Spontaneous Corneal Neovascularization in Nude Mice

To the Editor:

We would like to congratulate Drs. Kaminska and Niederkorn for an excellent description of spontaneously occurring corneal neovascularization in BALB/c mice. We have also noted that many BALB/c mice have had spontaneously occurring corneal neovascularization (unpublished observations). As we read the article, one piece of information that we did not note was a detailed description of the histopathologic findings in the transplanted vascularized corneas. A description of the histopathology of the spontaneously vascularized corneas was included in the Discussion section. We were wondering if the authors could comment on how much inflammation (and what type) was noted in the transplanted corneas. As the authors are aware, the role of acute and chronic inflammation in the pathogenesis of corneal neovascularization is being actively investigated, and we are certain that their observations would provide useful information in this regard. Finally, we were wondering if the authors could speculate on any possible relationship between the neovascularization that they observed in the BALB/c mice and that which we have previously reported in DBA mice. We were somewhat surprised to find that spontaneously occurring neovascularization in DBA mice appeared to be associated with an irido-corneal endotheliopathy.

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References


The authors reply:

We appreciate the comments and insights offered by Drs. Epstein and Stulting regarding their observations on spontaneous neovascularization in corneas of DBA/2 and BALB/c mice. Although we occasionally discern spontaneous corneal neovascularization in normal euthymic BALB/c mice, the incidence in our experience is quite rare. By contrast, we have consistently observed spontaneous corneal neovascularization in the overwhelming majority of euthymic hairless mice and athymic BALB/c nude mice. We wish to also emphasize that although these two mouse strains share the hairless phenotype, they originated from entirely different genetic stock. We feel that the hairless phenotype, not the BALB/c background, influences the development of corneal neovascularization.

As we mentioned in the Discussion section of our manuscript, the possible role of chronic inflammation in the spontaneous neovascularization in the nude mouse cornea remains unanswered. Although we are attracted to the explanation that persistent inflammation contributes to this neovascularization, we are reluctant to make this a definitive conclusion because some corneas contain numerous PMNs yet are free of corneal vessels, whereas other corneas contain extensive vessels but are free of PMNs.

In our studies on the orthotopic transplantation of BALB/c nude mouse corneas to syngeneic euthymic BALB/c recipients, we did not examine the corneal grafts at the histologic level. These grafts were followed clinically for two months. Our initial interests focused on the long-term behavior and fate of the blood vessels in the graft. Thus, it was not feasible to perform time course histologic analyses of these grafts. Although we agree that it would be of interest to examine the grafts for the presence of inflammatory cells, we suspect that interpreting such findings would be extremely difficult based on the previously mentioned inconsistent association between PMN infiltration and corneal neovascularization.

We are familiar with Drs. Epstein and Stulting’s previous report on the occurrence of spontaneous corneal neovascularization in DBA/2 mice. The neovascularization that occurs in DBA/2 mice offers an interesting contrast to that which occurs in hairless euthymic mice and athymic BALB/c mice and suggests that different angiogenic/pathogenic stimuli are involved. No signs of ocular inflammation were observed in any of the DBA/2 mice displaying corneal neovascularization, whereas a large number of nude and hairless mice display corneal inflammatory cell infiltration. Moreover, neovascularization occurred primarily in DBA/2 mice expressing large corneal opacities. By contrast, we did not observe similar corneal opacities or irido-corneal endotheliopathies in either nude or hairless mice.

We appreciate the comments offered by Drs. Epstein and Stulting and feel that they have brought an important issue to the attention of corneal angiogenesis researchers. It is clear that spontaneous vascularization of the cornea can occur under a variety of conditions in genetically different mouse strains. The observation that spontaneous corneal vascularization in the DBA/2 mouse can occur in the absence of inflammation but in close association with corneal opacities may provide important insights into corneal angiogenesis. We think the use of these and other mouse strains displaying spontaneous angiogenesis may shed light on the complex processes involved in corneal neovascularization.

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References