Saving a species bedeviled by cancer

The Tasmanian devil (*Sarcophilus harrisii*), the world's largest surviving carnivorous marsupial, is endangered by a fatal transmissible disease called devil facial tumor disease (DFTD). DFTD is a naturally occurring infectious cancer first observed on the east coast of Tasmania in 1996. This cancer is rapidly spreading across the island, the devil's only native habitat. DFTD is predicted to spread throughout Tasmania within 5 years. Because the disease has a 100% mortality rate, preservationists are concerned that the devil may face imminent extinction.

It has been suggested that low genetic diversity among Tasmanian devils has contributed to the success of DFTD. Efforts to conserve the species include captive breeding programs to maintain a group of devils that could be re-released into the wild to repopulate the island after DFTD has run its course. Recently, an international group of researchers led by Webb Miller and Stephan C. Shuster (Pennsylvania State University, University Park) and Vanessa M. Hayes (Children's Cancer Institute

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Australia and University of New South Wales, Australia) contributed to the conservation effort by using a revolutionary approach. They sequenced the genomes of two Tasmanian devils from opposite ends of the animal's native range, as well as the genome of a DFTD tumor isolated from one of the devils (*Proc. Natl. Acad. Sci. USA* doi:10.1073/pnas.1102838108; published online 27 June 2011). They also analyzed a set of genetic markers from 175 additional devils, some of which were museum specimens. The sequencing project had a two-part goal: first, to quantify genetic diversity within the population and evaluate whether it has decreased during recent history, and second, to identify which animals should be selected for inclusion in captive breeding programs in order to preserve the population's existing genetic diversity.

Their analysis indicates that the level of genetic diversity among Tasmanian devils has been relatively low and unchanged for more than 100 years, well before DFTD arose in the population. The researchers also suggest that animals included in captive breeding programs should be genetically characterized and selected to represent the full extent of genetic diversity among the population today.

The group expressed cautious optimism that Tasmanian devils can survive, given adequate habitat space, population size and preservation of existing genetic diversity through captive breeding. Furthermore, the scientists believe that this project exemplifies the potential of sequencing and genetic analysis to aid species preservation efforts. They hope this approach can be applied to other endangered species as well.

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A POSSIBLE MECHANISM OF AIDS RESISTANCE

One of the major questions remaining in AIDS research is how the progressionπ of HIV to AIDS might be prevented. Progression rates in infected individuals vary, suggesting that there might be an innate immune mechanism involved in determining how the disease progresses. New research on the simian immunodeficiency virus (SIV), the equivalent of HIV in monkeys, highlights a possible means of protection from AIDS.

SIV infection in natural host species, such as sooty mangabeys, tends to be nonpathogenic. In contrast, SIV infection in rhesus macaques and HIV infection in humans tends to be pathogenic. Recent findings indicate that fundamental differences between the immune responses of sooty mangabeys and of rhesus macaques to SIV may explain the lack of SIV pathogenicity in natural host species (*Nat. Med.* doi:10.1038/nm.2395; published online 26 June 2011).

Sooty mangabeys possess fewer immune cells that express CCR5, a co-receptor of the SIV virus that enables its infection of cells, than do rhesus macaques. In this study, Mirko Paiardini of Emory University in Atlanta, GA, and colleagues found that, following immune activation in response to SIV infection, levels of CCR5 in activated immune cells were significantly lower in sooty mangabeys than in rhesus macaques. This difference seemed to be due to a resistance of the sooty mangabey cells to CCR5 upregulation. Additionally, the researchers found lower levels of CCR5 mRNA in sooty mangabey T cells that had been activated *in vitro* than in activated rhesus macaque T cells.

Further analysis revealed that cells positive for CCR5 proliferate more slowly than cells lacking CCR5, suggesting that CCR5 impedes the ability of cells to proliferate in response to viral infection. Progression to AIDS in SIV-infected rhesus macaques is predicted by depletion of immune cells. The immune cells of the sooty mangabey may be protected from depletion by their lack of CCR5. These results could explain why SIV progresses to AIDS in macaques but not in sooty mangabeys.

The authors propose that in SIV-infected sooty mangabeys, low CCR5 upregulation following immune cell activation protects immune cells from virus-mediated depletion and protects the cells from infection. These results highlight a new and important mechanism of AIDS resistance despite continuous viral infection. This mechanism may prove to be a useful target for treatment approaches that could reduce the pathogenicity of HIV and increase the life expectancy of those living with the disease.

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