

Accepted Manuscript

Single-cell RNA sequencing reveals diverse intratumoral heterogeneities and gene signatures of two types of esophageal cancers

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PII: S0304-3835(18)30572-X

DOI: [10.1016/j.canlet.2018.09.017](https://doi.org/10.1016/j.canlet.2018.09.017)

Reference: CAN 14062

To appear in: *Cancer Letters*

Received Date: 30 May 2018

Revised Date: 7 August 2018

Accepted Date: 9 September 2018

Please cite this article as: H. Wu, J. Yu, Y. Li, Q. Hou, R. Zhou, N. Zhang, Z. Jing, M. Jiang, Z. Li, Y. Hua, F.C. Brunicardi, S. Wu, Single-cell RNA sequencing reveals diverse intratumoral heterogeneities and gene signatures of two types of esophageal cancers, *Cancer Letters* (2018), doi: <https://doi.org/10.1016/j.canlet.2018.09.017>.

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Abstract

Single-cell RNA sequencing and transcriptome analysis enable novel discovery and precise characterization of new cell types and states, which improves the understanding of the cellular context of tumorigenesis. Herein, we applied this powerful approach to analyze 368 single cells from three esophageal squamous cell carcinoma (ESCC) and two esophageal adenocarcinoma (EAC) tumors. Using inferred copy number variation analysis, we successfully distinguished carcinoma cells from heterogeneous cellular populations, identifying gene signatures and crucial cancer-related signaling pathways related to ESCC and EAC. In particular, we found that NOTCH signaling was exclusively activated in ESCC, but not in EAC. ESCC tumors with higher NOTCH activity were associated with significantly worse survival rates than those with lower NOTCH activity. Collectively, this study revealed that ESCC and EAC are distinct in terms of cellular transcriptome profiles, which leads to a wide range of intratumoral cellular heterogeneity. The findings suggest that different therapeutic strategies that target the differences between two types of esophageal cancers are required, guiding cancer-specific future drug development.

Keywords: Esophageal squamous cell carcinoma, esophageal adenocarcinoma, single-cell transcriptome sequencing, NOTCH signaling

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