Nature Reviews Clinical Oncology | Published online 20 Feb 2017; doi:10.1038/nrclinonc.2017.23

BIOMARKERS

ANEUPLOIDY AND IMMUNE EVASION — A BIOMARKER OF RESPONSE

> “…indicating that aneuploidy restricts cytotoxic immune processes during tumorigenesis”

Many tumours are characterized by the presence of aneuploidy (an abnormal number of chromosomes), and somatic copy-number alterations (SCNAs). Immune evasion is another hallmark of cancer, with important implications for resistance to therapy. Studies have shown that cytolytic immune infiltrates correlate with the tumour mutational load, although the mechanisms underlying this link are not well understood. Now, results of a large analysis indicate that most tumours with extensive aneuploidy have a reduced number of infiltrating immune cells, which might have predictive potential.

Researchers examined data from 5,255 tumour and normal samples from The Cancer Genome Atlas (TGCA). A positive correlation was found between the number of mutations and SCNAs in 8 of 12 tumour types assessed. Overall, the analysis showed that a high degree of aneuploidy was linked with increased cell proliferation markers, but was also accompanied by reduced infiltration of cytotoxic imune cells, especially of $CD8^+$ T cells and natural killer cells. A notable exception to this trend was observed in brain tumours. The type of SCNA is important: immune signatures related to chromosomal-arm SCNAs were more predictive than focal SCNAs. Furthermore, tumours with a high number of chromosomal-arm SCNAs had a significantly decreased immune signature score, indicating that aneuploidy restricts cytotoxic immune processes during tumorigenesis.

In light of the correlation between SCNAs and immune activity, researchers investigated the potential link between SCNAs and patient survival following immunotherapy. In a TCGA dataset of patients with metastatic melanoma treated with anti-CTLA-4 blockade, tumour SCNA levels were significantly lower in patients with long-term survival than in those with shorter survival. In patients who did not receive immunotherapy, a higher number of mutations predicted a significantly better survival, whereas a higher SCNA burden was associated with poorer survival, but this latter association was not statistically significant. Thus, data on tumour mutational load and SCNA levels can be combined to predict patient survival after immunotherapy.

Lisa Hutchinson

ORIGINAL ARTICLE Davoli, T. *et al.* Tumor aneuploidy correlates with markers of immune evasion and with reduced response to immunotherapy. *Science* **355**, eaaf8399 (2017)