Title: Tertiary lymphoid structures are associated with higher tumor grade in primary operable breast cancer patients.

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Author's response to reviews: see over
Dear Editor,

Please find enclosed our manuscript entitled: “Tertiary lymphoid structures are associated with higher tumor grade in primary operable breast cancer patients”.

The topic for this study is tertiary lymphoid structures (TLS) formation in breast carcinoma and its association with clinicopathological factors. The background for our study is the described phenomenon of lymphoid neogenesis in developing tumors and the postulated involvement of TLS in locally generated antitumoral responses. TLS that develop within the tumor resemble immune cell organization and function of conventional secondary lymphoid organs.

This is, to our knowledge, the first time the characterization of TLS has been described in a larger series of cancer patients. In the present manuscript we show that the intra- and peritumoral TLS formation was associated with higher levels of immune cell infiltration, organized immune cell aggregates and hormone receptor status. The major finding of this study demonstrated that TLS was associated with histological grade 3 tumors which are known to be the most aggressive types and with worst patients’ prognosis.

Taken together, this study shows that TLS are frequently observed in primary operable breast tumors that highlights the importance of defining the immune cell contexture in developing tumors. Hence, this may provide new insight in the host immune response against tumors that could hopefully result in more advanced targeted therapies and improvement of patients’ clinical outcome.

This manuscript has previously been submitted to Breast Cancer Research, but was not accepted for publication. All authors have contributed to the manuscript as defined in the instructions, read the manuscript and the submission to Breast Cancer Research is approved by all authors. There are no financial, personal or professional competing interests from our side that have influenced the construction of the manuscript. We therefore declare no conflict of interests.
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