifications have been reported, but if and how they contribute to the dicing cycle, and particularly to the structural flexibility of Dicer, is unknown.

Notably, both studies highlight cancer-associated mutations that correspond to prominent structural positions in Dicer. For example, the sequence encoding a pocket in the platform domain that accommodates the 5′ end of the pre-miRNA is often mutated in cancer. In addition, cancer-associated mutations in the dsRBD lead to reduced binding of Dicer to the GYM motif.

It is tempting to speculate that many more such mutations exist, which might not only affect cleavage by Dicer but potentially also later, post-dicing steps. What are the consequences of such mutations for cell growth and cancer development? Is there solely a reduction of global miRNA levels owing to impaired processing, or could there even be pre-miRNA-specific processing effects? Future mechanistic and structural work will provide further functional insights into the fundamental cellular process of miRNA formation and its link to disease.

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Atmospheric chemistry

How wildfires deplete ozone in the stratosphere

V. Faye McNeill & Joel A. Thornton

Unexpected smoke-particle chemistry is shown to be the link between intense wildfires and stratospheric ozone loss. As the climate changes, more-frequent and more-intense fires might delay the recovery of the stratospheric ozone layer. **See p.259**

The devastating Australian bushfires of 2019–20 sent massive plumes of smoke high into the atmosphere, where it was transported around the world, affecting air quality as far away as South America[1]. Satellite data showed that this smoke also caused changes in the composition of the upper atmosphere, including a decline in stratospheric levels of ozone[2,3] — a gas that forms a protective layer around Earth, shielding terrestrial life from damaging short-wave ultraviolet radiation. But the mechanism by which wildfire smoke might enhance ozone depletion has remained uncertain. On page 259, Solomon *et al.*[4] make the case that particulate matter from wildfire smoke contributes to the destruction of stratospheric ozone, and suggest how it does this.

In 1974, modelling first pointed to increasing levels of chlorofluorocarbons (CFCs, which were often used in aerosol spray cans, foams and cooling devices) as a source of chlorine radicals in the stratosphere that could

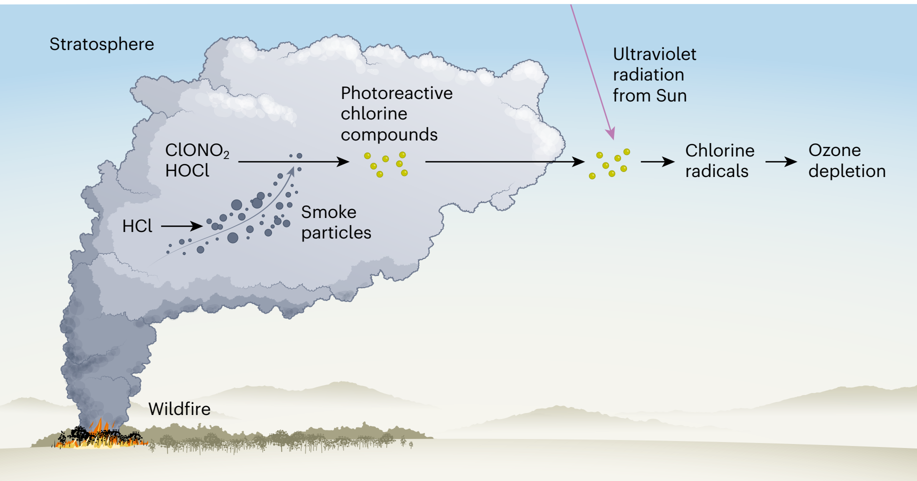

Figure 1 | A mechanism for wildfire-driven ozone depletion. Smoke particles from intense wildfires can enter the stratosphere. Solomon *et al.*[4] report that smoke particles in the stratosphere can absorb hydrogen chloride (HCl) gas, derived mostly from the breakdown of anthropogenic chlorofluorocarbon compounds (not shown). This allows the particles to catalyse the conversion of other chlorine-containing gases, such as chlorine nitrate ($ClONO_2$) and hypochlorous acid (HOCl), to 'photoreactive' chlorine compounds. When irradiated by ultraviolet light from the Sun, the photoreactive compounds produce chlorine radicals that catalytically destroy ozone, depleting its concentration in the stratosphere.

catalytically destroy ozone[5]. The dramatic discovery in the mid-1980s of the seasonal 'hole' in the ozone layer over the Southern Hemisphere polar region led to the 1987 Montreal Protocol on Substances that Deplete the Ozone Layer, the phasing out of CFCs worldwide and the expected gradual recovery of the stratospheric ozone layer – which is still not complete, owing to the long residence time of CFCs in Earth's atmosphere. When the ozone hole was first observed, the challenge for atmospheric chemists was to explain its unique seasonal and spatial characteristics. At the time, observations clearly linked the hole's appearance to anthropogenic chlorine, but there was no chemical explanation for its intensity and timing.

A major breakthrough came from theoretical and laboratory studies that pinpointed reactions occurring on the surfaces of stratospheric ice particles[6,7], which make up the iridescent 'mother-of-pearl' clouds seen in polar regions. Throughout the dark polar winter, those surfaces efficiently catalyse reactions of hydrogen chloride (HCl, mostly derived from the breakdown of CFCs) with other relatively inert chlorine-containing gases, including chlorine nitrate ($ClONO_2$) and hypochlorous acid (HOCl), to release 'photoactive' forms of chlorine that become reactive when irradiated by light. The return of sunlight in the polar spring transforms those forms of chlorine into a burst of highly reactive chlorine radicals, which catalyse processes that cause ozone loss. The ice particles further contribute to ozone depletion by removing certain nitrogen oxides (N_2O_5 and HNO_3) from the atmosphere; these compounds act as reservoirs for nitrogen oxide radicals, which, if present, limit the efficiency of chlorine-catalysed ozone destruction[6,7].

The properties of ice make it particularly well suited to catalysing chlorine activation and to removing nitrogen oxides at the low temperatures of the stratosphere, but there are clues that other particle types might also have a role. The powerful eruption of Mount Pinatubo in the Philippines in 1991 injected large amounts of sulfur dioxide gas into the stratosphere. After being transported long distances and oxidized, this gas became a layer of reflective sulfuric acid particles over much of the globe. In addition to reducing global average surface temperatures by 0.5 °C for more than a year, these particles also catalysed ozone loss in the stratosphere – not just over polar regions, but throughout the mid-latitudes[8].

Fast-forward 30 years to the 2019–20 Australian bushfires, which were another source of stratospheric particles, but with a very different chemical profile. The heat from large fires can lead to efficient lofting of smoke and its gas and particle constituents to high altitudes, where they enter the stratosphere. Solomon *et al.* now report that particulate matter from wildfire smoke contributes to the destruction of stratospheric ozone by efficiently absorbing HCl gas, thereby enhancing chemical activation of ozone-destroying chlorine radicals (Fig. 1). The authors also provide a glimpse of the properties of wildfire smoke particles in the stratosphere, which are challenging to observe directly or to recreate in the laboratory owing to their compositional complexity and the extreme conditions of the stratosphere.

Particles in wildfire smoke consist mostly of soot and organic carbon material, and are not immediately obvious candidates for enhancing chlorine activation and nitrogen oxide sequestration. Under dry conditions, such particles are generally less reactive than in ice or aqueous solutions[9]. Moreover, particles that are made up mostly of oxygenated organic compounds (such as those in smoke), and that might otherwise take up liquid water to better facilitate chlorine activation, can be glass-like at the cold temperatures and dry conditions of the lower stratosphere[10]. Reactant gases would not dissolve and diffuse into glassy particles as well as they would into liquid droplets. However, efficient HCl ionization and chlorine-activation reactions can occur on frozen polar stratospheric ice-particle surfaces as a result of the formation of disordered surface regions under stratospheric conditions[11], and this could also be true for glassy particles.

The first clue that smoke particles in the stratosphere might not be in a dry, glassy state came from an analysis of data acquired by the Atmospheric Chemistry Experiment Fourier Transform Spectrometer, a project in which the atmosphere is monitored by a spectrometer on a space satellite. This suggested that the Australian wildfire particles in the stratosphere contain both oxygenated organic material and adsorbed water[2].

Solomon *et al.* now build on this observation, using thermodynamic arguments to assert that complex mixtures of oxygenated organic material are likely to be liquid-like, even at low stratospheric temperatures. They also draw on an intriguing, albeit limited, set of laboratory studies of HCl solubility in mixtures of organic acids and water. These show that the potential for such mixtures to absorb HCl is even higher than that for sulfuric acid (the more common component of stratospheric particles). In other words, smoke particles have a higher potential to promote ozone depletion than was previously thought. On this basis, Solomon and colleagues are able to reproduce the ozone depletion observed during the Australian wildfires, using numerical modelling that combines their proposed process with the known chemistry of chlorine activation and chlorine-catalysed ozone destruction.

The study makes it clear that chlorine activation by smoke particles is the missing piece of the wildfire ozone-depletion puzzle. However, the findings raise questions about the physical state and chemistry of smoke particles in the stratosphere, questions that should now be further explored with field observations and laboratory studies under realistic conditions. Are these particles liquid-like, glassy or in some other state? And is a liquid-like state necessary to catalyse chlorine activation efficiently?

The findings also raise further questions about proposals to intentionally inject particles into the stratosphere to reflect sunlight and cool the planet – a climate-engineering approach called solar-radiation management. It has been proposed that, by using particles other than sulfuric acid, negative side effects such as ozone depletion and stratospheric warming could be bypassed or reduced[12]. Solomon and colleagues' study underscores the possibility that various particle types, fresh or after chemical transformation in the stratosphere, might still promote ozone depletion for a few decades as stratospheric chlorine levels slowly decline. Any candidate material for stratospheric injection must, at a minimum, be studied carefully in the laboratory, under simulated conditions of the stratosphere.

The Australian bushfire season of 2019–20 was extreme, but large wildfires and the resulting pyrocumulonimbus clouds are likely to become increasingly frequent and intense as the climate changes. The resulting injections of smoke into the upper atmosphere might therefore slow or temporarily disrupt the recovery of the stratospheric ozone layer. In this context, Solomon and colleagues' findings emphasize the need for atmospheric chemists to better understand the properties and reactivity of common, but complex, atmospheric particle types, such as those produced from biomass burning, in the cold and dry upper atmosphere.

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Condensed-matter physics

Hopes raised for ambient superconductors

ChangQing Jin & David Ceperley

A hydrogen-rich compound has taken the lead in the race for a material that can conduct electricity with zero resistance at room temperature and ambient pressure — the conditions required for many technological applications. **See p.244**

A superconductor is a metal that conducts electricity without resistance. In our increasingly electrified world, the implications of such a material are astounding — just imagine transmitting electrical power over thousands of kilometres with essentially no losses. But as promising as superconductivity might sound, this state has been achieved only at low temperatures[1] or very high pressures[2], both of which are unsuitable for many applications. For this reason, finding a material that can superconduct under ambient conditions has long been a focus of materials research. On page 244, Dasenbrock-Gammon *et al.*[3] report possible evidence for remarkable progress in this search.

When a material is in a superconducting state, its electrons form bound pairs known as Cooper pairs. These pairs avoid further collisions, and therefore encounter less resistance, than do single electrons moving alone. In some materials, crystal-lattice vibrations enable these Cooper pairs to form because the movement of positive ions in the lattice draws the electrons together. Materials containing hydrogen are particularly amenable to this pairing mechanism because hydrogen is the lightest chemical element, which means it has the highest vibration frequency. According to theory[4], this high frequency should increase the temperature at which a material can superconduct.

In 1968, physicist Neil Ashcroft predicted that pure hydrogen could superconduct at room temperature[5]. However, hydrogen becomes metallic only when H_2 molecules are dissociated at intense pressures of around 500 gigapascals (1 GPa is 10^9 Pa)[6]. This is about five million times that of atmospheric pressure, and extremely difficult to achieve with current experimental techniques. Ashcroft later suggested that hydrogen-rich compounds could become superconducting at lower pressures than can pure hydrogen, owing to the chemical compression induced by the other elements[7].

Experiments have since shown that several polyhydride compounds transition to a superconducting state at temperatures higher than 200 kelvin (some 93 K below room temperature). These compounds include sulfur hydride[2], rare-earth hydrides[8,9] and alkaline-earth hydrides[10,11]. But the pressures required are still very high — typically, hundreds of gigapascals.

Other materials exhibit a state of 'unconventional' superconductivity induced by lattice vibrations, as well as other physical processes that set these systems apart from their conventional counterparts[12,13]. A process called doping, in which impurities are deliberately added to a material, can induce, modify or enhance superconductivity in these materials — changing a non-superconducting state into a high-temperature superconducting state.

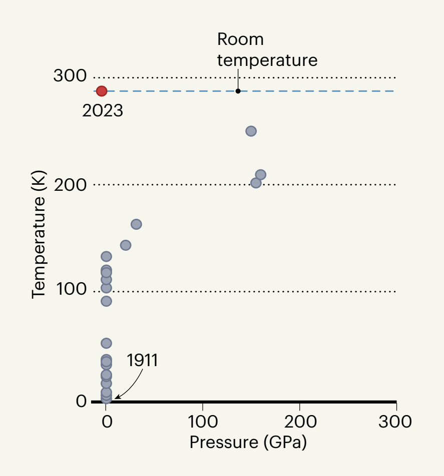

Figure 1 | The road to high-temperature superconductors. Researchers have been trying to achieve a superconducting (zero electrical resistance) state at ambient temperatures and pressures for more than a century. Several superconductors have been reported, albeit at very low temperatures. In 1968, it was predicted that pure hydrogen could superconduct at room temperature[5]. Dasenbrock-Gammon *et al.*[3] provide possible evidence that a hydride compound superconducts at 294 kelvin and 1 gigapascal (10^9 Pa), close to ambient conditions. (Adapted from Fig. 1 of ref. 20, with extra data from refs 10, 11.)