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ABSTRACT

Cancer stands as the most significant challenge in terms of clinical, societal, and economic impact among all human diseases. It arises from the disruption of the orderly process of cell senescence. Genomic instability is a prominent hallmark of cancer, it facilitates for mutations that can contribute to the disorderliness in the senescence process and aids in tumours survival, progression, as well as immune evasion. Evading immune response is another hallmark of cancer. The immune system, which is ordained to protect self from non-self or altered self is either suppressed or manipulated to support cancer cells in a process termed as immune editing. In immune editing, initial immune surveillance is followed by an equilibrium phase, where immune resistant and immune susceptible clone coexist in equilibrium. The equilibrium is tilted by accumulation of mutations favouring immune escape leading to expansion of immune resistant clones that manipulate the tumour immune microenvironment to facilitate secretion of immune-suppressive molecules and infiltration of immune suppressive cells fuelling tumour growth. It can therefore be hypothesized that mutations in immune response related genes have the potential to influence tumor growth, prognosis and survival. In this doctoral research we focus on exploring immune related genes with genomic instability in order to better understand how changes in these genes affect the disease. For the study, immune-related genes exhibiting genomic instability in cancer were selected to evaluate their influence on disease outcome, altered gene expression, enriched pathways and immune cell infiltration to the tumour immune microenvironment.

Datasets for 24 types of cancer and a list of immune-related genes were downloaded from cBioPortal and ImmPort, respectively. Mutation data for genes in the immune-related gene list was obtained and analysed for mutational summaries and screening frequently mutated genes using maftools. CNA data from the 24 different cancer dataset was analysed using GISTIC 2.0. Given the potential of secondary nucleic acid structures, such as G-quadruplexes, to induce genomic instability and their association with the immune system, we investigated their relationship with mutations in immune-related genes in cancer. FASTA sequences for the human genome were downloaded from NCBI, and G4Hunter was used to examine the

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