replication as tested *in vitro*. When NK cells from healthy individuals were treated with TGF-β1 *in vitro*, the cells were less able to form connections with infected target cells and were less able to degranulate and produce cytokines.

Witkowski and colleagues report high levels of TGF-β1 in the blood of people with severe COVID-19, but not in those with no or minimal signs of the disease. Notably, the authors reveal that serum from people with severe COVID-19 can limit, to some extent, the *in vitro* degranulation and control of viral replication mediated by NK cells from healthy donors, and that this effect can be prevented by adding an antibody that blocks TGF-β1. Together, these findings indicate a correlation between severe COVID-19, the presence of a high level of TGF-β1 in the bloodstream and an impaired defensive response by NK cells.

Several questions remain. The first is whether NK cells are necessary to fight SARS-CoV-2 infection. Several studies of mouse models of respiratory viral infections, such as influenza A virus, respiratory syncytial virus and Sendai virus, have shown that NK cells contribute to virus control and aid host survival[5]. Consistent with this, the only characteristic shared by people with various types of NK-cell deficiency is a predisposition to viral infections, especially of herpesvirus[12]. The fact that type I interferons are strong activators of NK cells also suggests a link between deficiencies in type I interferons and impaired NK-cell-mediated antiviral immunity. All these findings, together with the inverse correlation between the number of functional NK cells and the severity of COVID-19, support a role for these cells in controlling SARS-CoV-2 infection, but formal proof of this hypothesis remains to be obtained.

A second question to be addressed is, what are the mechanisms underlying the high production of TGF-β1 during COVID-19? SARS-CoV-2 contains a spike protein that interacts with the ACE2 receptor on human cells[1]. This receptor is an enzyme that converts the protein angiotensin II (AngII) to a peptide called Ang1-7. The enzymatic activity of ACE2 is disturbed during SARS-CoV-2 infection, resulting in a rise in AngII levels that promotes TGF-β1 expression[1]. Thus, excessive damage to lung tissue caused by a high viral load might induce a high level of TGF-β1, which could affect NK cells. Moreover, TGF-β1 is known to promote a type of tissue damage called fibrosis, which is a hallmark of severe COVID-19. A rise in the level of AngII is a common feature of coronary artery disease, hypertension and diabetes[13], and high levels of TGF-β1 are observed in obesity[14]. It will therefore be interesting to investigate whether the association of such conditions with severe COVID-19 involves defective functioning of NK cells mediated by TGF-β1.

Ways of manipulating NK cells are of increasing interest in anticancer therapy, using approaches such as immune-checkpoint inhibitors, NK-cell 'engagers' and off-the-shelf infusions of NK cells[15]. The importance of NK cells in the control of viruses should similarly prompt the design of innovative treatments based on harnessing these cells to fight viral infections. In the case of severe COVID-19, the high levels of TGF-β1 present might compromise strategies to boost the activity of NK cells. Instead, the use of TGF-β1 blockers[16] might be a way to promote NK-cell-mediated antiviral defence and prevent lung fibrosis, although the safety of such treatment in this context is a concern that should be addressed. In addition, monitoring TGF-β1 levels in plasma, along with TNF-α-mediated gene expression in NK cells from the bloodstream[7], might help to predict the outcome of infection and to guide a patient's care appropriately.

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Astronomy

Giant planet imaged orbiting two massive stars

Kaitlin Kratter

Direct imaging has revealed the existence of a large planet orbiting a binary system that contains the most massive planet-hosting stars detected so far. The discovery challenges existing models for how planets and stars form. **See p.231**

If a child had been asked to draw a planet 30 years ago, they would have had a relatively straightforward task. Perhaps they would draw Earth in orbit around the Sun, or maybe Saturn with its beautiful ring system. Now, the options are dizzying: as detection techniques have become more powerful, myriad planetary systems have been discovered, hosting planets with a range of masses, charting varied orbits around a diverse population of stars. On page 231, Janson *et al.*[1] have further stretched our collective imagination of what a planetary system looks like, by directly imaging a planet of roughly ten times the mass of Jupiter, orbiting not one, but two stars, whose combined mass is nearly ten times that of the Sun.

Astronomers are continually transforming and expanding our notion of planetary systems. In 1992, tiny, rocky worlds were revealed to be in orbit around the dense cores of massive stars known as neutron stars – these were the first planet-like objects to be detected outside the Solar System[2]. Three years later, we were treated to the discovery of the 'hot Jupiters', giant planets that have days the same length as their years, and orbital periods shorter than a week in Earth time[3]. In the 2010s, the Kepler space telescope delighted us with the knowledge that not only are planets diverse compared with those in our Solar System, they are also incredibly common. Suddenly it became clear that the Milky Way is filled with more planets than stars[4].

These planetary surprises have all relied on indirect detection techniques, in which the presence of a planet is inferred from changes in the light of a star. But the past three decades have also witnessed extraordinary discoveries

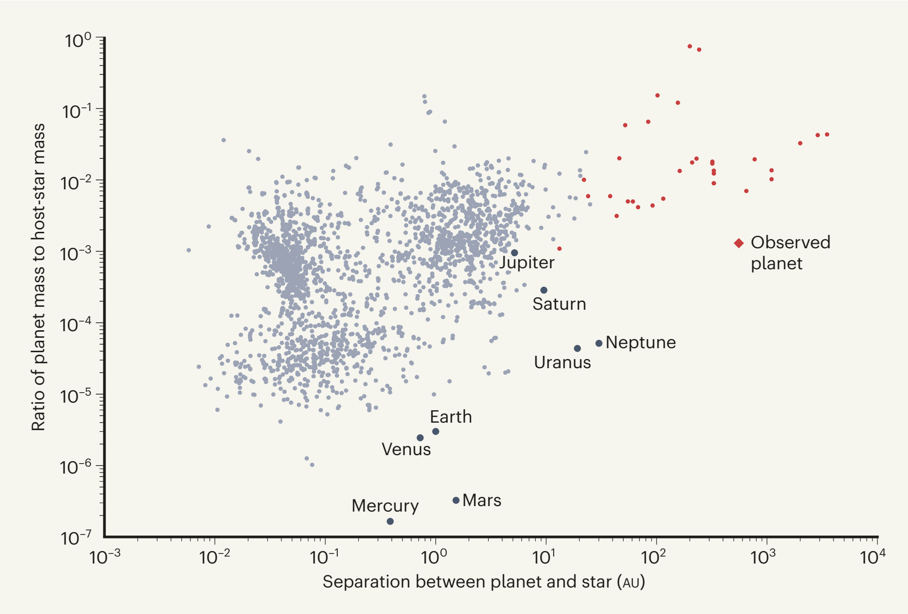

Figure 1 | The mass ratio of detected planets to their host stars as a function of their separation. Each point represents a confirmed planet orbiting a star whose mass is known with at least 30% precision. The observed separation between planets and their stars is measured in astronomical units (AU), where 1 AU is the distance between Earth and the Sun. Janson *et al.*[1] used direct imaging to detect a planet orbiting two stars, shown here with a red diamond marker. Other points in red represent planets also detected through direct imaging. Among these planets, Janson and colleagues' discovery has an unusually low planet-to-star mass ratio compared with those with similarly wide orbits. (Adapted from Fig. 2 in ref. 1.)

using a technique known as direct imaging[5]. This approach is similar to taking a photograph – except that it requires a sensitivity equivalent to capturing a single Christmas light in a football stadium illuminated by 500 floodlights.

Planets discovered through direct imaging have so far been strange bedfellows for their indirectly detected brethren. The separation between these planets and the stars they orbit is typically hundreds of times the distance between Earth and the Sun, and their masses as much as ten times that of Jupiter (Fig. 1). Are they even planets? Or do they have more in common with stars – but never grow massive enough to commence nuclear fusion, which is the definition of stardom?

The system identified by Janson *et al.* stands out in several ways. It orbits not one, but two stars, which are each more massive than any planet-hosting star previously detected[6]. Although it is not the first planet to be found orbiting two stars[7], it joins only a dozen or so others like it. It also has one of the widest-known orbits detected so far: the separation between the planet and the stars it orbits is roughly 500 times that between Earth and the Sun (Fig. 1). This orbit is comparable to that of Sedna, the dwarf planet orbiting at the edge of the Solar System, but the newly discovered planet's mass is a million times greater than Sedna's.

Given the system's extraordinary properties, this discovery challenges existing planet-formation models, while also improving our understanding of how very large stars form. Most planets form through a bottom-up process known as core accretion. In the disk of dense gas surrounding a new star, known as a protoplanetary disk, small dust grains coagulate, become concentrated and eventually collapse into objects spanning 10–100 kilometres[8]. These objects then interact gravitationally: they collide with each other and sweep up nearby debris until they begin to resemble small, rocky planets.

"Direct imaging requires a sensitivity equivalent to capturing a single Christmas light in a football stadium illuminated by 500 floodlights."

At this point, the planets' fates diverge. If their mass is sufficiently large, these rocky bodies begin to accumulate gas from the protoplanetary disk, amassing a sizeable hydrogen and helium atmosphere like that of Jupiter or Saturn. In other cases, they fail to accrue enough gas, and instead become rocky or icy planets without a substantial atmosphere – the most common type of planet.

But there is an alternative mechanism for planet formation. Planets with large mass might instead form through gravitational instability, like some binary star systems and brown dwarfs[9]. This top-down model requires that the mass of the protoplanetary disk be so large that it causes part of the disk to collapse in on itself under the pull of its own gravity. When this happens, a small secondary body is created, and starts to orbit the star.

If the planet detected by Janson *et al.* were orbiting a star similar to the Sun, this top-down model would be a fitting description of its formation. However, the ratio of planet mass to star mass has been predicted to be more relevant to planet formation than mass itself – and the mass ratio in this system is much like that of Jupiter and the Sun (Fig. 1). In this context, the typical core-accretion mechanism seems plausible.

The gravitational-instability mechanism also tends to create objects that are very large – so large, in fact, that they fail to become planets[9]. Compared with the stars it orbits, this planet is small, making gravitational instability less likely than core accretion. Perhaps it is just a planet similar to Jupiter, flung out to the far reaches of its stellar system through an interaction with the stars it orbits. A broad census of planets associated with large stars will help to clarify the exact mechanism of its formation.

It comes as no surprise that the most massive stars known to host a planet are bound together in a close binary: nearly all massive stars have stellar companions[10]. Despite their frequency, the formation mechanisms for such massive stars are still a subject of debate. Janson and colleagues' detection of a planet in orbit around a close star pair provides evidence that the binary hosted a long-lived, massive disk of gas and dust. It therefore suggests that this massive binary formed in a similar way to stars with lower mass – by accreting gas from a disk. It is even possible that one of the stars formed through gravitational instability.

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