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Title

Genomic and transcriptomic analyses of desmoid tumor reveals enrichment of transforming growth factor beta responsive signature

Presenter/Authors

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Abstract

Introduction: Desmoid tumor is a rare aggressive tumor where there is no satisfying systemic treatment. Previous studies showed increased expression of transforming growth factor-β (TGF-β) in the desmoid tumor. Here, we analyzed genomic and transcriptomic data of tumor samples from patients with desmoid tumor to evaluate therapeutic applicability of inhibition of TGF-β response.

Methods: We collected pre-treatment desmoid tumor samples from 31 patients in Yonsei cancer center, (YCC)-desmoid cohort and performed targeted next-generation sequencing and whole RNA sequencing. To compare the data with other cancer types, we used whole exome sequencing and whole RNA sequencing data from sarcoma patients from Yonsei Cancer Center (YCCsarcoma cohort, n = 17 and n =53, respectively) and The Cancer Genome Atlas (TCGA, n = 9,235). Transcriptomic data was normalized throughout the three cohorts to reduce batch effect. To evaluate the enrichment of TGF-β responsive signature (TBRS) in tumor and microenvironment, we calculated the mean expression values of fibroblast-TBRS (F-TBRS) from previous study.

Results: In the two sarcoma cohorts (YCC-desmoid and YCC-sarcoma cohorts), desmoid tumor samples had the highest F-TBRS score among the various types of sarcoma. When compared with other cancer types in TCGA, desmoid tumor samples showed the higher F-TBRS than all other cancer types except for pancreatic adenocarcinoma. In the desmoid tumor samples, *CTNNB1*, *GNAQ*, and *APC* mutations were the top 3 frequent mutations (23, 19, and 2 samples, respectively). In the merged two sarcoma cohorts, *CTNNB1*/*APC* mutation and *GNAQ* mutation were both associated with higher enrichment in F-TBRS ($p < 0.001$, respectively).

Conclusion: Desmoid tumors are enriched with expression of genes associated with TGF-β response of fibroblast compared with other cancer types including other sarcomas. In addition, *CTNNB1*, *APC* and

GNAQ mutations were associated with higher enrichment in TBRS. Therapeutic intervention to decrease the TGF-β response of fibroblast by using TGF-β receptor inhibitor may show clinical benefit in patients with desmoid tumors.