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Nanobyte

Immune Checkpoint Inhibitors and Gut Biota

Immune checkpoint inhibitors targeting PD-1/PD-L1 can have differing effects in various individuals. Recent studies published have suggested a role in the gut microbiome composition in contributing to the efficacy of these drugs. Patients who took antibiotics showed a poorer response to PD-1 inhibitors compared to those who did not take any antibiotics.[1] In another study, fecal transplants to mice from patients that improved on PD-1 blockers showed improvement on the drugs, while mice receiving transplants from poor responders showed similar lack of efficacy of PD-1 blockers. [1] New clinical trials and metagenomics studies are anticipated in the near future that could allow us to understand better the mechanisms of the gut microbial role in the effectiveness of immune checkpoint blockers.

Oncolytic Viruses in Targeting Immune Checkpoint Inhibitors

Oncolytic viruses are tumor-specific, self-replicating viruses that cause cancer cell lysis. Oncolytic viruses were recently delivered in two clinical studies to infect brain[2] and breast tumor[3] cells to assess the effect of pretreatment with these viruses on subsequent immune checkpoint inhibitor activity. Both studies showed enhancement of immune checkpoint inhibitor effect on the targeted tumors when administered in these patients. These studies potentially widen the repertoire of immune checkpoint inhibitors to include other tumors.

Molecular mechanism of the "Warburg Effect"

The Warburg effect is a well-known and long discussed cancer metabolism phenomenon described almost a century ago. It was the observation that tumor cells required high amounts of glucose to grow and that this was in the absence of oxygen (anaerobic). It is this very property that is exploited in positron emission tomography scans, to predict prognosis of a tumor based on its glucose utilization. Recently, a molecular connection between yeast cells and cancer cells was discovered, which would explain both types of cells' preference for sugar fermentation rather than mitochondrial respiration. The missing link was all too familiar Cdc25 that activated Ras.[4] It has been known for some time that glucose catabolism in glycolysis is necessary activation of the Ras proteins and cAMP synthesis. However, the molecular connection was so far unclear. It is now clear that glucose, on entering the cell, is converted to fructose 1,6 bisP which interacts with Cdc25 which in turn leads to the activation of Ras.

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