

Transcript Details

This is a transcript of an educational program. Details about the program and additional media formats for the program are accessible by visiting: <https://reachmd.com/programs/project-oncology/resistance-transformation-egfr-mutant-lung-cancer/39982/>

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Resistance and Transformation in EGFR-Mutant Lung Cancer

Announcer:

This is *Project Oncology* on ReachMD. On this episode, Dr. Triparna Sen will share new findings on immunosuppression during histologic transformation in EGFR-mutant lung adenocarcinoma, which she presented at the 2026 World Conference on Lung Cancer. Dr. Sen is the Max Morehouse Endowed Chair in Cancer Research and Associate Director of Research for the Division of Medical Oncology at The Ohio State University, as well as the Director of the Lung Cancer Preclinical Therapeutics Platform at The Ohio State University Comprehensive Cancer Center. Let's hear from her now.

Dr Sen:

The study that we are presenting at World Lung this year in Seoul is titled, "Multiomic Spatial Analysis That Reveals Immunosuppression During Therapy Resistance and Histological Transformation in EGFR-Mutant Lung Adenocarcinoma."

So when EGFR-mutant lung adenocarcinoma is treated with a tyrosine kinase inhibitor, we have seen that one of the significant ways by which patients become resistant to these drugs is by transformation to small cell lung cancer, which is one of the most aggressive forms of lung cancer. Our group has studied this phenomenon for quite a few years now, and we have proposed in a previous study what could be the molecular drivers and therapeutic targets for this process of resistance. It's actually a very important process to study because this kind of histological transformation is seen a lot in these EGFR-mutant tumors, which typically happens in never smoker, younger patients, and typically women. It's seen a lot in Asian populations, so it's a quite significant mechanism of resistance.

In our study, what we saw was that one of the typical pathways that was getting suppressed during this process of histological transformation was immunosuppression. So that prompted us to really study the immune pathways that were actually typically getting suppressed during this process of histological transformation. Our study focuses on multiomic spatial profiling. And what I mean by spatial profiling is we took matched samples pre- and post-transformation, so we were able to get matched tissues, and we performed Xenium-based spatial transcriptomics on the pre- and post-transformation samples with the corresponding annotated cells. And we were also able to perform Orion, which is a method of looking at immunofluorescence. So this is essentially looking at immunofluorescence proteomic analysis Orion-based platform. And we focused on the immune compartment on these and the area around the tissue, and we were able to capture what happens on the immune cells.

So what we were able to first see is that in the Xenium dataset, all the immune subsets were poorly represented in the post-transformation samples compared to the pre-transformation samples. So what I mean by that is that all the immune pathways were suppressed, so there was a global suppression of immune pathways. Particularly, we saw that CD8-positive T cells, which were the good, active T cells, were going down. But interestingly enough, there were certain percentages of immunosuppressive macrophages that were not good that were actually going up in the post-transformation samples.

So now, in our follow-up studies, we are actually performing more validation on a different population of these immunosuppressive macrophages that are emerging as these key regulators in the initiation process and the maintenance of this histological transformation. And we also believe that targeting these macrophage populations could represent a promising therapeutic strategy to prevent this process of histological transformation and support the development of combination approaches with EGFR TKIs in the high-risk patients who can develop this process of therapeutic resistance through transformation.

Announcer:

That was Dr. Triparna Sen discussing her research on therapeutic resistance in EGFR-mutant lung adenocarcinoma. To access this and other episodes in this series, visit *Project Oncology* on ReachMD.com, where you can Be Part of the Knowledge. Thanks for

listening!