

Tumor Immune Microenvironment: A Holistic Approach Workshop

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Sox2 expression in NSCLC impairs tumor T cell infiltration and promotes resistance to checkpoint blockade therapy

Elen Torres, PhD Spranger Lab, MIT April 22, 2022



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Disclosure

• I have no financial disclosure or conflicts of interest to report.



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Checkpoint blockade therapy improves overall survival of NSCLC patients



Hellmann et al., NEJM, 2019



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The absence of tumor-infiltrating T cells is associated with unresponsiveness to CBT

Inflamed tumor



- Exhausted T cells
- Regulatory T cells
- Myeloid suppressors
- Expression of inhibitory factors by tumor cells



Based on Chen and Mellman, 2017



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Sox2 overexpression in NSCLC patients correlates with low T cell infiltration into the tumor





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T cells are excluded from Sox2-positive tumor regions in NSCLC patients



Hypothesis

In NSCLC, Sox2 overexpression acts as a tumor cellintrinsic mechanism to mediate T cell exclusion from the tumor microenvironment







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Sox2 overexpression in lung adenocarcinoma cells increases tumor growth and induces T cell exclusion from the tumor microenvironment





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Sox2 overexpression in tumor cells mediates resistance to checkpoint blockade therapy





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T cells fail to infiltrate Sox2-positive lung tumors



Currently working on studying the response to checkpoint blockade therapy in Sox2-positive lung tumors.



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Ex-vivo activated 2C T cells are recruited to the TME but failed to infiltrate Sox2-positive



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Sox2 expression in cancer cell induces changes in the extracellular matrix



<u>GO: cellular component – significantly upregulated genes</u>

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Sox2 expression in cancer cell induces changes in the extracellular matrix



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Sox2 overexpression in cancer cells may impair CD8 T cell trafficking from blood vessels to the tumor



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Summary



- Sox2 overexpression in lung cancer cells induces T cell exclusion from the tumor core.
- Extracellular matrix component are differentially upregulated in Sox2-positive tumors.
- Laminin 4 expression is increased in Sox2-positive tumors.
- Sox2-positive tumors have a higher vessel density, however, the size of the vessels is smaller.

BioRender.com

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