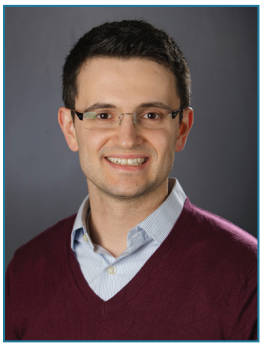

Hair Sciences

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Sandalwood Demonstrated to Promote Human Hair Growth through Olfactory Receptors Present on the Hair Follicle

In their September 2018 publication in Nature Communications, Cheret and colleagues showed that a synthetic sandalwood odorant stimulated the olfactory receptor OR2AT4 located in the outer root sheath of the hair follicle to promote human hair growth *ex vivo*.[1]

BACKGROUND

Our smell sensation results from molecules called odorants interacting with olfactory receptors. This results in signals being sent to our brain that we interpret as our sense of smell. Olfactory receptors (ORs) have physiological functions in the body that extend beyond smell sensations and have been found in spermatozoa and in the gastrointestinal system.[2,3] In fact, several olfactory receptors, including OR2AT4, are present in the human epidermis. Selective activation of OR2AT4 by synthetic sandalwood odorant (Sandalore®) promoted keratinocyte migration *in vivo* and wound re-epithelialization *ex vivo*.[4] Given the connection between wound healing and hair growth, the authors hypothesized that ORs may have a role in hair growth. Study techniques and key findings:

1. Using immunofluorescence, qRT-PCR (polymerase chain reaction), and western blots, the authors demonstrated that OR2AT4 was expressed in human hair follicles (HFs). Specifically, it was expressed predominantly in the suprabulbar keratinocytes of the outer root sheath (ORS) in the anagen (V1) stage of the hair cycle.
2. Treatment of organ cultured human HFs in vitro with the selective OR2AT4 agonist Sandalore inhibited catagen development and reduced hair matrix keratinocyte apoptosis. These effects were shown to be specific to OR2AT4 since they were partially counteracted by the co-administration of the OR2AT4 antagonist Phenirat. Also, si-RNA (si = small interfering) knockdown of OR2AT4 in the presence of Sandalore promoted catagen induction and hair matrix keratinocyte apoptosis, further supporting that Sandalore's effects are specific to OR2AT4 activation.
3. The authors examined the effects of Sandalore on two key growth factors that control the anagen-catagen transformation during human HF cycling: catagen-promoting TGF-β2 and anagen-maintaining IGF-1. Sandalore treatment resulted in a decrease in TGF-β2 and an increase in IGF-1 in the proximal ORS.
4. Using microarray analysis, the authors showed that Sandalore promotes anti-apoptotic genes while down-regulating pro-apoptotic genes in HFs. Sandalore promoted the IGF-1 pathway as well as another anagen promoting growth factor, FGF-7.
5. The authors tested the hypothesis that the anagen promoting effects of Sandalore are mediated through IGF-1-related signaling in the HF. While the IGF-1 neutralizing antibody promoted catagen, the co-administration of Sandalore with this IGF-1 neutralizing antibody reversed the catagen promoting effects of the antibody alone.

Collectively, the data presented in this publication showed that human HFs have an olfactory receptor that is important to sustain HF growth. The synthetic agonist of the HF olfactory receptor, Sandalore, promotes anagen. It does so by suppressing catagen and HF apoptosis through the upregulation of IGF-1. So, in effect, HFs have evolved to employ a proverbial sense of "smell" in the fact that they are responsive to the stimulation of an olfactory receptor, OR2AT4. While Sandalore is a synthetic OR2AT4 receptor, we currently do not know the identity of endogenous OR2AT4 agonists. The authors suspect these endogenous agonists may be molecules with a Sandalore-like structure such as short-chain fatty acids and metabolites of HF microbiota. While in vivo and clinical data are necessary prior to making assumptions about the clinical effects of Sandalore on androgenetic alopecia, these results may form a foundation on which further investigation will take place.

References

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