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The devil is in the detail

Two transmissible cancers that have been circulating in Tasmanian devils in recent decades continue to pose complex and interrelated ecological and evolutionary questions.

Transmissible cancers are rare, and the most well-known example of a species experiencing such a disease is the Tasmanian devil. Wild devils are already confined to Tasmania, and populations of the marsupial have been decimated in recent years by devil facial tumour diseases. Writing in this issue, Beer et al. explore the population genomic consequences of this disease for a subordinate predator, the spotted-tailed quoll. Using a landscape community genomics approach, the authors show that population structure in the quoll increases as the devil declines and that there is evidence of selection on genes involved in muscle development and locomotion. This demonstration of the knock-on effects of the transmissible tumours prompts a recap of current knowledge of the disease.

Two independent transmissible cancers are circulating in Tasmanian devils, both of which are of relatively recent origin. Devil facial tumour 1 (DFT1) is thought to have emerged around 1986, whereas devil facial tumour 2 (DFT2) arose around 2011 (ref. 1). Both arose in the eastern part of Tasmania, but whereas DFT1 has now affected populations across the island (about 90% of the range) DFT2 is thought to remain restricted to the area near its origin[2]. There is evidence that some individuals have been infected with both tumours. The tumours, particularly DFT1, have been associated with substantial population declines. From an estimated 56,000 individuals in 1996 (when the disease was first identified), numbers had declined to 16,900 by 2020 (ref. 3).

The Tasmanian devil has therefore become a species of great interest to evolutionary geneticists, cancer biologists and conservationists. These unusual cancers pose a series of basic biological questions. We currently know of just a handful of cases of transmissible cancer — one in domestic dogs, these two independent examples in Tasmanian devils, and the others in molluscs. To an extent, this patchy distribution may reflect limited investigation. Other, undiscovered transmissible cancers may be less aggressive than the severe visible facial tumours seen in devils. However, it is notable that not only are there two independent contagious cancers in this one species, but also that they have both arisen very recently. This has led researchers to ask whether aspects of the Tasmanian devil's biology or ecology might make it particularly prone. The existence of two tumours also enables a comparison of their parallel evolutionary histories that explores commonalities and differences. Indeed, transmissible cancers in general have been compared with long-term evolutionary experiments[4].

Both tumours arose from Schwann cell cancers, and genome rearrangements involving chromosome ends occurred in both, which possibly indicates a role for telomeres[1,5]. However, DFT1 arose in a female and shows equal ability to infect males and females, whereas DFT2 arose in males and shows a strong male bias (possibly due to an immune reaction in females against the Y chromosome of the tumour cells). DFT1 is deficient in MHC1, which may be how it escapes control by the immune system, whereas DFT2 expresses normal MHC1. DFT1 is also predominantly found as a facial tumour, whereas more DFT2 tumours are found on other parts of the body[2]. The mutations identified in the two cancers are largely different, particularly the small number in each that are thought to be under positive selection. The two cancers also have different mutation rates — overall mutational elevation is found only in DFT2, but a specific hypermutator lineage has been identified within DFT1.

What, then, are the common factors that enable these two lineages with different evolutionary strategies to thrive? It is likely that there have been other tumours that have come and gone in this species before we had the tools to identify them as being transmissible cancers. One possibility is that external factors such as viruses or environmental mutagens could have given rise to similar tumours. Another possibility is that germline mutations in the individuals within which the tumours arose might have made them more susceptible. However, a recent study did not find evidence for either of these possibilities[6]. Instead, it seems likely that some shared aspect of the devil's genome and population structure allows for tumours to arise and have the potential to avoid immune suppression; and the role of biting in their behavioural ecology may be a major factor in enabling transmission and spread. As with all infectious diseases, there is a complex interplay between host and pathogen population and evolutionary dynamics. Although population declines to date have been sharp, some modelling suggests that they may level off in the near future[3].

It may not be immediately clear what this all means for conservation efforts. For Tasmanian devils (as with many predator species), human land use has been the major driver towards extinction. Even without disease, these human pressures — which include habitat loss and roadkill — need to be mitigated. Although there are conservation interventions that rightly focus on the disease, there is probably little that can be done to alter the chances of new tumours arising and causing further threats. Indeed, evidence suggests that the population dynamics of the host and the pathogen may not exactly align, which complicates attempts at intervening in the disease process[7]. However, the more we know about tumour dynamics — both within individuals and at a population level — the more precisely we can monitor and anticipate potential declines, and the better conservation efforts can be prioritized. With Beer and colleagues' study now showing the genetic effects of devil declines on quolls, there is the beginning of the possibility of taking a more ecosystem-based approach to such work that moves beyond a focus on a single species.

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Editorial

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