

Lack of specificity of cytokeratin-15 loss in scarring alopecias



To the Editor: A recent letter by Kolivras et al¹ ascertains whether the loss of cytokeratin-15 (CK15) is specific for lichen planopilaris (LPP) by assessing CK15 expression in 19 cases of LPP, 9 cases of frontal fibrosing alopecia, and 7 cases of alopecic lupus erythematosus (LE). The authors find a loss of CK15 in affected follicles in all 3 entities and recommend exploring CK15 expression in other scarring alopecias, such as central centrifugal cicatricial alopecia and folliculitis decalvans. Expression of CK15 in these entities and those in the original letter has, however, been previously ascertained in earlier studies, and while this letter references some of them,²⁻⁴ it is notable for omission of 2 key early references, which is the reason for our letter.^{5,6}

In the first, involvement of the bulge region was studied by assessing the expression of CK15 in scarring alopecias of diverse etiopathogenesis (eg, LPP, LE, central centrifugal cicatricial alopecia, and traction and dissecting cellulitis).⁵ The authors observed a loss of CK15 in 8 of 16 cases, all of which were characterized by a moderate to dense perifollicular inflammatory infiltrate. Based on this, the authors proposed involvement of the bulge region in early/active stages of primary scarring alopecia. In the second, also a study on scarring alopecias of

diverse etiopathogenesis (eg, LPP, LE, folliculitis decalvans, dissecting cellulitis, and traction and end-stage scarring alopecia), CK15 loss was observed in 20 of 43 cases.⁶

In the epidermis, keratinocytes in the basal cell layer express keratins 5 and 14, while keratins 1 and 10 are expressed by cells in the suprabasal layer.⁷ The hair follicle expresses both these and other keratins (ie, keratins 6, 16, and 17). Restriction of CK15 expression to cells of the bulge region of murine and human hair follicles has led some to suggest that CK15 is a specific stem cell marker.⁷ Contradicting this, we have previously noted that CK15 expression is not merely restricted to the bulge, but also involves part or all of the outermost layer of the outer root sheath of the human hair follicle, the basal layer of the epidermis, and secretory cells of the eccrine glands.⁶ Based on its expression in the mitotically active basal cell layers of the hair follicle, it is believed that CK15 may play a role in regulating an early stage of keratinocyte differentiation and one that actually predates the fate of a cell becoming epidermal or hair-like.⁷

Since CK15-positive cells possess stem cell characteristics of multipotency and a high proliferative potential,⁸ it seems reasonable to hypothesize that any insult (internal or external) to these cells will result in destruction of the follicle and clinically manifest as alopecia. Given this, the conclusions made by Kolivras et al, although neither novel or

Table I. Chronologic literature overview of studies on cytokeratin-15 in scarring alopecias

Reference	Scarring alopecias studied	Conclusions
Pozdnyakova and Mahalingam, ⁵ 2008	16 cases of scarring alopecia (8 LPP, 4 CCCA, 1 LE, 2 traction, and 1 dissecting cellulitis)	Paucity of CK15-positive cells in cases with a moderate to heavy peribulbar inflammatory infiltrate; the bulge region is a target in "active" scarring alopecia
Hoang et al, ⁶ 2009	43 cases of scarring alopecia (12 LE, 11 LPP, 7 FD, 5 end-stage, 3 CCCA; 3 traction; and 2 dissecting cellulitis)	CK15 expression lost in 47% of cases; the bulge region is a target in scarring alopecia
Al-Refu et al, ³ 2009	46 cases of cases of scarring alopecia (36 DLE, 10 SCLE)	CK15 expression alters with density of inflammation: normal/moderate expression in cases with a mild/moderate inflammatory infiltrate; absent/weak expression in cases with dense inflammation
Sperling et al, ⁴ 2011	23 cases of scarring alopecia (all CCCA)	Loss of CK15 expression is not specific for cicatricial alopecia
Habashi-Daniel et al, ² 2014	55 cases of scarring alopecia (all LPP)	Damaged follicles that have lost CK15-positive stem cells disappear when they enter catagen
Kolivras et al, ¹ 2016	35 cases of scarring alopecia (19 LPP, 9 FFA, and 7 LE)	Loss of CK15 expression found in all 3 entities; CK15 loss is not specific for cicatricial alopecia

CCCA, Central centrifugal cicatricial alopecia; CK15, cytokeratin-15; DLE, discoid lupus erythematosus; FD, folliculitis decalvans; FFA, frontal fibrosing alopecia; LE, lupus erythematosus; LPP, lichen planopilaris; SCLE, subacute lupus erythematosus.

surprising, are supportive of previous research (summarized in Table I).

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