Immunoediting instructs tumor metabolic reprogramming to support immune evasion

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一、簡訴論文概要及重大發現

To overcome diverse environmental cues and selective pressures in the tumor microenvironment (TME) by the host anti-tumor immunity. It has been reported that tumor cells will undergo metabolic reprogramming in response to hypoxia and oncogenic mutation, but this is not the whole story.

The tug-of-war between tumor cells and tumor-infiltrating immune cells have shown to be a critical event for immune evasion. Previous study suggested that the metabolic competition between T cells and tumor cells might empower tumor cells to undergo immune evasion by promoting T cells dysfunction and establishing an immunosuppressive TME.

Here, the author proposed that immune evasion of tumor cells through metabolic reprogramming is guided by immunosurveillance, termed as “immunometabolic editing”. They suggested that IFNγ guided immunosurveillance impacts epigenetic architecture for modulating cMyc-dependent signaling cascade. cMyc is not the only player in the tug-of-war, the author proposed a non-canonical IFNγ-STAT3 signalling which will dampen T cell anti-tumor immunity.

Thus, those findings suggested that the metabolic crosstalk between tumor and tumor-infiltrating T cells is the outcome of immunoediting and tumor cells can adapt to the TME by adjusting their metabolic preferences.

二、對論文內容的提問

Genomic instability might be one of the causes in human cancers while Braf/Pten melanoma mouse model is used, does the phenomenon observed will be the same as in human case?

三、論文的缺點與評論

This is an integrative way to study the metabolic crosstalk between tumor cells and tumor-infiltrating T cells in TME.

Is in vivo tracing possible to perform? To check whether glucose in the TME is involve in immune evasion, since the author analyze OCR/ECAR as the indicator for immune evasion.

I wonder how other immune cells work in this setting, because T cell is not the only one immune cell that will secrete IFNγ.

Article

Cell Metabolism

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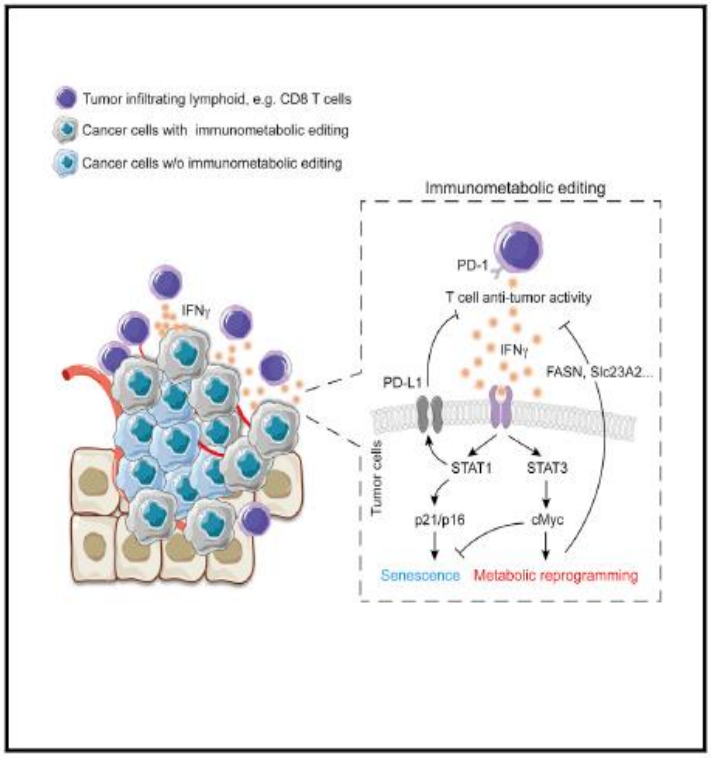
Graphical abstract



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In brief

Metabolic reprogramming, generally believed to be controlled by oncogenic mutations and hypoxia, supports tumor proliferation, anti-apoptosis, and metastasis. Here, we uncover an unexplored action of IFNγ by which T cell-mediated immunosurveillance impacts epigenetic architecture and gene expression in tumor cells that boosts cMyc-dependent metabolic reprogramming and tumor immune evasion.

Highlights

- Immunometabolic editing orchestrates metabolic preferences in tumor cells
- Metabolic program acquired by edited tumor cells supports tumor immune evasion
- IFNγ-driven editing modulates cMyc expression in a non-canonical STAT3 pathway
- Immunosurveillance impacts tumor epigenetic program for boosting aggressiveness

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