Published OnlineFirst March 22, 2017; DOI: 10.1158/0008-5472.CAN-16-3440

Letter to the Editor

Cancer Research

EGFR-Dependent Regulated Intramembrane Proteolysis of EpCAM—Response

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We would like to thank Dr. Gires for the letter concerning our article (1). We are very glad that Dr. Gires considers our data on how EGFR activation affects endometrial cancer cell invasiveness via EpCAM activity novel and interesting. The study highlights not only the function of EpCAM as a cell adhesion molecule but also its transcriptional activity and the interplay of both functions on the invasiveness of endometrial cancer cells. Regarding the mechanism of EpCAM cleavage, we agree with Dr. Gires that using inhibitor of ADAM17 with and without EGFR inhibition would have provided additional detail on EpEX release. We understand the ectodomain shedding by α- and/or β-proteases is a prerequisite for the regulated intramembrane proteolysis of EpCAM (2, 3). As our studies have mainly focused on the transcriptional activity of EpICD, we have not pursued experiments to inhibit ADAMs and TACE. Future studies using these inhibitors will shed light on the mechanisms underlying the shedding of EpEX.

In conclusion, we would like to clarify here, based on our data, that EpICD release mediated by EGFR activation may depend on γ-secretase activity; however, additional studies beyond the scope of this article are needed to dissect the mechanisms underlying the release of EpEX by EGFR.

Disclosure of Potential Conflicts of Interest

No potential conflicts of interest were disclosed.

Received December 16, 2016; accepted December 20, 2016; published OnlineFirst March 22, 2017.

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doi: 10.1158/0008-5472.CAN-16-3440

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Cancer Research
The Journal of Cancer Research (1916–1930) | The American Journal of Cancer (1931–1940)

AACR American Association for Cancer Research

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Cancer Res 2017;77:1777. Published OnlineFirst March 22, 2017.