Many questions remain. For example, how are the different types of PCD integrated and controlled to achieve optimal release of DAMPs? What precisely triggers NINJ1-induced pore formation? Finally, the identification of antibodies that can function to inhibit NINJ1's pore-forming activity *in vivo* raises the intriguing question of whether NINJ1 might represent a therapeutic target for certain chronic inflammatory diseases.

James C. Whisstock and **Ruby H. P. Law** are at the Monash University Biomedicine Discovery Institute, Clayton, Melbourne 3800, Australia, and at EMBL Australia, Monash University, Clayton.
e-mails: james.whisstock@monash.edu; ruby.law@monash.edu

1. Bertheloot, D., Latz, E. & Franklin, B. S. *Cell. Mol. Immunol.* **18**, 1106–1121 (2021).
2. Degen, M. *et al. Nature* **618**, 1065–1071 (2023).
3. Kayagaki, N. *et al.* **618**, 1072–1077 (2023).
4. Frank, D. & Vince, J. E. *Cell Death Differ.* **26**, 99–114 (2019).
5. Xia, S., Hollingsworth, L. R. IV & Wu, H. *Cold Spring Harb. Perspect. Biol.* https://doi.org/10.1101/cshperspect.a036400 (2019).
6. Xia, S. *et al. Nature* **593**, 607–611 (2021).
7. Kayagaki, N. *et al. Nature* **591**, 131–136 (2021).
8. Araki, T. & Milbrandt, J. *Neuron* **17**, 353–361 (1996).
9. Jumper, J. *et al. Nature* **596**, 583–589 (2021).
10. Law, R. H. P. *et al. Nature* **468**, 447–451 (2010).
11. González-Juarbe, N. *et al. PLoS Pathog.* **11**, e1005337 (2015).
12. Wang, H. *et al. Mol. Cell* **54**, 133–146 (2014).

The authors declare no competing interests.
This article was published online on 17 May 2023.

Atmospheric chemistry

Halogen-containing gases cool the climate

Laura Revell

Simulations using a model of the Earth system have shed light on the role of short-lived halogen-containing gases in climate change. The findings suggest that these gases should now be included in all Earth-system models. **See p.967**

Short-lived gases that contain the halogen elements chlorine, bromine or iodine are widespread in Earth's atmosphere. These compounds, which last for no longer than six months, are involved in numerous chemical processes in the lower atmosphere, and affect the abundance and lifetimes of gases and particulates that contribute to climate change. However, the collective influence of short-lived halogen-containing (SLH) compounds on the global climate has remained unknown. On page 967, Saiz-Lopez *et al.*[1] provide a comprehensive assessment of the role of these compounds in global climate change, and find that they contribute to climate cooling through their involvement in atmospheric chemistry.

Nearly five decades ago, research into halogen-containing gases was sparked by the realization that they posed a threat to Earth's protective ozone layer[2]. Of particular concern were chlorofluorocarbons (CFCs), which are inert in the lower atmosphere, but deplete ozone in the stratosphere, around 10–50 kilometres above Earth's surface. In 1987, the Montreal Protocol on Substances that Deplete the Ozone Layer was implemented to phase out the use of CFCs and protect the ozone layer. However, it has since become apparent that some SLH compounds also reduce the levels of ozone in the stratosphere[3,4], whereas others have crucial roles in the chemistry of the lowermost atmosphere[5] (the troposphere).

Understanding the behaviour of halogen-containing compounds in the troposphere has been a challenge. Short-lived compounds are emitted by a wide array of sources, both natural (such as the ocean, polar ice and volcanic plumes[5]) and human-induced[3]. Their brief lifetimes, ranging from seconds to months, mean that it is difficult to measure atmospheric concentrations accurately[6].

Nevertheless, over the past few decades, scientists have come to realize that SLH compounds are ubiquitous in the troposphere, and contribute to climate change by warming and cooling the atmosphere (Fig. 1). The cooling occurs through their ability to destroy ozone, which heats the stratosphere by absorbing sunlight and acts as a greenhouse gas in the troposphere[6]. Warming happens when SLH compounds slow the formation of atmospheric aerosols, which cause cooling at ground level by reflecting sunlight back to space[7]. Furthermore, SLH compounds decrease the abundance of the hydroxyl radical[5] – a chemical species known as the detergent of the atmosphere, because it efficiently removes pollutants from the air. Reduced levels of hydroxyl radicals mean that the greenhouse gas methane is removed less rapidly from the atmosphere, resulting in a small amount of atmospheric warming.

Assessing the overall impact of the multitude of chemical reactions involving SLH compounds and their various climate feedbacks is challenging, especially considering that atmospheric composition and climate are changing rapidly. In their study, Saiz-Lopez *et al.* used an Earth-system model – a type of simulation used to inform assessments such as those made by the Intergovernmental Panel on Climate Change (IPCC) – to quantify how

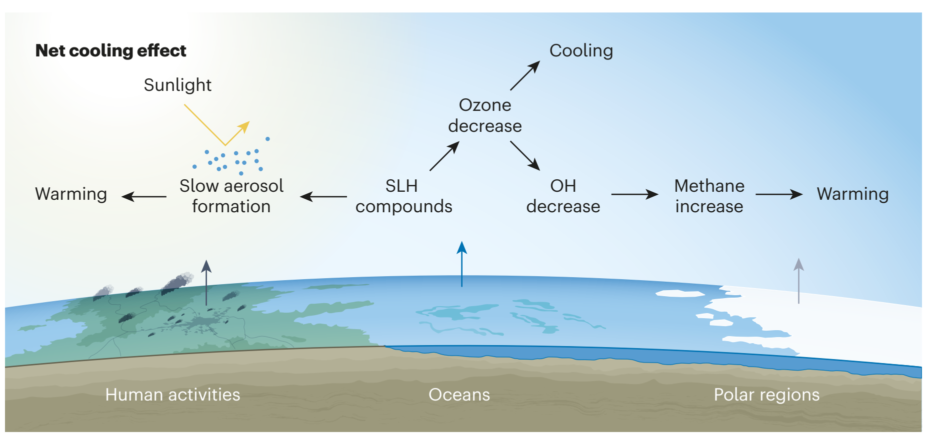

Figure 1 | How short-lived halogen-containing compounds affect climate. Gases that contain the halogen elements chlorine, bromine or iodine are produced naturally (for example, from the ocean surface and polar ice) and from human activities (such as industry and biomass burning). Saiz-Lopez *et al.*[1] analysed the pathways through which short-lived halogen-containing (SLH) compounds influence the global climate. The biggest effect is climate cooling, which occurs because SLH compounds deplete ozone (a gas that causes atmospheric warming). This cooling is partly offset by warming through two pathways: SLH compounds slow the formation of atmospheric aerosols (which cool the climate by reflecting sunlight back to space); and they decrease the levels of hydroxyl radicals (OH) in the atmosphere, which causes an increase in the abundance of the greenhouse gas methane. However, the net cooling effect is not sufficient to counteract global warming caused by carbon dioxide emissions.

SLH compounds influence the global climate. By running simulations for past, present and future climates, the researchers identified changes in the effects of SLH compounds on the climate that have occurred since the pre-industrial period, and projected how those effects might develop further with continued atmospheric warming.

Overall, the findings reveal that SLH compounds have a net cooling effect on the climate. The authors' simulations indicate that cooling due to ozone destruction has the biggest impact. However, this is partially offset by indirect warming caused by the extended atmospheric lifetime of methane, among other factors. It should be noted that the cooling effect of SLH compounds is insufficient to counterbalance the warming produced by carbon dioxide, which has increased around 40 times more than the cooling from SLH compounds since pre-industrial times[1,7]. In other words, these compounds are not a silver bullet for climate change.

Notably, Saiz-Lopez *et al.* report that most of the increased cooling associated with SLH compounds can be attributed to the human-induced enhancement of natural emissions from the oceans (a consequence of climate change and air pollution), rather than to a straightforward upsurge in emissions associated with human activities – although the latter also plays a part[8]. This human-induced increase in natural halogen-containing emissions seems to be a key climate feedback that is missing from current IPCC models.

Looking ahead, Saiz-Lopez *et al.* expect the climate impacts of SLH compounds to strengthen in some respects and weaken in others, depending on future socio-economic development, greenhouse-gas emissions and atmospheric warming. However, these projections are based on a single model and would benefit from comparisons with predictions from other Earth-system models. This is not yet possible, because most of the models do not take into account the emissions and chemistry of SLH compounds. If SLH compounds were included, it is possible that their impacts under future climate scenarios would fall outside the range estimated by Saiz-Lopez *et al.*, because different models represent atmospheric chemistry and aerosols in different – sometimes vastly different – ways.

In general, the more models that can be used, the better. The Coupled Model Intercomparison Project, the sixth phase of which informed the 2021 IPCC assessment[7], is a useful initiative for performing coordinated multi-model assessments. The challenge now is for more research groups to incorporate the sources, chemistry and climate feedbacks of SLH compounds into their models.

Ultimately, Saiz-Lopez and colleagues' study underscores the role of SLH compounds in the global climate system. By deepening our understanding of the contributions of these compounds both to the baseline climate state and to climate change, scientists can refine current projections, which will enhance our ability to tackle the challenges posed by climate change.

Laura Revell is at the School of Physical and Chemical Sciences, University of Canterbury, Christchurch 8140, New Zealand.
e-mail: laura.revell@canterbury.ac.nz

1. Saiz-Lopez, A. *et al. Nature* **618**, 967–973 (2023).
2. Molina, M. J. & Rowland, F. S. *Nature* **249**, 810–812 (1974).
3. Hossaini, R. *et al. Nature Geosci.* **8**, 186–190 (2015).
4. Villamayor, J. *et al. Nature Clim. Change* **13**, 554–560 (2023).
5. Simpson, W. R., Brown, S. S., Saiz-Lopez, A., Thornton, J. A. & von Glasow, R. *Chem. Rev.* **115**, 4035–4062 (2015).
6. Finlayson-Pitts, B. J. *Anal. Chem.* **82**, 770–776 (2010).
7. Szopa, S. et al. in *Climate Change 2021: The Physical Science Basis. Contribution of Working Group I to the Sixth Assessment Report of the Intergovernmental Panel on Climate Change* (eds Masson-Delmotte, V. *et al.*) 817–922 (Cambridge Univ. Press, 2021).
8. Hossaini, R. *et al. Nature Commun.* **8**, 15962 (2017).

The author declares no competing interests.