Mapping the surfaceome of circulating colon tumor cells to discover immune evasion mechanisms and therapeutics targets

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Abstract

Background & Objectives

Metastasis accounts for the vast majority of cancer-related deaths, and circulating tumor cells (CTCs) play a pivotal role in this lethal process. Unfortunately, the vast majority of patients fail to respond to conventional immunotherapies due to relapse or immune evasion mechanisms that remain poorly understood. Moreover, CTCs exhibit poorly understood immune evasion mechanisms and may express phenotypes distinct from the primary tumor, potentially limiting treatment efficacy. These immune evasion mechanisms, such as PD-L1, CD47 or AXL, involve the recognition of proteins on the surface of CTCs by the various cells of the immune system. Identifying novel therapeutic targets on CTC surfaces is a critical challenge in oncology, given that over 66% of approved human drugs listed in the DrugBank database target surface proteins known as the “surfaceome”.

Methods

CTC lines developed by our group were cultured in RPMI 1640 supplemented with L-glutamine, ITS, EGF, FGF and 10% FBS at 37°C, 5% CO_2. HT-29 and SW620 colon cancer cell lines were maintained in DMEM (HT-29) or RPMI 1640 (SW620) with L-glutamine and 10% FBS. Once cells reached confluence, surface proteins were selectively isolated using hydrazide chemistry, followed by identification through liquid chromatography-mass spectrometry (LC-MS) analysis.

Results

Our preliminary analysis of the CTC surfaceome identified a unique set of membrane proteins, including immune evasion markers. Some of these proteins are already known therapeutic targets, while others could represent novel avenues for CTC-specific treatments. Future studies will expand this analysis to additional CTC lines and patient-derived samples to identify conserved markers of immune escape.

Conclusion

CTCs remain underexplored in the search for immune evasion mechanisms and therapeutic targets, largely due to their rarity and the difficulty of their isolation. By characterizing the CTC surfaceome, our study provides a new framework for identifying immune escape markers and therapeutic targets, paving the way for novel immuno-oncology strategies.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.