NATIONAL CENTER FOR CASE STUDY TEACHING IN SCIENCE

A Devil of a Disease

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Part I – The Mystery

In 1996, field researchers first noticed small, soft tissue lesions occurring on the face and heads of *Sarcophilus harrisii,* a spirited creature better known as the Tasmanian devil (Hawkins et al., 2006). Tasmanian devils are endemic to Tasmania, an island off the coast of Australia. Tasmanian devils are small marsupials weighing on average 10 kg (McGlashan et al., 2006) with an average life expectancy of 7–10 years. Male devils are generally larger than their female counterparts and are very aggressive. For example, during mating season males will often rip off chunks of flesh from each other's faces as they vie for mates (McCallum et al., 2009).

Devils are genetically similar due to eradication efforts during the 19th century until the species was protected in 1941, followed by generations of inbreeding. There appears to be some genetic diversity between devils on different sides of the island. O'Neill (2010) and Siddle et al. (2010) correlate this genetic inbreeding with the increased homogeneity of immune-related major histocompatibility complex (MHC) among devils. The MHC loci control the recognition of self and non-self in species such as the Tasmanian devil and humans through the production of cell recognition proteins on cells involved in immunity. This homogeneity suggests that the MHC loci are more uniform and would restrict the organism from recognizing a large number of potential pathogens or foreign cells. Tasmanian devils face no natural predators, but habitat destruction and newly introduced species have impacted population numbers within the last decade. Similarly, cocktails of pesticides and herbicides are employed in Tasmania each year to increase crop yield. These chemicals have the potential to affect devils and other animals, including those the devil scavenges and seeks as prey.

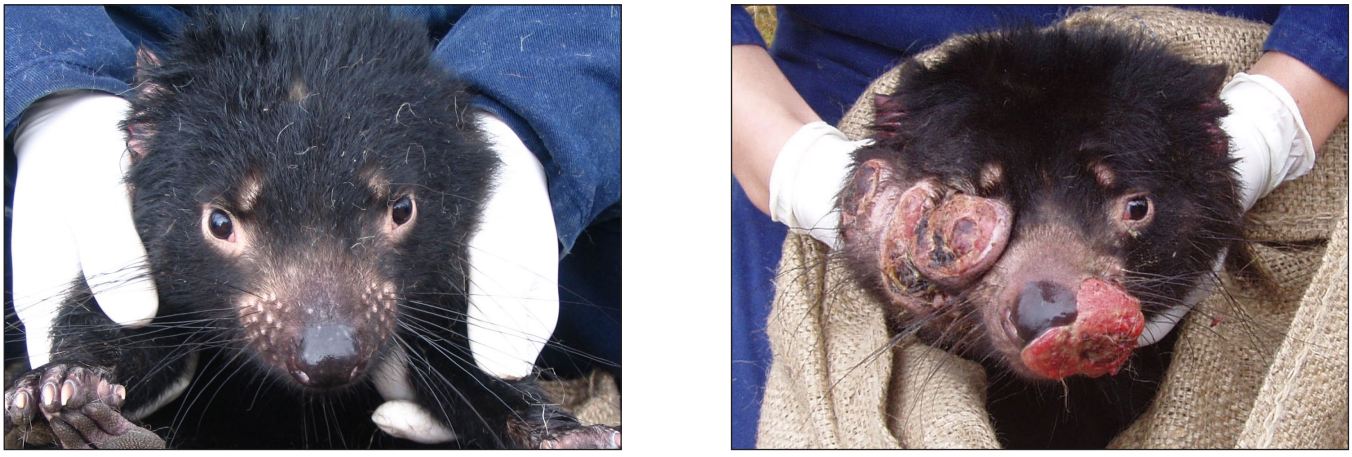

Figure 1. Comparison of a normal Tasmanian Devil (left) to an animal showing a facial tumor (right). (Images used with permission of "Save the Tasmanian Devil Program," http://www.tassiedevil.com.au/tasdevil.nsf.)

Between the years 1996 and 2007, the frequency of the facial lesions among devils increased rapidly and the population of devils drastically decreased throughout the eastern part of Tasmania. Scientists determined that these lesions were tumors. The tumors were most numerous in and around the mouths of the devils. At first viewed as an isolated problem, scientific curiosity quickly turned to panic as the Tasmanian devil population plummeted and the Australian media inflamed the public to action. In some eastern areas, the number of Tasmanian devils has declined by 85%. This disease, which sparked so many questions, demanded the answer to just one: *Why?*

Questions

1. What are some known causes of cancers in humans?
2. Propose a hypothesis to test one or more of the potential known causes of human cancer in the development of Tasmanian devil facial tumor disease.
3. Describe an experiment to test your hypothesis.

Part II – The Twist

Tasmanian devils with facial tumors would die, on average, within three months after being afflicted (McGlashan et al., 2006). Facial tumors occurred at the same frequency in areas where there are varying levels of chemical products found in the environment, suggesting that chemicals may not be the cause of the cancer. Certain sites experienced an 85% population decrease within 12 years (McCallum et al., 2009). Oncogenic (cancer-causing) viruses were also considered, but in laboratory experiments the immune responses of Tasmanian devil cells to viruses were excellent and viruses were not identified. Thus, a virus was probably not the cause of the tumors. With the devils' differential diagnosis dwindling, scientists turned to genetics to further analyze the properties of these singularly aggressive tumors.

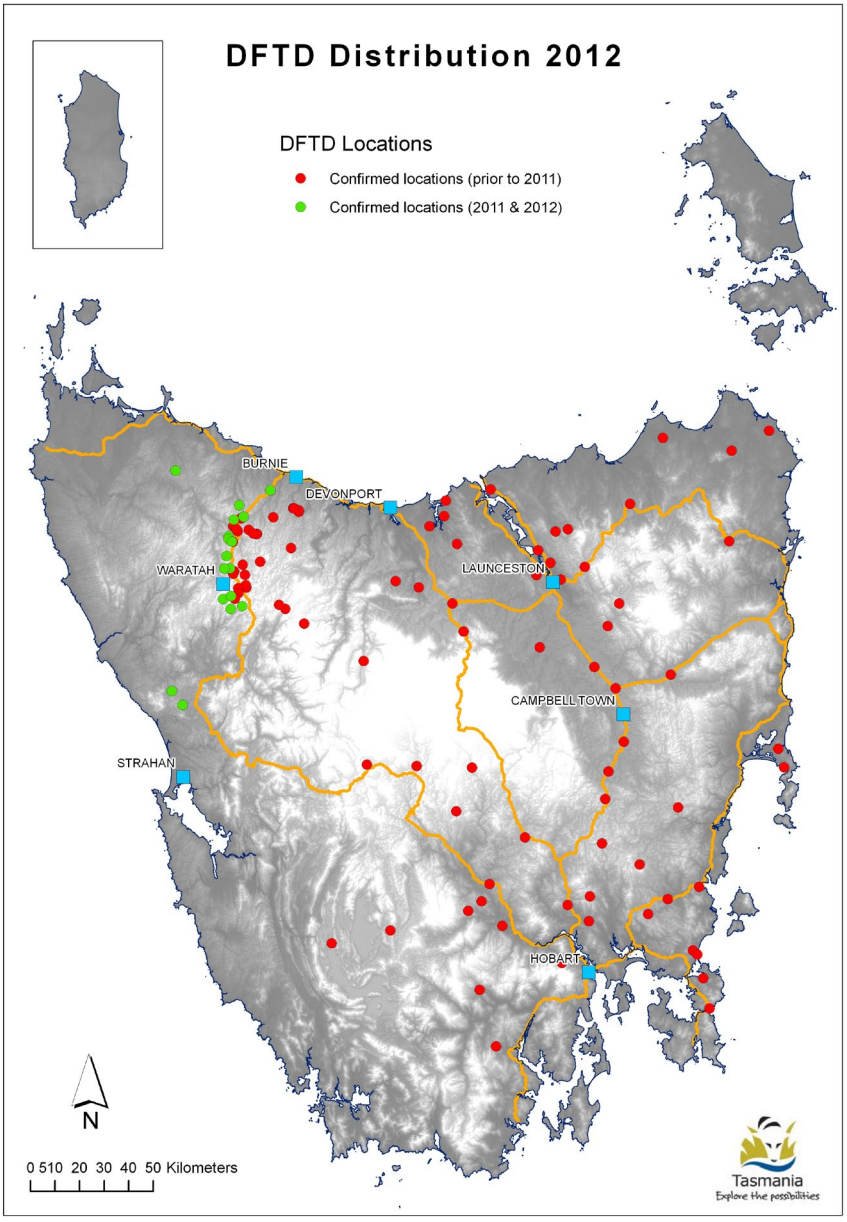

Figure 2. Map of Tasmania detailing the relatively homogenous nature of disease transmission in devils. (Map used with permission of "Save the Tasmanian Devil Program.")

A biopsy of the tumors revealed that they were cancerous (Murchison et al., 2010). Cytogeneticists analyzed the chromosome content (karyotype) from the tumor as well as cells from non-infected tissue. One test subject, nicknamed Errol, displayed a curious genetic anomaly in his karyotype. A single pair of homologous chromosomes from his healthy tissue was not identical (not shown in Figure 3). One chromosome demonstrated an inversion relative to the other chromosome. In the cancerous cells, the homologous chromosomes matched, although other differences were observed (see Figure 3). Furthermore, the karyotypes of the tumor cells were found to be identical in all affected devils and distinct from the healthy cells of the infected individuals. Karyotypes of the normal cells from individual animals were not identical. Cytogenetics thus provided a clue to the cause of the Tasmanian devil cancer. There was only one problem: *What did it mean?*

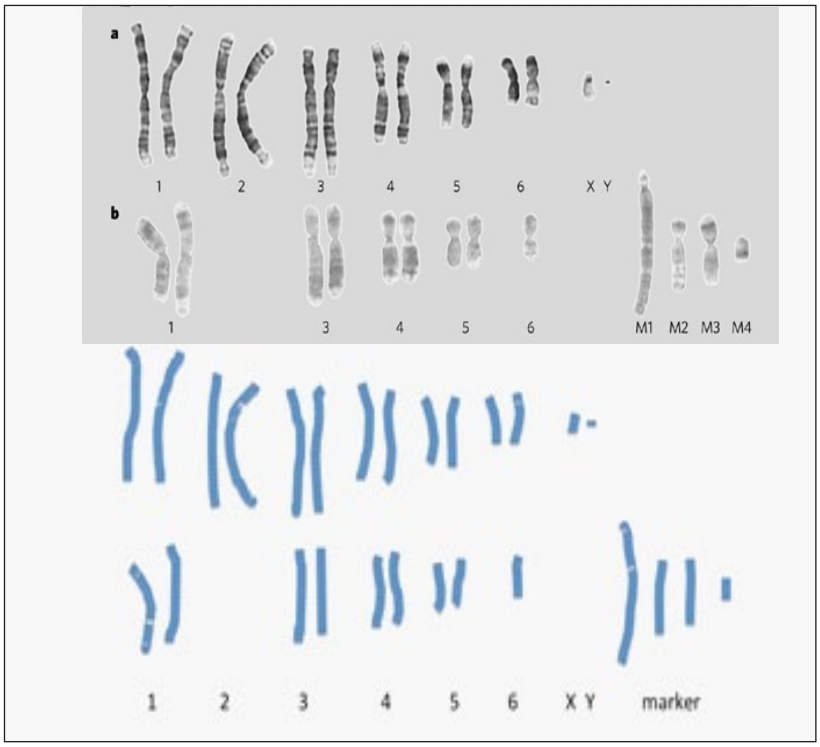

Figure 3. Top: A comparison of the devil karyotypes shows the unique non-homologous chromosomes and the various homologous chromosomes of the tumor tissue. Bottom: Schematized version. Numbers at the bottom identify the chromosomes. X and Y indicate the sex chromosomes. Marker chromosomes that are unique to the cancerous tissues are a composite of different chromosomes that are absent in the normal cell karyotype. *Credit:* Top panel reprinted by permission from Macmillan Publishers Ltd: *Nature* (Pearse, A.-M., and Swift, K., Allograft theory: Transmission of devil facial-tumour disease, *Nature* 439: 549–549), copyright 2006. Bottom panel schematized by case author., K. A. Johnson.

Questions

1. What feature(s) of a chromosome is a cytogeneticist looking for in a karyotype?
2. In the case of Errol's karyotype of normal cells, explain why one chromosome showed a different structure than the homologous chromosome?
3. What about the cancerous cell karyotype appears different from the normal karyotype based on Figure 3?
4. Explain the phenomenon of identical cancers among devils in terms of transmission.

Part III – Case Closed

Chromosomally, identical tumors suggest that the cancer cells originated in a single Tasmanian devil. This first diseased devil became the "index case" in what has proven to be a disastrous epidemic that continues to the current time. Although the index devil died many years ago (probably before disease outbreak was first reported), its immortal cancerous cells continue to spread throughout the Tasmanian devil population. The cancer is not rejected by the devils' immune system possibly because of the genetic similarity of the devils or through suppression of the immune system. The "foreign" cancerous tissues are not detected by the immune system, allowing propagation of the cancerous tissues (O'Neill, 2010). This inability to detect the tumors may be due to the genetic bottleneck and lack of heterogeneity in the MHC loci or to other factors. Tumors appeared on the face more often than the body of Tasmanian devils because they were more likely to bite each other on the face during mating or when competing for food or mates.

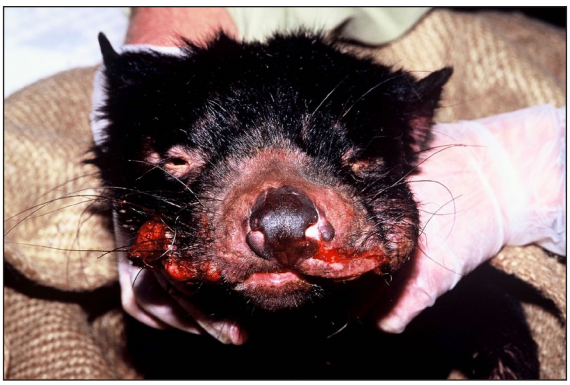

Figure 4. Variation on the Tasmanian Devil Facial Tumor disease. ("Save the Tasmanian Devil Program," http://www.tassiedevil.com.au/tasdevil.nsf.)

Only one other organism has been found to have a naturally transmissible cancer—dogs. Dogs experience the cancer as a venereal disease. This is referred to as "Sticker's sarcoma" (reviewed in Welsh, 2011). Canine transmissible venereal tumors are usually fought off by the dogs' immune system, ridding them of the tumor and preventing further tumors from manifesting. The relative ease with which dogs handle transmissible cancer means that scientists have spent little time investigating the problem of how to abate the spread of such cancers. Humans can "catch" cancer, but only as the result of an organ transplant or direct integration at the cellular level; for example, a mother might spread cancer to her fetus or cancer in one Siamese twin could metastasize to the other. Accidental transfer in surgeries also has been reported. The extinction of Tasmanian devils is a real threat, and one that needs to be dealt with immediately. In addition to the intrinsic value of such an iconic figure as the Tasmanian devil, further ramifications, such as a harsh disturbance to the ecological web of life, are motivation to investigate this intriguing and morbid disease.

Questions

1. Propose some possible methods of containing or eliminating Devil Facial Tumor Disease (DFTD) from the Tasmanian devil population.
2. Discuss the consequences of allowing the disease to spread unchecked. For example, Tasmanian devils and kangaroos are both marsupials. Could the disease spread to kangaroos? To humans? (Diseases capable of spreading from animals to humans are called zoonoses.)
3. What are possible dangers associated with relocating Tasmanian devils in order to protect a select group from the epidemic?
4. If scientists can determine that a particular group of devils is genetically dissimilar enough from other devils to produce an immune response to the tumors, then these may be the only devils that survive the current epidemic. Suggest possible problems these select devils may face in the future. How will fitness ultimately be affected?
5. What would happen in another organism, perhaps humans, if a naturally transmissible cancer were to develop similar to the cancer described here in the Tasmanian devil? What could happen to the human population?

Part IV – What Is Being Done?

Scientists investigating DFTD have made several significant observations, and efforts to contain the spread of the disease have begun. It is believed that the wild Tasmanian devil may be extinct by 2025 without an answer to this disease. Some efforts that have already begun include:

- *Population monitoring:* Scientists have placed additional field cameras in the wild on known devil trails to gather information regarding the health and number of devils in a given area.
- A disease-free population of devils was identified in Western Tasmania early in the investigations, with hopes that the genetic diversity of this population was distinct and rendered the devils immune to the cancerous tissue. This population unfortunately was observed to show susceptibility to DFTD. *Note:* Genetically diverse devils have now been shown to be susceptible to the disease. In June 2012, it was suggested that the cancerous cells are acting to suppress the host immune system (Hall, 2012)—which has been observed in some other cancers—and that the genetics of the devil population is not an issue with regards to the disease.
- *Wildlife management:* In order to create an isolated and disease free population, animals were captured and moved to a peninsula from 2004–2009. Observations in 2009 suggested that this effort was not effective, possibly due to either the inclusion of one or more infected animals or the migration of infected animals onto the peninsula.

Figure 5. Healthy Tasmanian devil protecting his food (remains of a kangaroo), Cleland Wildlife Park, near Mount Lofty, Adelaide, South Australia. Photo by Peripitus, http://commons.wikimedia.org/wiki/File:Sarcophilus_harrisii_feeding.jpg, CC BY-SA 2.5.

- *Insurance populations:*
  - One place for an insurance population has been zoos, which have been able to keep free of DFTD. As this disease is spread through physical contact, these zoo-housed animals should serve as an insurance population. This may provide only a small breeding population, but may be sufficient to maintain genetic diversity as is managed in other zoo-kept animals.
  - Researchers have also initiated wild-insurance populations (called free range enclosures or FREs). These populations are located on islands. The first FRE, established in 2005, was surveyed and showed 277 disease-free animals in January 2010. Two additional FRE areas were established in late 2010.
- Scientists continue to investigate the disease with hopes of identifying a potential cure for DFTD and to save the Tasmanian devils.

Interestingly, the devils are also evolving to the presence of DFTD. Healthy female Tasmanian devils normally do not breed until their second year of age; however, in areas in which DFTD is present, females have been observed to begin to breed during their first year.

For additional information, visit the "Save the Tasmanian Devil" webpage at http://www.tassiedevil.com.au. Current news may also be found on the Facebook page for the "Save the Tasmanian Devil Program."

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Credit: The photo appearing in the case title block that depicts a gaping Tasmanian devil is used with permission of "Save the Tasmanian Devil Program," http://www.tassiedevil.com.au/tasdevil.nsf.