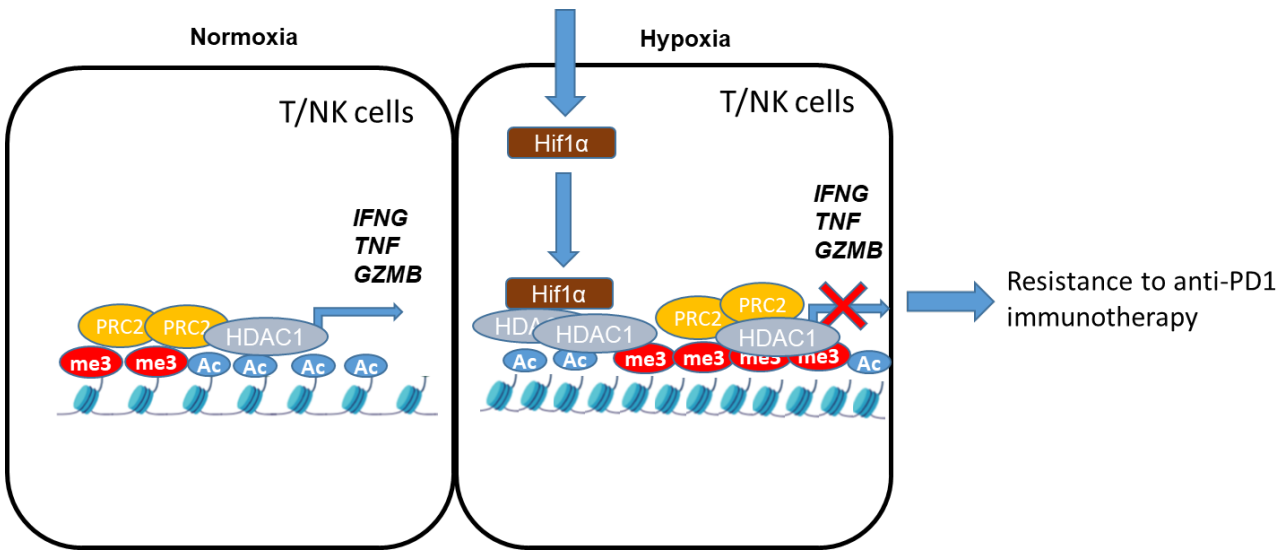
HYPOXIA PROMOTES IMMUNE CELL DYSFUNCTION TO CONFER RESISTANCE TO CANCER IMMUNOTHERAPY



Tumour hypoxia induces HIF1α-dependent epigenetic remodelling to suppress immune effector gene expression in T and NK cells, leading to resistance to PD-1 blockade.
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16 August 2022 – Triple-negative breast cancer (TNBC) is notorious for being one of the most incurable cancers worldwide that is highly recurrent, to the extent that it has been called "the kiss of death". Immune checkpoint blockade (ICB) therapy has been approved for treating TNBC, but the overall response rate is dismally low.

Our research found that tumour hypoxia (a hallmark of solid tumours that promotes tumour progression and metastasis) suppresses the anti-cancer activity of immune effector cells in triple-negative breast cancer (TNBC). This leads to resistance against ICB and enables cancer to evade our immune system.

We investigated the underlying mechanism and demonstrated that HIF1α contributes to hypoxia-induced T and NK cell dysfunctions through epigenetic silencing of immune effector expressions. We further demonstrated that targeting HIF1α-mediated epigenetic mechanism can rescue the immune effector dysfunction, and overcome TNBC resistance to ICB in our experimental models

The research was published in *Nature Communications* on 15 July 2022.

"We developed a new therapeutic strategy that can sensitise TNBC to ICB, which will aid future clinical trials. Our research revealed the underlying mechanism by which hypoxia promotes immune escape in solid tumours. It not only provides a rationale for supporting a future clinical trial in TNBC, but also sheds light on overcoming resistance against ICB in other solid tumours"

Dr Ma Shijun, Research Associate,
Laboratory of Precision Cancer Medicine, GIS

"TNBC is an aggressive and invasive cancer that lacks effective treatment. Although immunotherapies, including CAR-T therapy and ICB, have emerged as new breakthroughs in cancer treatment, they still failed to achieve satisfying outcomes in treating specific cancers, including TNBC. This unmet clinical issue needs to be addressed, which urged us to explore the mechanisms of immune evasion in TNBC, and formulate new strategies to treat it."

Dr Yu Qiang, Senior Group Leader
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