the targets of importin blocking activity. Both promote microtubule assembly and are found in complexes with importin α and β (*7–9*). TPX2 (*9*) anchors a microtubule-dependent motor (Xklp2) to the spindle poles (*10*); NuMA (*8*), when bound to the microtubule motor dynein, cross-links microtubules into the spindle poles during mitosis (*11*). A connection between NuMA and importin β explains the curious finding that mutations in mammalian RCC1 (the RanGEF) result in mitotic defects that can be overcome by increasing the expression of NuMA (*12*). Inhibiting the importin β block of NuMA activity restores formation of the spindle poles. Together, these findings strongly support a direct link between NuMA and Ran/RCC1 in mammalian cells.

Both NuMA and TPX2 are found in the interphase nucleus, presumably localized there by Ran and importin α and β. Their nuclear localization prevents them from interacting with microtubules in the cytoplasm until after breakdown of the nuclear membrane at the beginning of mitosis or meiosis (see the figure). In the absence of a nuclear membrane, chromatin-bound RCC1 and cytoplasmic RanGAP1 presumably produce a natural gradient of Ran-GTP that is most concentrated at the chromosomes and least concentrated at the cell periphery. Consequently, TPX2, NuMA, and probably other factors regulated by Ran-GTP are preferentially activated in the vicinity of chromatin. Ran mutants that cannot convert GTP to GDP increase net microtubule assembly by increasing the frequency at which disassembling microtubules are converted back into the assembly phase (*13*, *14*). There is also a Ran-GTP–dependent increase in the initiation of microtubule formation by centrosomes (*14*), although the factors involved in this additional Ran-dependent activity are not known.

In the absence of a nuclear membrane, commandeering the nuclear import machinery would prevent assembly of spindles except where there is an appropriate source of RCC1, that is, in or near the chromosomes. Ran stimulates microtubule polymerization and the nuclear import of proteins through similar mechanisms that depend on its ability to abrogate inhibitory interactions between proteins. The association of Ran with the importins and with known microtubule-associated proteins suggests that the nuclear transport machinery directly regulates microtubule organization. The identification of downstream effectors of Ran has provided valuable insights into the intricacies of spindle assembly.

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NOTA BENE: EVOLUTION

Wolbachia and Wasp Evolution

One of the strangest partnerships in nature is the pairing of the symbiotic bacterium *Wolbachia* with a remarkable range of insect hosts. *Wolbachia* live in the cytoplasm of insect cells and apparently do no harm. These endosymbionts do, however, have a startling effect on the reproduction of their insect hosts, which has led biologists to speculate that *Wolbachia* may contribute to reproductive isolation and the creation of new insect species (speciation). Bordenstein *et al.* (*1*) now provide evidence that this indeed may be the case.

When male insects infected with *Wolbachia* mate with uninfected females, no offspring are produced (because the cytoplasm of infected sperm is incompatible with the cytoplasm of uninfected eggs). Yet viable offspring result from all other mating combinations (uninfected males and infected females, infected males and infected females, and uninfected males and uninfected females). This arrangement ensures that *Wolbachia* (which are passed to offspring only through females) spread rapidly through the host species because uninfected females that mate with infected males cannot produce offspring. But is this partial reproductive isolation sufficient to drive the emergence of new insect species? Bordenstein and colleagues speculated that if a host insect population was infected with different *Wolbachia* strains that were incompatible (so that individuals infected with one strain could not produce offspring with individuals infected with the other), then this double reproductive barrier might be sufficient to drive speciation.

They set out to test their hypothesis in two closely related species of parasitic wasp, *Nasonia giraulti* (which inhabits eastern North America) and *Nasonia longicornis* (which inhabits western North America). In both species, individuals were infected with different *Wolbachia* strains and reproductive incompatibility was bidirectional: Matings between *N. longicornis* males and *N. giraulti* females, and between *N. giraulti* males and *N. longicornis* females produced few or no hybrid offspring. But when both species were treated with antibiotics to cure their *Wolbachia* infection, interspecies matings produced normal numbers of hybrid offspring. Working with uninfected wasps, the authors then tested several other reproductive barriers (unrelated to *Wolbachia* infection), such as reduced fertility and hybrid breakdown, that are known to precede the formation of two separate species. Interspecies matings did not reduce the number of eggs laid or the number of viable hybrid offspring produced, and sperm of one species was capable of fertilizing eggs of the other. There was also no evidence of hybrid breakdown because hybrid male offspring mating with female offspring of either species did not show abnormal courtship behavior or reduced fertility.

The authors conclude that microbial-induced reproductive isolation is already apparent between *N. longicornis* and *N. giraulti*, whereas genetically driven reproductive barriers have not yet been formed. Bordenstein *et al.* are careful not to endorse *Wolbachia* as the means of *Nasonia* speciation (geographical isolation is arguably a far more important factor in this case), but their work offers a tantalizing glimpse into how an apparently harmless endosymbiont could alter the course of evolution.

–ORLA SMITH

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