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### Possible mechanisms mediating complete regrowth of hair following scalp tattooing in alopecia universalis



*To the Editor:* Ramnot et al<sup>1</sup> recently described a fascinating case of the complete regrowth of hair following scalp tattooing in a patient with alopecia universalis unresponsive to previous treatment (local and systemic glucocorticoids, squaric acid dibutyl ester immunotherapy) despite high compliance. The causality between scalp tattooing and alopecia regression cannot be determined with certainty; however, the timeline of events, location, and size of the observed effect suggest that the regrowth of hair might have been triggered by tattoo ink and/or the process of tattooing via unknown mechanisms. This letter aims to propose possible mechanisms by which the process of tattooing and the presence of tattoo ink might promote hair growth in alopecia.

In the process of tattooing, insoluble pigments are deposited into the dermal skin layer with a specialized needle where they are either engulfed by dermal macrophages<sup>2</sup> or transported to the draining lymph nodes.<sup>3,4</sup> Tattooing is inherently traumatic as the skin is repeatedly punctured with multiple closely spaced needles which disrupt the epidermal basement membrane and damage epidermal and dermal cells that consequently undergo necrosis.<sup>4</sup> Traumatic injury of tattooed skin has the potential to activate hair follicles as physiological mechanisms regulating wound healing and hair growth are highly intertwined.<sup>5</sup> The aforementioned is considered to be the underlying principle of microneedling that has shown some promising effects on the skin,<sup>6</sup> as well as on hair loss.<sup>7-10</sup> Accumulating evidence show that hair follicles are involved in wound healing, and that wounding promotes the transition of follicles to the anagen phase, possibly by activating Wnt/ $\beta$ -catenin signaling and promoting follicle (re)vascularization by stimulating vascular endothelial growth factor.<sup>11-13</sup>

Tattooing-induced hair growth may also be mediated by the effects of bioactive components of tattoo inks (organic or inorganic pigments, binders, solvents, additives, impurities, and microorganisms<sup>14-16</sup>) on hair follicles and/or alopecia-associated pathophysiological processes (eg, autoimmunity,<sup>17-19</sup>

oxidative stress<sup>20,21</sup>). The direct effects of tattoo ink components on hair follicles are unexplored; however, there are several reports of henna (surface) tattoo-induced hypertrichosis.<sup>22</sup> Furthermore, some tattoo inks demonstrate immunomodulatory and antioxidant properties. Functional consequences of sequestration of tattoo ink pigments in dermal macrophages are still unexplored,<sup>2</sup> however, Devcic et al recently reported that tattoo ink pigment-exposed macrophages secrete less interleukin 6, tumor necrosis factor, and chemoattractant cytokines (monocyte chemoattractant protein-1, macrophage inflammatory protein-1 $\alpha$ ) after stimulation with lipopolysaccharide, suggesting that tattoo pigments might act as immunosuppressants.<sup>23</sup> Polycyclic aromatic hydrocarbons, often found in black tattoo inks,<sup>24</sup> have been proposed as mediators of the immunomodulatory effects of crude coal tar used in the treatment of psoriasis.<sup>25</sup> An N-of-1 study reported antioxidant properties of a blue tattoo in vivo<sup>26</sup> and an in vitro study reported that copper phthalocyanine-containing blue tattoo ink demonstrates catalase and superoxide dismutase mimetic properties.<sup>15</sup> The aforementioned results suggest that some tattoo ink constituents might theoretically promote hair growth by inhibiting etiopathogenetic factors of alopecia (inflammation and oxidative stress).

To conclude, the reported tattoo-induced regrowth of hair growth might be explained by stimulation of the transition of hair follicles to the anagen phase by the process of tattooing (by stimulating wound healing mechanisms) and/or immunomodulatory and antioxidant properties of some tattoo ink constituents.

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**Conflicts of interest**

None disclosed.

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