TUMOUR TRANSMISSION

Transmission possible

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URLs
MYC
http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?db=gene&cmd=Retrieve&dopt=full_report&list_uids=4609

Healthy humans cannot 'catch' cancer through direct contact with tumours, but dogs can. Claudio Murgia and colleagues show that in canine transmissible venereal tumour (CTVT) it is the tumour cell that is the transmissible agent.

CTVT is a histiocytic tumour that is transmitted between dogs primarily during coitus and was first characterized 130 years ago. It has long been thought that the CTVT cells are able to engraft onto new hosts, but other data have indicated the involvement of an oncogenic virus. The authors used molecular genetic markers as a means to resolve the issue of transmission and to investigate the origin of CTVT.

Matched tumours and normal tissues were used from dogs treated in Italy, India and Kenya, and these were compared with archive tumour tissue isolated from sources worldwide. CTVT cells have previously been shown to harbour a long interspersed nuclear element (LINE-1) inserted close to the *MYC* oncogene, and the authors confirmed that this is a characteristic of the CTVT cell and not an inherited predisposition in the dogs themselves. Analyses of polymorphisms within the canine major histocompatability complex (MHC) genes, genotyping of microsatellite markers and analyses of the polymorphic control region of mitochondrial DNA show that the tumour cells and their hosts are genetically distinct.

Further analyses indicate that CTVT might have originated in wolves, and that the current tumour clone is between 250 and 2,500 years old.

Interestingly, the microsatellite data also indicate that although the tumour cells are aneuploid, their genome is surprisingly stable. This could be because CTVT cells express telomerase, which can protect against DNA damage resulting from short telomeres.

CTVT cells can engraft in many different breeds of dog, but dogs that have recovered (gone on to reject the tumour) are immune on tumour rechallenge, indicating that the immune response must be suppressed by the tumour when it first establishes in a new host. Indeed, CTVT cells secrete transforming growth factor-β, a known immunosuppresive cytokine, and analysis of fresh tumour material from one of the dogs indicated reduced MHC expression compared with control tissue. So, CTVT seems to have adapted to initially evade the host immune response.

The expression of MHC genes is often reduced in tumours, so it is unclear why parasitic tumours have not emerged more frequently, over and above those identified in a colony of Syrian hamsters and the recent transmissible tumour outbreak in Tasmanian devils. The lack of genetic diversity in devils and hamsters might help to explain this in these species, but the confirmation that CTVT is also a parasitic tumour that has been stably aneuploid over many generations with a wide host range challenges many of our ideas about tumour development.

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ORIGINAL RESEARCH PAPER Murgia, C. *et al.* Clonal origin and evolution of a transmissible cancer. *Cell* **126**, 477–487 (2006)

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