Nature Reviews Cancer | AOP, published online 13 February 2014; doi:10.1038/nrc3686

CANCER GENETICS

The origin and evolution of an ancient cancer

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Canine transmissible venereal tumour (CTVT) is the oldest cancer in the natural world and one of only two known communicable cancers. CTVT is spread by the transfer of cancer cells between hosts during copulation, rather than arising *de novo* from the cells of each host. A new genomic analysis by Murchison *et al.* has refined the origin and evolution of this cancer.

Murchison *et al.* sequenced the genomes of two CTVT tumours and their hosts, located in Brazil and Australia. Despite massive karyotype abnormalities, the tumour genomes were found by copy number analysis to be mostly diploid. This indicates that these structural aberrations in karyotype are generally copy number neutral. Interestingly, unlike human cancers, the authors observed no subclonality in the tumours, suggesting that CTVT is fairly genomically stable, and this may indicate that it is well adapted to its niche. Moreover, at least 646 genes, which represent 2.8% of total protein-coding genes in the dog genome, were found to be lost by deletion or nonsense mutation, and are thus collectively dispensable for cell survival.

The authors also identified four mutational signatures in CTVT, which explained 98% of all mutations in the CTVT genome. Three of these signatures are also found in human cancers: one is correlated with patient age, one has an unknown aetiology and one corresponds to exposure to ultraviolet (UV) radiation. Forty-two percent of mutations in CTVT are associated with this latter signature, indicating that the CTVT cancer cells have been periodically exposed to UV light during the history of the CTVT lineage.

Finally, the researchers clarified the age of the cancer, which had been previously estimated to be 200–70,000 years old. They did this by examining the mutation signature associated with age in CTVT in comparison to the same signature in human medulloblastoma, which they used as a 'molecular clock'. By this estimate CTVT first arose 11,000 years ago. Interestingly, data from the two different tumours located on two continents also suggest that their most recent common ancestor existed 500 years ago, which corresponds to a period of history in which there were high levels of human exploration.

Collectively, this study of CTVT demonstrates the ability of a somatic cell to survive and to adapt to an enormous mutational burden over a vast period of time.

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This article originally appeared in *Nature Rev. Genet.* (http://dx.doi.org/10.1038/nrg3676).

ORIGINAL RESEARCH PAPER Murchison, E. P. *et al.* Transmissible dog cancer genome reveals the origin and history of an ancient cell lineage. *Science* **343**, 437–440 (2014)

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