THE ROLE FUSOBACTERIUM PLAYS IN ORAL CANCER PATIENTS IN INDIA

Relevant for: Science & Technology | Topic: Biotechnology, Genetics & Health related developments

A study identified the presence of a bacteria, *Fusobacterium nucleatum*, in oral tumours at a significantly higher burden than in the oral cavity of healthy individuals. | Photo Credit: Getty Images

Since the beginning of the 20th Century, it is known that infections could play a role in cancer, with 18-20% of cancers associated with infectious agents. This could be relatively higher in developing countries like India. Our team at ACTREC-Tata Memorial Centre developed a highly sensitive and specific automated computational tool HPVDetector to quantify the presence of human papillomavirus (HPV). This was done by subtracting human sequences from the cancer genome and comparing the rest with the HPV genome to identify the presence of HPV sequence trace and determine the range of all co-infecting HPV strains in the same individual.

The analysis revealed significant occurrence of HPV 16, 18, and 31, among others, in cervical cancer. But a surprising finding was that Indian patients with oral tumours showing a distinct tobacco usage gene signature were devoid of HPV infection. This was in sharp contrast to the oral tumours among Caucasian patients, wherein tobacco genetic signature is not common but is marked by a significant presence of HPV. Several groups have corroborated this finding, and it is well established that oral tumours among Indian patients are not driven by HPV infection.

In this study published on Mar 4, in *NAR Cancer,* Sanket Desai, the lead researcher from the group, developed another advanced automated computational tool — Infectious Pathogen Detector (IPD). Beyond HPV, IPD can detect the presence of 1,058 pathogens in the human cancer genome from datasets generated from any Next Generation Sequencing platform. This tool is publicly available for download from the ACTREC- TMC website. Using IPD, the DNA and RNA sequence from 1,407 cancer samples of oral, breast, cervical, gall bladder, lung and colorectal tumours derived from Indians were analysed and compared with Caucasian patients.

This has led to establishing the most detailed map of the abundance of 1,058 microbes present across Indian cancer patients. Rigorous statistical measures were adopted to distinguish the commensal microbes present as normal flora in a healthy individual compared with the diseased state. Systematic analysis of the data helped the group identify the presence of a bacteria, *Fusobacterium nucleatum*, in the oral tumours at a significantly higher burden than in the oral cavity of healthy individuals.

Interestingly, *Fusobacterium nucleatum* is known to play a vital role in colorectal cancer, wherein its presence affects the spread of the disease and the patient's response to chemotherapy. However, a similar role of *Fusobacterium* in oral cancer was not known earlier. The presence of the bacteria was found in Indian and Caucasian oral cancer patients, with a much higher incidence among the Indian patients. Moreover, oral cancer patients positive for *Fusobacterium* were found to be negative for HPV infection, suggesting they are present in a mutually exclusive way.

The finding underlines that while oral tumours in the West are more likely to be driven by HPV infection with a lower abundance of *Fusobacterium* infection, the oral cancer incidences in India are caused more by *Fusobacterium* infection. The tumours in oral cancer patients infected with the bacterium were found to spread to lymph nodes in the head and neck region or other distant

organs. This sub-class of the tumour was also found to have higher levels of genes responsible for inflammation and pro-cancer immunological response.

Consistent with this finding, infection with virus or bacteria causing chronic inflammation leading to cancer has been known across multiple cancer types, such as HPV in cervical cancer, HBV and HCV in liver cancer, *H. pylori* in gastric cancer, etc. This study also identified three novel small non-coding miRNA molecules among tumours infected with the bacteria. The discovery of these miRNAs allows the investigators to understand the biological pathway targeted by the *Fusobacteria*, when it infects the oral cells, and its detailed characterisation. The study continues in collaboration with IIT Bombay, where the researchers grow the oral cancer cells in the presence and absence of the bacterium.

Preventing cancer through immunisation against infectious agents such as HPV vaccination has been known to be effective in up to 90% of HPV-related cancers. Similarly, a significant reduction was observed in the incidence of gastric cancer across multiple studies when the patients infected with the bacteria, *Helicobacterium pylori*, were treated with antibiotics specific to the bacterium. The findings from the study carried out at ACTREC- Tata Memorial Centre opens an opportunity to treat oral cancer patients positive for *Fusobacterium*, occurring predominantly among Indian patients, with a *Fusobacterium*-specific antibiotic for selectively targeting the tumours. The study emphasises the impact of *Fusobacterium* infection on modulating conventional chemotherapy treatment or recurrence of the disease as frequently observed in oral cancer patients, similar to its role in colorectal cancer. The utility of community screening for the presence of *Fusobacterium* in the oral cavity in a population or among habitual tobacco chewers remains to be explored — though it could be a worthy exercise considering the alarming increase in tobacco-associated oral cancer in India.

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