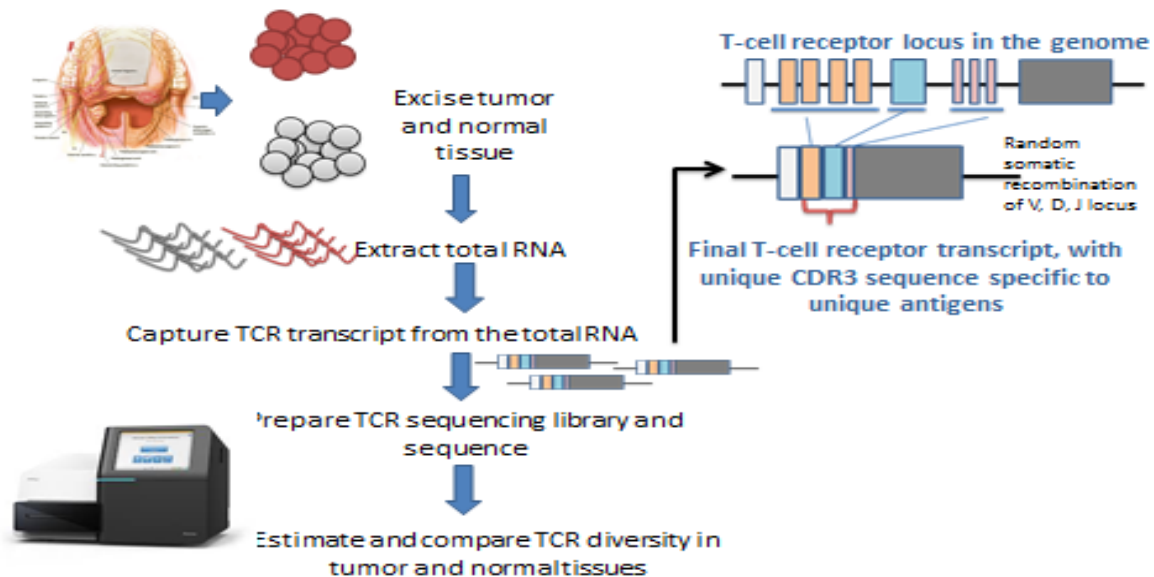


Understanding the anti-tumor immunity in oral cancer

Researchers at DBT's National Institute of Biomedical Genomics (NIBMG), Kalyani are investigating the T-cell receptor repertoire (TCR) repertoire diversity in oral cancer which was previously showed to carry high mutational burden. The preliminary findings on ten OSCC-GB patients showed higher TCR diversity in the tumors compared to tumor margins and adjacent normal tissues obtained from the cancer patients. This observation holds promising immunotherapeutic potential for OSCC-GB cancers.



Every cell replicates its own Deoxyribonucleic acid (DNA). The process of cell division is highly regulated by checkpoints and cells with erroneous replication are abolished. However, failure at checkpoints and uncontrolled cell division is one of the hallmarks of cancer, which leads to accumulation of nucleotide changes in DNA, also called mutations. Mutations can get translated to mutated peptides (Neopeptides), which when present on cancer cells, can be recognized as *foreign* by the immune system. Thus, as more and more *mutations* accumulate in the genomes of cancer cells (increase in mutation burden), there are increased chances of production of more *Neopeptides*. T cells are important players of cell-mediated immunity in our body. A highly diverse TCR is generated in the thymus by random recombination of V, D and J genomic segments. The divergent TCR can distinguish diverse foreign antigens, irrespective of

their sources of origin. CD8+ cytotoxic T-cells can induce death to the cell displaying the foreign antigen. However, T-cell induced killing activity is tightly regulated by immune checkpoints (ICs).

Recognition of cancer associated antigens, by T-cells and administration of active killing of the cancer cells is an important anti-tumor immune response. Identification of TCR repertoire in a tumor provides us valuable insights on the body's immune response against the cancer and is directly correlated with neo-antigen load. From the enormous researches done in the past decade, grossly, two distinct types of tumors have been identified- "Hot tumors" (where T-cells can infiltrate within the tumor) and "Cold tumors" (where T-cells are excluded from the tumor-microenvironment (TIME)). Studies also showed that patients with hot-tumors have better prognosis than those with cold-tumors. Thus, T-cells infiltration and functioning in the TIME is an important determinant of disease prognosis. In fact, current cancer therapy with IC inhibitors (which abolish the block to T-cell mediated killing by ICs) work better on hot tumors.

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