Knut the polar bear's medical legacy

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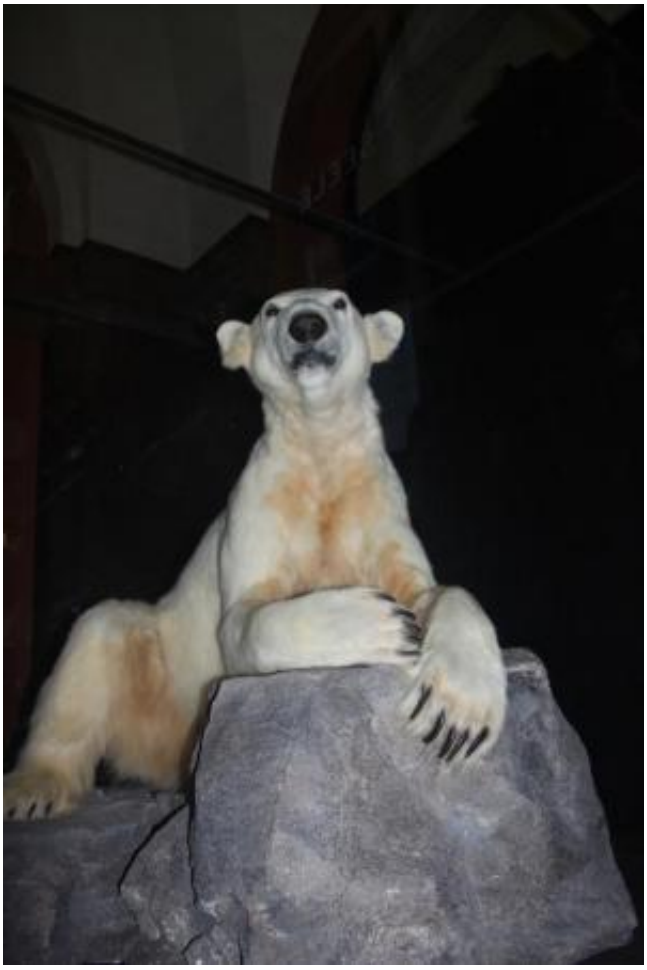

Credit: Forschungsverbund Berlin e.V. (FVB)

Keeping wild animals is an important component of the mission of zoos to educate the public and preserve endangered species. When animals die, tracking the potential cause becomes an investigation of pathogens

from around the world. This is because zoo animals are not only potentially exposed to pathogens occurring where the zoo is located, but also to those pathogens harboured by other zoo animals. In other words: the diagnostic challenge is enormous.

In the case of Knut, researchers from the Leibniz Institute for Zoo and Wildlife Research Berlin (IZW), the Freie Universität Berlin, the Friedrich Loeffler Institute – Insel Riems, the Max Delbrück Center for Molecular Medicine in Berlin, the University of California at San Francisco and many others combined their efforts to investigate Knut's death. Classical pathological, bacteriological, serological, molecular, histological and electron microscopical methods were combined with high throughput microarray and next generation sequencing methods to undertake the most extensive and exhaustive evaluation of the cause of death of any zoo animal to date. The necropsy was headed at the IZW by Dr Claudia Szentiks of the Department of Wildlife Diseases.

"After a detailed necropsy and histology that took several intense days to perform, the results clearly suggested that the underlying cause of Knut's seizures was a result of encephalitis, most likely of viral origin" says Dr Szentiks.

Encephalitis can be caused by a large number of viruses, bacteria and parasites, and identifying novel pathogens in wild animals is a huge and often insurmountable challenge. In the case of Knut, the team screened gene sequences from plausible causative pathogens from tens of millions of individual DNA sequences. "The sheer number of experiments undertaken and the sorting of results by many of the top diagnostics groups in Germany and beyond was extremely time consuming but also informative as to what we can and cannot do with current technologies. Many new directions for improvements and novel developments should come from this", says Professor Alex Greenwood, head of the Department of Wildlife Diseases of the IZW. Although frequently

suspected by many to be the likely culprit, the equine herpesviruses found in other polar bears in Germany and elsehwere was not responsible. The analysis of Knut also revealed a novel group of bear retroviruses whose presence was not related to his death. The only pathogen Knut seemed to have been exposed was an influenza A virus, as suggested by the detection of antibodies in his blood. However, it remains unclear and relatively unlikely that the flu was responsible for his death since the actual virus (in the form of viral RNA) could not be detected in his brain.

"After so much hard work, the results appear ultimately sobering. We cannot and therefore should not blame influenza as the source of death" stated Professor Klaus Osterrieder, holder of the chair for Veterinary Virology at the Freie Universität Berlin.

The results illustrate that while great strides in diagnostics have been made over the last decade, wildlife diseases present unique challenges because less is currently known than remains unknown about them. As a case in point, the research on Knut led to the discovery that a herpesvirus of zebras is able to kill polar bears as documented in the Wuppertal Zoo, infecting Knut's father Lars, who survived the infection, and his partner, Jerka, who died from the infection. This was a surprising result that has developed into an intensive project on herpesvirus transmission in endangered zoo animals. "It would have been impossible to check for all the suggested culprits without the support by the zoo community which willingly supplied samples from other animals for comparative purposes. This was exemplary. Although it will not help Knut any more, or other bears in the past, because of the new knowledge on pathogens in polar bears the zoos can now begin to develop management strategies to minimise their occurrence", commented Professor Heribert Hofer, head of the IZW.

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