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Immuno-metabolomics of tumor-associated T-regulatory cells

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Abstract

Metabolism plays a crucial role in shaping the interaction between cancer cells and immune cells and hence recent research has focussed in this new area of immuno-metabolism in the tumor microenvironment. Cancer cells show increased uptake of available nutrients and metabolically change the tumor microenvironment. Tumor-infiltrating immune cells often can't adapt to the glucose-depleted metabolic environment created by cancer cells and thus fail to survive. In the contrary, immunosuppressive T-regulatory (Treg) cells survive this inhospitable environment and facilitates tumor immune-evasion. The Treg cells adapt to the glucose-depleted tumor microenvironment by shifting their metabolic preferences from glucose to fatty acid. Our RNA-seq data showed that the key enzymes involved in fatty acid metabolism are up-regulated while those involved in glucose metabolism are down-regulated in Treg cells. Recent studies have revealed that other immune cells which strive on fatty acid metabolism for their generation and proliferation, scavenge the fatty acid molecule with the help of CD36, a fatty acid scavenger molecule. Interestingly, we observed that among all the CD4+ T cell subtypes, Treg cells from breast tumor patient showed significant higher level of CD36 expression than their normal counterparts. In the presence of fatty acid uptake inhibitor, the generation of Tregs was hampered which indicated an important role of CD36 in this regard. Bioinformatics analysis showed the presence of putative FOXP3-binding site at the CD36 promoter. In Treg cells FOXP3 binds to the promoter region of CD36 gene and induced its transcription which was confirmed by the bioinformatics and well as genetic ablation and biochemical studies. The genetic ablation of both FOXP3 and CD36 reduced fatty acid uptake by Treg cells and thus impaired their development and proliferation. Further extensive studies on the transcriptional control of CD36 will be pursued to elucidate the mechanism through which Treg cells metabolically adapt to the tumor microenvironment and thus to manipulate these immunosuppressive pro-tumor Treg cells to check tumor progression.

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Biography

Subhanki Dhar is a SRF in Immunology at the Bose Institute located at Kolkata in India. Her research works primarily focus on understanding the aspects associated with cancer cells and Identifying a viable solution for its treatment. Her expertise in this domain is relatively just begun but the works that are constantly done over a period has shown some decent results in the domain of cancer research. Her research works are focused on the design and development a viable solution for treating cancer cells.

Publications

- Regulation of cancer cell metabolism
- Tumors and mitochondrial respiration: a neglected connection
- The biology of cancer: metabolic reprogramming fuels cell growth and proliferation
- Metabolic Features of Cancer Treatment Resistance

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