mechanism of b12 action in a biologically relevant animal model. They inoculated monkeys with SHIV in order to study the protective effect of normal b12, as well as of two mutated versions, K322A and L234A–L235A (LALA). These differ from normal b12 by only one and two amino acids, respectively. The ability of the K322A variant to bind to complement proteins is compromised, whereas the LALA variant cannot bind to either complement proteins or Fc receptors[2]. *In vitro*, all three antibodies have similar virus-neutralizing potencies.

To test the potency of these antibodies *in vivo*, the authors intravenously infused female monkeys with individual antibody variants, then introduced SHIV vaginally. The normal b12 antibody, as well as the complement-defective K322A mutant, protected eight out of nine animals from SHIV infection, whereas the Fc-receptor-defective LALA variant protected only five out of nine.

There are two ways to look at these data. On the one hand, it can be argued that even without complement- or Fc-mediated effector functions, the b12 antibody can protect more than half of the animals. Such a conclusion substantiates our current belief that antibody-mediated protection against HIV is conferred mainly through direct neutralization of the virus. On the other hand, the work of Hessell *et al.* shows that Fc-mediated effector functions are necessary for the antibody to have its full protective effect. The group's findings indicate that clearance of antibody-coated viral particles by phagocytic cells, or the killing of virally infected cells by ADCC, could be contributing to maximal protection against HIV infection. Although the authors do not show how the binding of b12 to Fc receptors might contribute to protection *in vivo*, they provide *in vitro* data showing that normal b12 and K322A, but not the LALA variant, mediates ADCC. In addition, ADCC has been associated with antibody-mediated protection in monkeys infected with simian immunodeficiency virus[11,12].

So a picture emerges (Fig. 1) in which either passive infusion of antibodies or active immunization results in circulating antibodies in mucosal tissues. Subsequently, on inoculation of a mucosal surface with HIV-1, neutralizing antibodies react with most of the free virus particles to prevent the infection of $CD4^+$ T cells. Some free viruses are also coated by antibodies and destroyed by phagocytic cells. But a few $CD4^+$ T cells become infected and express viral antigens on their surface. Before these cells can initiate further rounds of productive infection, however, antibodies tag them for eradication by Fc-receptor-bearing natural killer cells.

That antibodies exert their protective effect by mobilizing an allied army of immune cells may have important implications for the design of HIV vaccines. The robustness of vaccine-mediated antibody responses are commonly measured by quantifying virus neutralization, but such analysis does not measure Fc-mediated effector functions of the antibody. From Hessell and colleagues' results, these commonly used neutralization assays might be unable to fully predict a vaccine's efficacy. Moreover, some might argue that the authors' findings suggest that an effective vaccine could elicit non-neutralizing antibodies that mediate ADCC, but do not block infection of target cells.

I would urge caution. Clearly, there is much we don't know about how protective antibodies work and the level of antibodies required for maximal protection. Nonetheless, results of previous animal and human studies[7–9,13] show that non-neutralizing antibodies alone have little or no protective effect. For example, a large clinical study[13] found that a vaccine consisting of a soluble form of the HIV envelope glycoprotein gp120 generates high levels of non-neutralizing antibodies that have no effect on HIV-1 infection.

As existing HIV-1 vaccines do not elicit potent neutralizing antibodies, the focus of vaccine researchers and funding agencies on identifying better vaccine antigens seems completely appropriate. At the same time, we should be aware of the complexity of the immune responses mediated by secretory antibodies. As Hessell and colleagues' findings[2] indicate, antibodies against HIV-1 are likely to exert a protective effect through more than one mechanism. So continued research should seek to elucidate and measure alternative biological functions of protective antibodies. ■

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SOLAR SYSTEM

Lethal billiards

Philippe Claeys and Steven Goderis

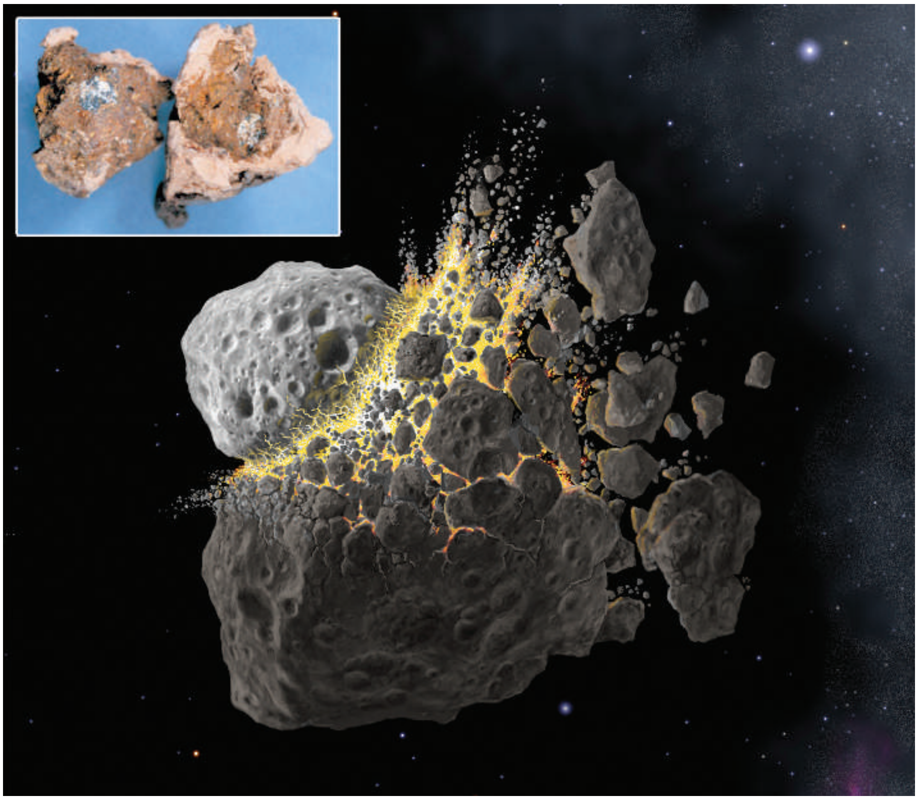
A huge collision in the asteroid belt 160 million years ago sent fragments bagatelling around the inner Solar System. One piece might have caused the mass extinction that wiped out the dinosaurs 65 million years ago.

What are the chances of the sky falling on our heads? If it's an asteroid hitting Earth that we're talking about, we can't be too sure. Not only do estimates of the current terrestrial meteorite impact rate differ by a factor of five to ten, depending on the approximations used[1], but we don't know for certain whether that rate has remained constant or has varied throughout geological time.

A current theory proposes that the impact rate has increased during the past 100 million years or so. On page 48 of this issue, Bottke *et al.*[2] present an intriguing explanation for why this might be, invoking errant fragments from a powerful ancient collision in the asteroid belt between Mars and Jupiter.

Clusters of impact craters and layers of material ejected in meteorite impacts, as well as higher levels of extraterrestrial material in some sedimentary rocks, seem to indicate that, during several glacial periods, the Earth–Moon system has suffered abnormally high rates of bombardment. The late Miocene epoch around 8 million years ago, for example, was marked by an increased flux of interplanetary dust particles between 1 μm and 1 mm across, which might have been produced by a collision within the asteroid belt[3]. An asteroid or comet shower has similarly been put forward to explain the higher dust-particle flux in the late Eocene around 35 million years ago, an event that seems to be coupled with an unusually high concentration of impact craters[4,5]. These include the two largest craters in recent geological history, Popigai in Siberia (100 km in diameter) and Chesapeake Bay off the Maryland coast (around 85 km in diameter).

And we can go even farther back in recording periods of heavy bombardment. The abundant micrometeorites in the 480-million-year-old Ordovician limestones of southern Sweden most probably reached Earth after a significant disruption had occurred in the asteroid belt[6]. Several impact craters also seem to cluster around this age, although here the geological record is rather poor. Farther back still, recognized ejecta layers are concentrated in two time windows between 2.65 billion and 2.5 billion years ago and 3.47 billion and 3.24 billion years ago[7]. Finally, the most dramatic series of events is undoubtedly the Late Heavy Bombardment of 3.8 billion years ago, the occurrence of which is inferred from the lunar cratering record[8]. Although its traces have been erased



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D. DAVIS/SWRI

Figure 1 | Breaking up is all too easy. **Bottke and colleagues[2] propose that the collisional break-up of an asteroid 160 million years ago was the ultimate cause of the mass extinction on Earth at the Cretaceous–Tertiary boundary some 95 million years later. This occurred when one particularly large fragment, the Chicxulub impactor, hit Earth. The inset shows an inferred remnant of this meteorite, retrieved from clays in the northern Pacific dating to the same time as that event[11].**

by geological activity on Earth, extrapolation of the lunar data indicates[9] the formation of up to 22,000 terrestrial craters with a diameter of more than 20 km. This catastrophic bombardment probably resulted from colliding asteroids disturbed by changes in the orbits of the giant gas planets[10].

Bottke *et al.*[2] have discovered the remnants of another huge collision hidden in the inner region of the main asteroid belt. These comprise the Baptistina asteroid family (BAF), a class of variously sized objects of similar composition and orbital geometry, typified by the 40-km-diameter asteroid known as (298) Baptistina. The authors use a computer simulation to track the orbits of these fragments back to the moment of their formation, and find that the collision must have taken place about 160 million years ago. The best fit to the data is given by an object of 60-km diameter colliding almost vertically with a 170-km-diameter body. This collision, at a velocity of 3 km s^{-1}, generated more than 1,000 large bodies greater than 1 km in diameter (Fig. 1).

The authors' dynamic modelling indicates that the Baptistina disruption took place in a region of the asteroid belt where the gravitational influence of Mars and Jupiter would have caused a number of large objects to be perturbed into Earth-crossing orbits. The collision of just a small fraction of these fragments with Earth would account for the increased cratering rate during the Cretaceous period (from around 145 million to 65 million years ago) and the early Cenozoic era that followed. The fragments would in fact have formed an asteroid shower in the inner Solar System lasting some 100 million years.

According to spectroscopic measurements, the composition of (298) Baptistina is similar to that of primitive 'carbonaceous chondrite' meteorites, a rather infrequent type of meteorite that contains unusually large amounts of water and organic compounds. This is front-page news, as a 10-km-sized carbonaceous chondrite is most probably the projectile that formed the Chicxulub crater on the Yucatán peninsula in Mexico[11,12] (Fig. 1, inset). This impact almost certainly triggered what is known as the K/T mass extinction, including the demise of the dinosaurs, at the boundary between the Cretaceous and Tertiary periods 65 million years ago.

By comparing the impact rate of BAF near-Earth objects with the background occurrence of objects with a similar composition, Bottke and colleagues[2] estimate that there is a 90% chance that the Chicxulub projectile came from the BAF. Other craters formed during the same period on the inner bodies of the Solar System could share the same origin: one candidate is Tycho on the Moon, which was formed 109 million years ago at what would have been the climax of the BAF asteroid shower.

This hypothesis is nothing if not provocative. It implies that a significant number of terrestrial craters that formed during the past 160 million years resulted from carbonaceous chondrite projectiles. The concentrations of platinum-group elements and the chromium-isotopic signatures measured in rocks melted in meteorite impacts provide precise information on the projectile type, and can be used to distinguish carbonaceous chondrites from other types of meteorite. Of the eight craters on Earth that are larger than 1 km in diameter (implying a projectile 50 m or more across) and less than 200 million years old for which the projectile composition has been unequivocally identified, Chicxulub stands out as an anomaly — it is the only one formed by a carbonaceous chondrite[13]. So did the other, smaller BAF objects miss Earth, or is this apparent anomaly due to the fact that projectile type is well characterized for relatively few craters?

That question must remain unanswered for now. Nevertheless, unless a rogue comet came from the outer edge of the Solar System (a rather unlikely event), the BAF remains a likely source for the Chicxulub projectile. It is a poignant thought that the Baptistina collision some 160 million years ago sealed the fate of the late-Cretaceous dinosaurs well before most of them had even evolved.

The most important point raised by Bottke and colleagues' discovery[2] of the Baptistina asteroid family is how severe the repercussions of cataclysmic collisions in the asteroid belt can be for the Earth–Moon system. The terrestrial impact record needs to be scrutinized more closely to identify and understand these periods of more intense bombardment, and to link them to the huge and dangerous game of billiards continuously being played out between the orbits of Mars and Jupiter. ■

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