腫瘍微小環境での免疫抑制ネットワーク

Immune suppressive network in the tumor microenvironment

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Upon the clinical application of cancer immunotherapy, particularly immune checkpoint blockade (ICB) in which treatment efficacy is dependent on the immune system, more than half of treated patients yet fail to respond to immune checkpoint blockade, even in combination, uncovering a limited window of clinical responses. It is therefore required to develop more effective cancer immunotherapies and define biomarkers for stratifying responders and non-responders via the detailed analyses of immune responses in the patients.

According to the cancer immunoediting hypothesis, cancers select low-immunogenic tumor cells such as cells with decreased immunogenic antigens and employ multiple immune suppressive mechanisms including immune checkpoint molecules to create an immunosuppressive tumor microenvironment (TME) to escape immunosurveillance. Thus, cancers in the clinic can be divided in immunologically hot and cold tumors, and clarifying the immunological phenotypes with comprehensive genomic and immunological assays is necessary to optimize cancer immunotherapies with suitable predictive biomarkers.

Certain oncogenic signals such as WNT signal reportedly control immune responses in tumors. We have found that driver mutations in EGFR promoted Treg-infiltration and inhibited effector T-cell infiltration into the TME by directly targeting chemokine expression to establish the immune suppressive TME. Thus, integrated analyses of immunological and genomic assays revealed the comprehensive immune suppressive network in the TME, leading to the optimal cancer immunotherapies.