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Correspondence

The Baader–Meinhof phenomenon in ductal carcinoma *in situ* of the breast

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Sir: We read with interest the review of Pang *et al.* published in the annual review issue of *Histopathology* in January 2016, entitled 'Ductal carcinoma *in situ*—update on risk assessment and management', wherein a concise overview of the diagnosis and present management of ductal carcinoma *in situ* (DCIS) is provided, as well as a comprehensive summary of the histopathological assessment and currently available prognostic markers.[1] We are aware that an extensive overview of the potential role of the tumour microenvironment in breast cancer progression was beyond the scope of this review. Nevertheless, we would like to draw attention to Figure 1 in the article of Pang *et al.*, wherein microphotographs of a low-grade and a high-grade DCIS lesion are shown.[1] The accompanying figure legend points out the differences between the size and features of the nuclei, but another remarkable morphological characteristic is strikingly overlooked: the low-grade lesion is surrounded by a dense sclerotic stroma, whereas the high-grade lesion is surrounded by an aberrant stroma that consists of loosely arranged collagen fibres interspersed with an amorphous, slightly basophilic substance.[1] We previously described this architectural change of the periductal stroma in DCIS, and designated this phenomenon as 'myxoid' stroma (Figure 1).[2] In another review on current concepts in DCIS, a similar omission of periductal stroma is observed, despite its overt presence in a photograph of high-grade DCIS.[3] Similarly, Shatat *et al.* did not comment on the presence of extensive myxoid stroma in their series of microinvasive carcinomas, whereas Figure 1 in their article shows a nice illustration of myxoid periductal stroma in both DCIS and microinvasive carcinoma.[4]

Wernicke *et al.* were probably the first to describe myxoid stromal changes in invasive breast cancer,

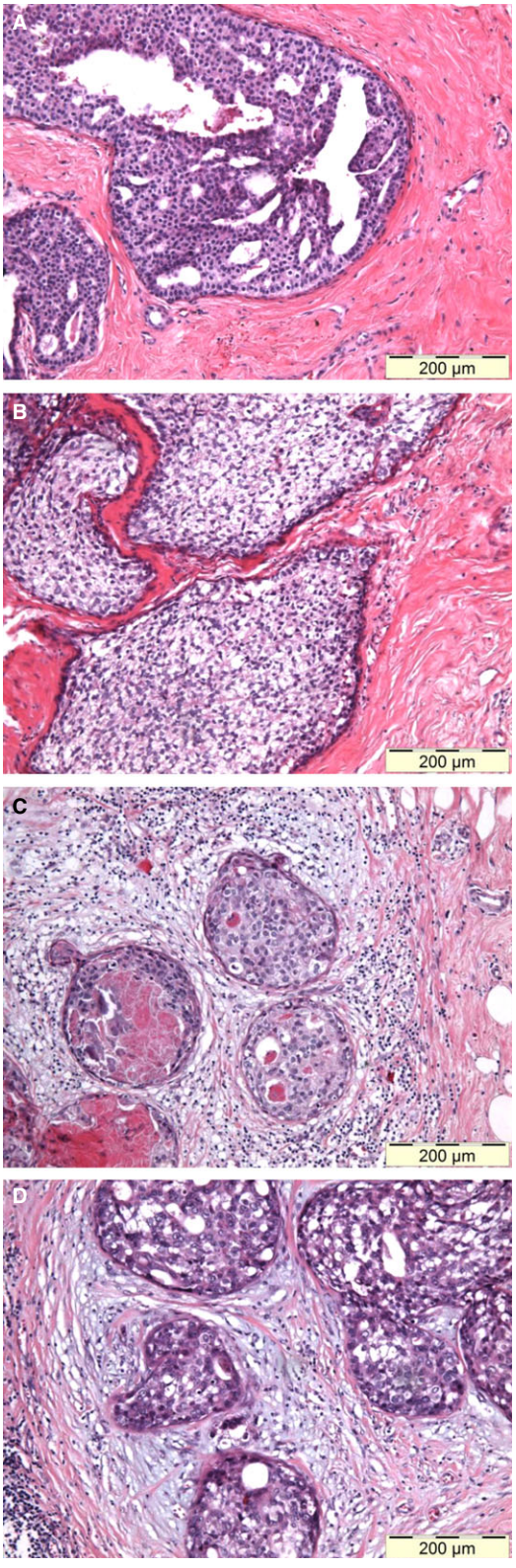

Figure 1. Microphotographs of two ductal carcinoma *in situ* (DCIS) lesions with predominantly sclerotic periductal stroma (**A**,**B**) and two DCIS lesions with predominantly myxoid periductal stroma (**C**,**D**).

and they observed a significant association between the presence of myxoid stroma and lymph node involvement.[5] To our knowledge, no other studies on myxoid stroma in breast cancer have been reported yet.

We previously observed that myxoid periductal stroma in DCIS was associated with an increased overall recurrence risk, and with an increased risk of invasive recurrence in particular.[2] The presence of myxoid stroma was associated with reduced periductal decorin expression.[2] Although these observations require validation on larger, independent patient cohorts, we hypothesize that this myxoid architecture might mirror an invasion-permissive microenvironment. We speculate that the normal breast stroma functions as a protective barrier against invasion, and that its remodelling is likely to enable invasion. Some preinvasive lesions are able to influence neighbouring fibroblasts in order to modulate the composition of their surrounding extracellular matrix.[2] Future translational studies should aim at targeting these adverse stromal changes, in order to prevent or disrupt the process of cancer cell invasion.

In summary, we noticed the regular appearance of several photographs of DCIS with myxoid periductal stroma in both original reports and review articles, after we described myxoid stromal changes in DCIS. In psychology, such a phenomenon is referred to as 'selective attention bias' or 'frequency illusion', which is better known as the 'Baader–Meinhof phenomenon' in popular literature.[6] Remarkably, myxoid stroma is generally overlooked by authors who publish photographs of DCIS: myxoid stroma is often overtly present, but, as the authors had not yet learned about it, they did not perceive it. In a certain way, this is a kind of cognitive bias as well.

We hope that this letter will lead to the acknowledgement of the existence and potential importance of myxoid stroma in DCIS by other researchers and experts in this field, including the authors of the aforementioned articles. Subsequently, this might stimulate researchers to include assessment of stromal features in future studies on DCIS, especially in large ongoing trials such as NSABP B-43, the LORD trial, and the LORIS trial. If such investigations lead to the validation of our findings regarding its prognostic value, myxoid stroma might become part of standard reporting on DCIS in daily histopathological practice.

Conflicts of interest

The authors state that they have no conflicts of interest.

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Reply to the Baader–Meinhof phenomenon in ductal carcinoma *in situ* of the breast

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Sir: We thank Van Bockstal *et al.*[1] for their letter, entitled 'The Baader–Meinhof phenomenon in ductal carcinoma *in situ* of the breast', in response to our review 'Ductal carcinoma *in situ*—update on risk assessment and management'.[2] Van Bockstal *et al.*[1] raise the issue of the often ignored ductal carcinoma *in situ* (DCIS) microenvironment, in particular myxoid-appearing stroma, and its role in modulating disease outcome in DCIS.

As Van Bockstal *et al.*[1] acknowledge, detailed appraisal of the prognostic significance of the DCIS