

# Transmissible cancer in marine bivalves: Implications for mode of cancer transmission

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## Abstract

Cancer spread away from the primary tumour towards other parts of the body is what is most feared in cancer treatment, and is the leading cause of relapse for patients who are in remission after initial rounds of treatment with surgery, radiation or chemotherapy. Typically more aggressive than the primary tumour, secondary tumours developed through the process of metastasis are seeded by circulating tumour cells that migrate away from solid tumours to distant body sites. But increasingly, there is another method by which cancer is able to spread: transmission between members of the same or different species. Dangerous for the implications that it portends, the intra- and interspecies transmission of cancer highlights the potential infectious nature of the disease of neoplastic cell growth, and the implications it may have on transmission of cancer through the food chain, even though the latter link find no verifiable reported episode, but which remains a possibility to be vigilant for. Currently, transmissible cancers have been detected in dogs, Tasmanian devils, and molluscs. In a recent report in *Nature*, Goff and coworkers reported the widespread transmission of independent cancer lineages within and between marine bivalves species (“Widespread transmission of independent cancer lineage within multiple bivalve species”, [Link](#)). Field studies conducted along the Pacific Northwest coast led to the identification of neoplastic bivalves, which upon sequencing of the mitochondrial cytochrome c oxidase gene proffer a set of single nucleotide polymorphisms (SNP) that could be clustered into distinct cancer lineages in a phylogenetic tree. Using sequence information as guide and histology observations as clues, clear evidence of cancer transmission between and within bivalves species were confirmed, with affected bivalves showing clear phenotypic neoplasms. Given that bivalves are a source of nutrients and vitamins in the delicacy segment of Asian cuisine, possible transmission of cancer between bivalves and humans as well as mammals such as bears that feed on them is an important direction for future research.

**Keywords:** cancer transmission, infectious disease, bivalves, single nucleotide polymorphism, cancer lineages, DNA sequencing, phylogenetics,

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## Perspective

With their rapid growth rate and need for nutrition, cancer cells move as they seek new niches for nutrients and space for colony expansion. Thus far, the most well studied movement mechanism for cancer cells is metastasis, where a cancer cell from a primary tumour migrate, through the bloodstream, to a new site suitable for growth and establishment of a new clonal population that later morphs into a secondary tumour distant from the primary tumour.

But, is cancer transmissible like infectious diseases such as flu and chicken pox are? Answering the question in a *Nature* article, “Widespread transmission of independent cancer lineages within multiple bivalve species”,<sup>1</sup> *Nature*, 2016, Vol. 534, pp. 705-708, Goff and coworkers discovered transmission of cancer between and within three marine clam shell and mussels species; thereby, corroborating the possibility of cancer transmissions between members of the same species documented by earlier discoveries of transmissible cancer in dogs and Tasmanian devils. More importantly, the research revealed another facet of cancer transmission: the ability to cross the species barriers at least in closely related marine clam like species.

Using mitochondrial cytochrome C oxidase I (*mtCOI*) as marker gene for profiling the phylogenetics of cancer cells in neoplastic bivalves obtained from Vancouver Island, the study revealed the transmission of cancers in the following species: (i) mussels (*Mytilus trossulus*), (ii) cockles (*Cerastoderma edule*), and (iii) golden carpet shell clams (*Polititapes aureus*). Specifically, gene sequencing highlights the specific nucleotide changes characteristic of individual lineage of cancer cells. Known as single nucleotide polymorphism (SNP), the approach allows the clustering of individual cancer lineage within a single type of cancer in a species; thus, enabling the delineation of the genetic map of the cancer. Together with histology study where tissue specific dyes are used to label cellular tissue prior to optical microscopy, SNP sequencing should be able to inform the particular gene allelic changes that manifest as observable phenotypic change at the tissue level.

Overall, the discovery research detailed in the paper adds to our nascent understanding of transmissible cancer, which was previously reported in only 8 lineages: one lineage in dogs, two lineages in Tasmanian devils, and five lineages in four species of molluscs. Of greater importance is the discovery of another instance of cross species transmission of cancer; thus, providing more evidence supporting the hypothesis that cancer may be able to cross species barriers, which makes it a greater medical threat. Beyond the broad themes highlighted, the paper also demonstrates the utility of profiling for SNP changes via gene sequencing for understanding the lineage present in a cancer and correlating genetic changes to observed phenotypic manifestations.

Further work may look into how marine environment conditions affect the transmissibility of cancers between and within marine bivalves species. Since environmental conditions feed into epigenetic changes that impact on gene transcription and metabolic programmes utilized, understanding how different modifications at the DNA and histone level could open up a deeper layer of information for the specific triggers or genetic repertoire that endow a cancer to cross the species barrier. Various bisulphite based chromatin sequencing techniques such as chromatin immunoprecipitation sequencing (ChIP seq) could be used for elucidating epigenetic marks in bivalves with and without cancer, where possibility exists for decoupling the interactions between epigenetic modifications at the DNA and histone levels, which could help advance our understanding of environmental triggers for cancer transmission. Such information would provide us with a framework to better understand transmissibility of cancer in other species, for example, humans. Finally, from an evolutionary perspective, it would be interesting to explore possible cases where cancer is able to cross a large species barrier such as that between different mammal species, given that the transmission of cancer documented in this study is that between fairly closely related species.

One area where the authors could improve the manuscript is to describe the basis for characterizing cancer lineages using the mitochondrial cytochrome C oxidase I gene. Information such as the above would help readers better understand the phylogenetic significance of the gene and the role it played in either potentiating the cancer or enable its transmissibility.

### Conflicts of interest

The author declares no conflicts of interest.

### Author's contribution

The author read the original publication and wrote a perspective describing the research.

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1. Metzger, M. J. *et al.* Widespread transmission of independent cancer lineages within multiple bivalve species. *Nature* **534**, 705–709 (2016).

