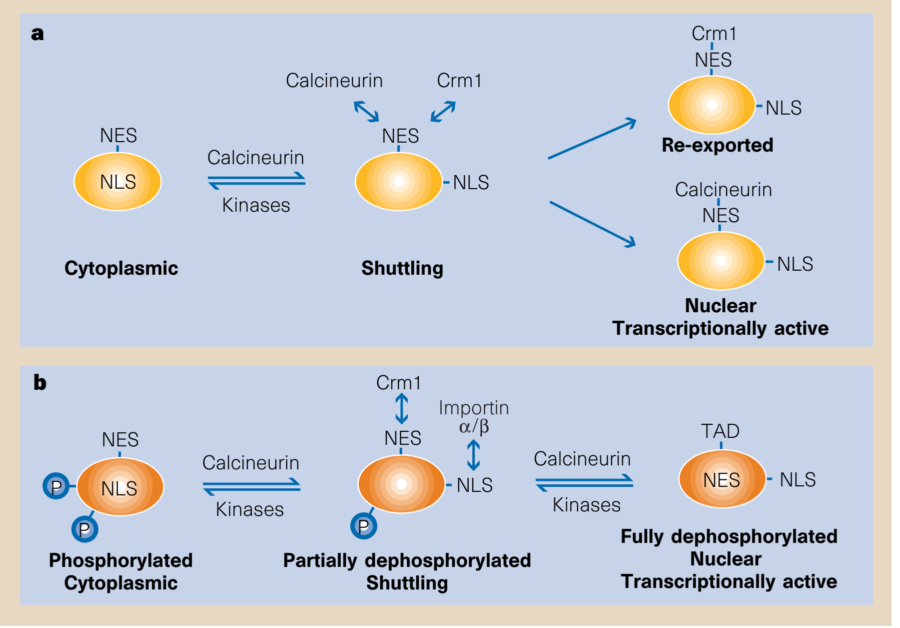

Figure 1 **Regulation of the nuclear import and export of NF-AT4.** a, **The model of Zhu and McKeon[3]. In activated cells, import is initiated by calcineurin-mediated dephosphorylation of NF-AT4. This results in exposure of the nuclear-localization signal (NLS), yielding a protein with an exposed nuclear-export signal (NES) and an exposed NLS. Calcineurin and Crm1 compete for binding to the NES. Crm1-bound NF-AT4 is re-exported from the nucleus. But binding of active calcineurin to NF-AT4 blocks the access of Crm1 to the NES, and the NF-AT4 is incorporated into an active transcriptional complex.** b, **Alternative model. Partial dephosphorylation uncovers the NLS but does not confer full transcriptional activity. Full activation requires further dephosphorylation, which may result in increased affinity for DNA, increased exposure of the transactivation domain (TAD) and, possibly, blocking of the NES.**

probably does not resemble the transcriptionally active, fully dephosphorylated form. It would not be surprising if, by further dephosphorylation, calcineurin causes changes that increase the transcriptional capacity of NF-AT4ΔZ (Fig. 1b). There is good evidence that, on full dephosphorylation, another family member (NF-AT1) is converted to a form with a higher affinity for DNA and increased transcriptional function[4,5,13].

How generalizable is Zhu and McKeon's model? Can it be applied to other members of the NF-AT family? The NF-AT proteins are all controlled by calcineurin, and the overall organization of the NF-AT regulatory domain is conserved in all four proteins. However, the regulatory domains show considerable primary sequence diversity — in particular, NF-AT2 and NF-AT4 differ in the locations of their NLS-masking sequences[8,12] and NES[3,9], and distinct kinases seem to be involved in their export[11,12]. In other words, the NF-AT proteins are likely to differ in the details of their regulation, and we must be careful when making generalizations. It is conceivable, however, that the basic characteristic of the model (calcineurin–Crm1 competition) is preserved throughout the family. The calcineurin-binding surface of NF-AT is likely to encompass not only the major calcineurin-binding loop, conserved in all four NF-AT proteins[14], but also regions that are not contiguous in the primary sequence. Competition between calcineurin and Crm1 will occur if the calcineurin- and Crm1-binding sites overlap, regardless of where the NES is in the primary sequence. It will be a challenge to decipher which regulatory mechanisms are common to all NF-ATs, and which are unique to each family member. □

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Daedalus

Sweeping the seas

The polar seas abound in krill, the tiny crustacea that live on plankton. The main predator of krill is the whale; now that the whaling industry has driven whales almost to extinction, the krill is richly abundant. So Daedalus plans to harvest it directly.

What is needed, he says, is some sort of automatic, self-propelled submerged vehicle that would wander at random around the polar seas, sucking in the krill like a giant vacuum-cleaner. When fully laden, it would return with its catch to a home port or a mother-ship. Modern robotics and satellite navigation techniques make this fairly simple in principle. But the devil, as ever, is in the details.

Daedalus's 'oceanic filter-feeder' is essentially an open framework whose bow is a huge filter. Its mesh is chosen to admit krill, but to exclude bigger fish, weed, flotsam and so on, which would complicate the processing downstream. As the craft travels round the ocean, it will strain the krill continuously from its densest stratum just under the surface. The main problem, of course, is that each voyage will continue for many days or weeks; the captured krill will die and rot long before it reaches port. Hence the need for processing: some form of on-board chemical engineering to preserve the catch. Daedalus's design cunningly splits the krill intake into two streams. The smaller stream will indeed be allowed to die and rot. It will ferment to methane gas, the fuel for the propulsion and electronics of the craft, and to carbon dioxide, which will be catalytically reacted with methane to give acetic acid (vinegar). The vinegar will pickle the larger stream of krill, preserving it in a huge flexible plastic 'stomach'. When sensors on the stomach detect that it is full, they will switch the navigation system from 'cruise' to 'homing', and the filter-feeder will return to base with its catch.

Bulk pickled krill will be an intriguing new resource. Since filter-feeders could take over the whole ecological niche now being vacated by whales, there will be a lot of it. But despite the popularity of lobsters, prawns and other large crustacea, Daedalus doubts that krill as such will be welcomed by the chef and housewife. It may have to be ground up to a nutritious 'fish-flour', partially hydrolysed to a proteinaceous pabulum, or even fed to chickens. But one way or another, the ever-ingenious factory-food industry will put it to good use.

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