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# Letter to the Editor

# Reply to Rosen

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**To the Editor:** We read with interest the comments of Dr Rosen regarding our study of the genetic analysis of microglandular adenosis and acinic cell carcinoma,[1] and would like to acknowledge his pioneering work on microglandular adenosis and carcinoma arising in microglandular adenosis.[2,3] Dr Rosen and colleagues provided histologic evidence consistent with the notion that acinic cell carcinomas of the breast constitute invasive carcinomas with acinic cell differentiation arising in microglandular adenosis. Our studies[4,5] were the first to employ massively parallel sequencing to decipher the molecular profiles of these lesions and to provide molecular evidence to support the histologic observations made by Dr Rosen and colleagues.

Our group has employed a combination of histologic analysis and massively parallel sequencing to study rare forms of breast cancers and their potential precursors.[6] We have demonstrated the existence of low-grade forms of triple-negative breast cancer, which differ from the common high-grade forms of the disease on the basis of unique molecular profiles (e.g. breast adenoid cystic carcinomas often being underpinned by *MYB-NFIB* fusion genes) and better outcomes.[6] We have also demonstrated that pure microglandular adenosis, microglandular adenosis associated with carcinoma, and carcinoma with acinic cell differentiation harbor somatic *TP53* mutations and/or similar patterns of gene copy number alterations,[4,5] supporting the notion that these lesions share the same driver genetic alterations and constitute a family of closely related neoplastic lesions.[1] We fully acknowledge the importance of the morphological similarities and coexistence of these lesions as demonstrated by Rosen and colleagues in their studies of microglandular adenosis and carcinomas arising from it,[2,3,7] but caution that morphology alone is insufficient to demonstrate histogenesis, clonal relatedness and molecular evolution, given that morphologically similar tumors may show different genomic profiles and *vice versa*.[8] In the study cited in his letter[9] that applied chromosomal comparative genomic hybridization to a series of microglandular adenosis and associated lesions, the associated carcinomas were invasive ductal carcinomas rather than acinic cell carcinomas, and the authors reported clonal relatedness between synchronous microglandular adenosis, atypical microglandular adenosis, and/or carcinoma arising in microglandular adenosis but only in a single case.[9] Importantly, our study[1] represents a genomic comparison between microglandular adenosis and acinic cell carcinomas with other triple-negative breast cancers as well as with breast carcinomas of estrogen receptor-positive and/or HER2-positive phenotype.

Therefore, our findings provide strong molecular evidence to support the contention that microglandular adenosis and acinic cell carcinoma of the breast are part of the same spectrum of lesions that appear to represent low-grade forms of triple-negative disease with indolent behavior. We would contend that our findings also provide genetic evidence to support and expand rather than contradict the prior astute morphological observations of Dr Rosen and colleagues.[2,3,7] Further studies, however, are still required to define the molecular basis of the acinic cell features in breast cancers.

## Disclosure/conflict of interest

The authors declare no conflict of interest.

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