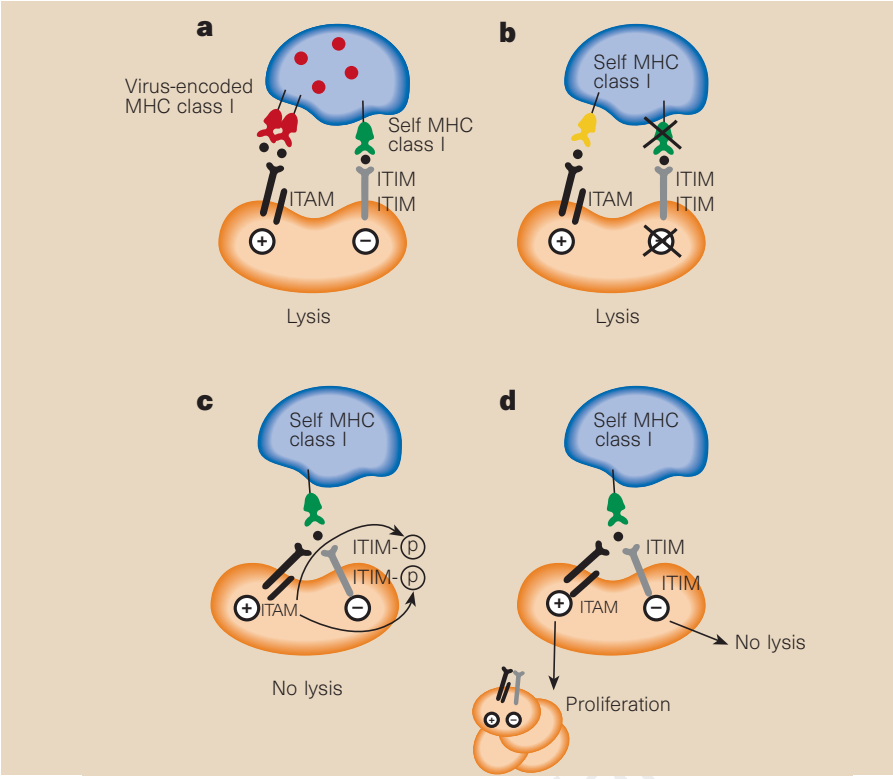

Figure 2 **Hypothetical interactions between activating and inhibitory MHC class I receptors. Inhibitory and activating receptors may recognize self and non-self class I molecules, respectively** (a), **or distinct self-class I molecules** (b) **on the same cell. Activating receptors may allow NK cells to recognize target cells that express virally encoded MHC class I molecules/ self class I molecules carrying viral peptides** (a), **or target cells that have selectively lost one class I molecule** (b). **Alternatively, inhibitory and activating receptors may recognize the same class I molecules on a target cell. In this case, activating receptors may regulate inhibitory receptors by phosphorylating cytoplasmic immunoreceptor tyrosine-based inhibitory motifs (ITIMs;** c), **or may control distinct NK-cell functions. Activating receptors may promote NK-cell proliferation, whereas inhibitory receptors may control effector responses such as cytotoxicity** (d).

enigmatic. How can inhibitory and activating MHC class I receptors interact to regulate the activity of NK cells? Does the existence of activating receptors violate the 'missing self' model? One hypothesis is that inhibitory receptors recognize self MHC class I molecules (preventing autoreactivity), whereas activating receptors detect non-self MHC class I molecules, such as those encoded by cytomegalovirus to deceive NK-cell inhibitory receptors[14] (Fig. 2a). Another possibility is that individual NK-cell clones express both activating and inhibitory receptors that are specific for different self-MHC class I ligands. These receptors may cooperate to identify class I deficient cells. For example, the preferential loss of a class I ligand specific for an inhibitory receptor could allow activation of the NK cell through an activating receptor, which recognizes another class I ligand on the target cell (Fig. 2b). Alternatively, if both inhibitory and activating receptors see the same MHC class I molecule on a given target cell, the activating receptor may cooperate with the inhibitory receptor by recruiting tyrosine kinases to phosphorylate the cytoplasmic ITIMs (Fig. 2c). Finally, inhibitory receptors may regulate effector and cytotoxic responses, whereas activating receptors could mainly control NK-cell proliferation, promoting NK-cell expansion during development (Fig. 2d). Now that Lanier *et al.*[2] have discovered the mechanism by which the activating receptors signal, it will be easier to define the biological function of activating receptors in NK-cell recognition of tumours and virally infected cells. □

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Daedalus

Craters of doom

The Earth is under heavenly threat. Every so often, a comet or asteroid hits it with sufficient violence to bring about a mass extinction of higher species. Many people advocate a nervous watch for such celestial missiles, and the building of huge nuclear-armed rockets to deflect them.

Yet, oddly, recent mass extinctions seem nonrandom, having occurred at about 26-million-year intervals. One theory gives the Sun a companion star ('Nemesis'), in a highly eccentric orbit with just this period. Every time Nemesis swings past the Sun, she disturbs the Oort comet cloud, and may bring comets of her own into the Solar System. In the resulting storm of comets, several hit the Earth. If even one is moderately big, disaster follows.

So far, Nemesis has proved elusive, but Daedalus plans an indirect check. The Moon must also come under cometary attack; and craters on the Moon are not smoothed away by weather. So he advocates examining the Moon for impact craters whose ages are multiples of 26 million years. If found, they would confirm the theory, and allow us to predict the next likely attack.

But how to tell the age of a lunar crater? Daedalus notes that the Moon's surface is steadily eroded by meteoritic dust impacts, whose debris forms a layer of 'regolith'. A meteoritic or cometary impact would excavate the regolith at the impact site, replacing it with characteristic 'new crater' surface. Subsequent dust impacts would slowly cover this surface deeper and deeper in standard regolith.

The pristine crater surface and regolithic debris must differ in thermal capacity and conductivity. These can be measured by the rate of cooling when sunlight is cut off by a lunar eclipse. Daedalus wants to do this continuously, by infrared and microwave imaging of the dark Moon's surface just beyond the 'terminator' defining local sunset. The longer wavelengths of this thermal emission will have come from deeper layers of the surface. As the terminator sweeps across the lunar disc, the changing temperature profile behind it should disclose recent craters. The wavelength-dependence of their thermal emission will show their depths of regolith, and hence their ages. Statistical study should reveal the period of Nemesis, and when she is due to strike next. With luck, the results will set our minds at rest. If we turn out to have (say) 13 million years in hand, the nuclear defence programme will lose its urgency.

David Jones