Reply to: "Lack of specificity of cytokeratin-15 loss in scarring alopecias"

To the Editor: We read with great interest the letter by Mahalingam[1] supporting our published findings concerning the lack of specificity of loss of cytokeratin-15 (CK15) in affected follicles in cicatricial (scarring) alopecia.[2] Because of the limited authorized number of references in research letters in the *Journal*, we were unable to cite the multiple relevant publications, including the 2 studies authored by Pozdnyakova and Mahalingam[3] and Hoang et al.[4] It is nowadays obvious that bulge stem cell exhaustion cannot have any discriminating value in lymphocytic cicatricial alopecias because isthmic outer root sheath injury is nonspecifically seen in lichen planopilaris, frontal fibrosing alopecia, lupus erythematosus, and central centrifugal cicatricial alopecia. Neutrophil-poor folliculitis decalvans could be added to the aforementioned differential diagnosis. Use of this immunostain in the so-called "neutrophilic" cicatricial alopecia is without interest because the inflammatory infiltrate in dissecting cellulitis is deeper than in folliculitis decalvans and does not affect the follicular isthmus. We also find it pointless to further explore CK15 in biphasic alopecias (eg, chronic traction alopecia, pattern hair loss, chronic alopecia areata, and nonscarring alopecia of systemic lupus erythematosus) because in these disorders permanent follicular dropout results from follicular stem cell exhaustion. CK15 loss would also be seen after direct toxicity on the follicular stem cells, as seen in permanent alopecia after chemotherapy.[5] For the above reasons, further debate on this topic is useless; our focus should no longer be whether follicular bulge stem cells are preserved on not, but why they are lost.

Expanding knowledge on hair follicle immunology stresses our need to step away from the conventional North American Hair Research classification of scarring alopecia based on the nature of the inflammatory infiltrate.[6] Lichen planopilaris and the related frontal fibrosing alopecia can clearly be regarded as follicular bulge immune privilege (IP) collapse disorders. The bulge is a target for an interferon-gamma–induced immune injury, similarly to the anagen hair bulb IP collapse seen in alopecia areata.[7,8] Studying the follicular suppression of major histocompatibility complex class I antigens, the accumulation of no danger signals (such as CD200) and the accumulation of IP guardians could contribute to better delineate the spectrum of follicular bulge IP collapse disorders, as well as positioning fibrosing alopecia in a pattern distribution and central centrifugal cicatricial alopecia in this spectrum. Current knowledge has also revealed the coexistence of the activated hair germ cells engaging in the follicular growth and the quiescent bulge stem cells maintaining the long-term stem cell pool. The follicular stem cell and dermal papilla niche interdependency has also shifted our attention from the former to the critical role of the latter.[9] We wish that our research letter would be considered as concluding remark concerning the limited value of bulge stem cell marker immunostaining and a challenge to the researchers to focus their interest on hair follicle immunology and follicular cell kinetics.

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