

# Sandalwood as hair tonic

**Hair roots may share a sense of smell with the outer layer of the skin**

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The skin is the largest organ in the body. Adults have about 3.5 kilograms of skin, and 20 square feet of it. Skin is the body's waterproof cover, an insulator that guards the body against extreme heat and cold, water loss, the harmful part of sunlight and damage by chemicals. It produces antibacterial substances that save us from infection and it generates Vitamin D, which enables absorption of calcium for healthy bones.

It is also the body's communication centre. The skin has nerve tissues that tell the brain about the environment — hot and cold — and a sense of touch that can make out shapes and surfaces, with such sensitivity that it all but replaces the sense of sight in the sightless. The nerve endings on the tongue and in the nose also detect and convey information about chemicals in the environment. And then, skin is flexible, for it can bend and stretch, and it repairs itself if damaged.

Jérémy Chéret, Marta Bertolini, Leslie Ponce, Janin Lehmann, Teresa Tsai, Majid Alam, Hanns Hatt and Ralf Paus, from industry and the university at Münster, Germany, Ruhr-University and Universities of Manchester and Miami write in the journal, *Nature Communications* about the multiple roles of the hair that grows on skin. While hair, which is present on all parts of the skin, protects it and helps to sense touch or movement, it is also a powerful initiator of healing when the skin is injured.

And a further finding that the group reports is that the olfactory faculty, or the capacity to detect chemicals in the air, is not confined to the nose, it appears to be there over most of the skin too. But a remarkable discovery the group reports is that a synthetic sandalwood odorant (sadly, not the natural sandalwood) promotes the action of hair follicles both in wound healing and in promoting the growth of hair! The paper first recounts the ample records there are of the role of



hair follicles in the repair of tissue when damaged by injury or after surgery. The earliest and most comprehensive study of the subject may be the 1945 report by Dr G H Bishop of Washington University, St Louis. Dr Bishop inflicted skin wounds, at different tissue depths, on his own forearm, and recorded the progress of healing. He found that the presence of hair follicles was the main skin structure that affected the pace of healing.

Dr Bishop reported that fresh skin begins to grow around the remaining hair follicles and the edge of the damaged skin. And scar tissue forms only if the injury is so deep in the inner layer of the dermis (see picture) that the base of the hair follicles are destroyed.

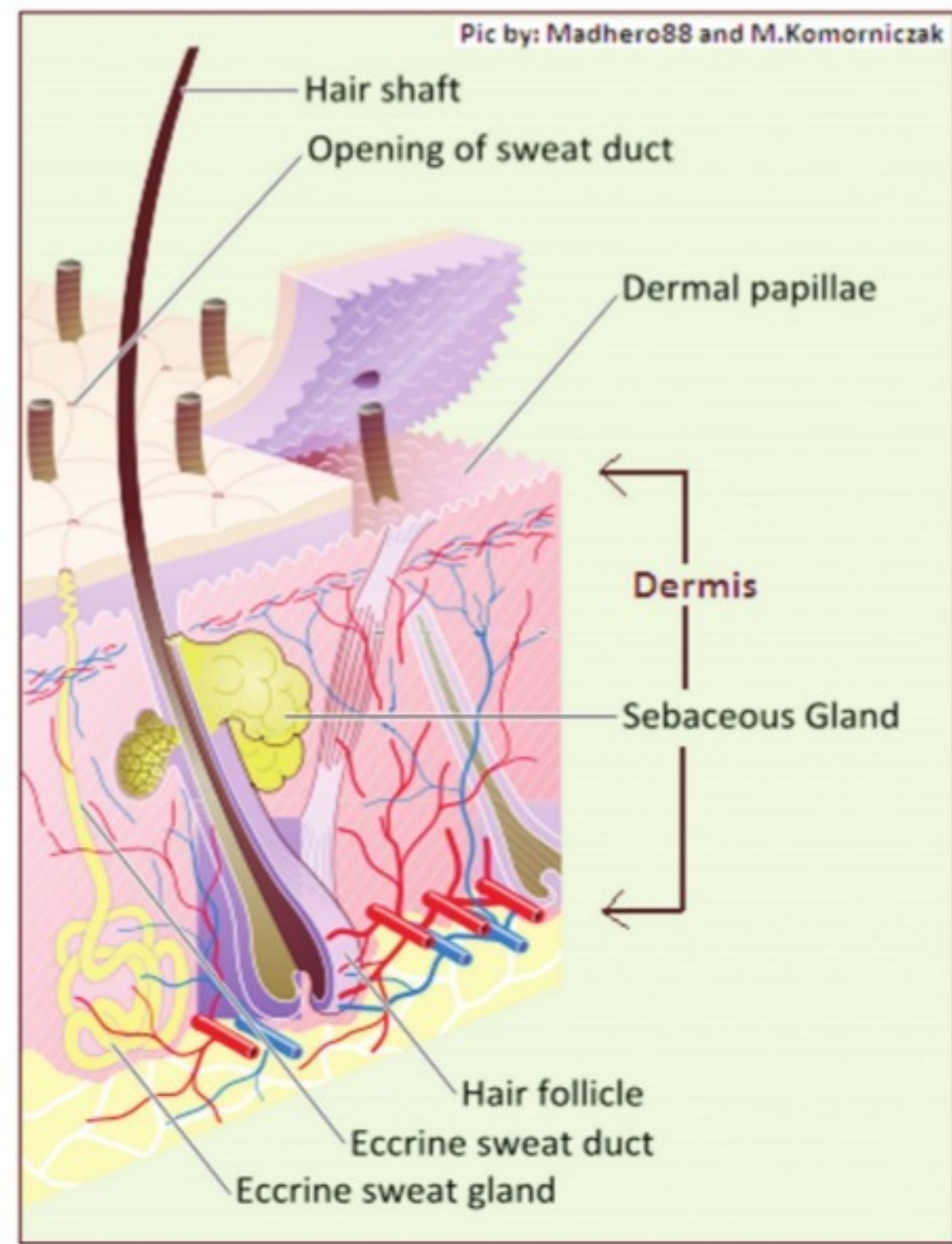
A clear demonstration of the utility of hair follicles in wound healing is the fact that wounds in areas that abound in hair follicles, like the scalp, heal rapidly. Wounds in areas that lack hair follicles, like the palm of the hands, take longer. When skin grafts are done, it is known that the healing time is five to six days if the source of the graft was the scalp, against 10 to 14 days if the source was the thighs or abdomen.

But coming back to detection of chemicals, it is on record that humans can distinguish over a trillion different odours. *The Nature Communications* paper, however, says that "olfactory reception" is a chemo-sensory signalling system of great evolution-

ary antiquity, which predates the development of smell sensation. Olfactory receptors, the cellular structures that sense chemicals, are hence not restricted to the nose but are present in other tissues as well. Non-smell roles of these receptors in such tissue have also been studied, the paper says.

Several of such receptors, called "ORs", are also there in the outer layer skin tissue, the paper says. Among them is OR2AT4, which, when activated, promotes the migration of cells that produce keratin, the material of the skin. This OR has been now found to be expressed by the hair follicles. It is otherwise well known that the hair follicle is a reservoir of stem cells, which can differentiate into other types of cells. Stem play their greatest role in the developing embryo for the formation of different organs. They are, however, needed throughout life, for normal regeneration of tissue and for repair. The recorded effect of the presence of hair follicles in promoting wound healing is hence, apparently, as a result of stem cells playing a role.

What *The Nature Communications* paper points out is that a commercial, synthetic preparation, Sandalore®, which has an odour similar to sandalwood, has been found to promote the activity of the olfactory receptor, OR2AT4. Faster migration of skin cells has been observed in the lab, and better progress of actual healing of



wounds, the paper says. That OR2AT4 is the substance involved has been confirmed by adding Phenirat®, a known antagonist of OR2AT4. Sandalore®, induced activity in cells with OR2AT4 was to be blocked by Phenirat®.

Given the association of the presence of hair follicles with wound healing, the authors of the paper surmised that OR2AT4 may also impact hair growth. It was then seen that activation of OR2AT4 by Sandalore® prolongs the active growth phase of hair follicles, during which the root of the hair is dividing rapidly, adding about one centimetre to the hair shaft every 28 days. This action appears to arise by decreasing the pace of death cells that create keratin, through increasing the production of a growth stimulating

hormone in the outer root sheath. Conversely, when OR2AT4 was suppressed, it was seen that Sandalore® did not have the growth promoting effect, which shows that the effect of Sandalore® is specific to OR2AT4.

The conclusion of the exercise, the paper says, is that "hair follicles are able to 'smell' in the sense that they recruit the evolutionarily oldest and largest of all receptor families (the olfactory system) for regulating key organ functions". The study, in any case, holds out a tantalising hope that Sandalore®, a preparation that is used in perfumes, moisturisers and cleansing agents, could find application to help hair growth!

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PLUS POINTS

## Death by plastic



Baby sea turtles are particularly vulnerable to the harmful effects of plastic pollution, according to a new study, which found around half of the recently hatched reptiles had stomachs full of plastic.

In recent years, scientists have realised that animals ranging from plankton to whales are regularly consuming plastic, since around 10 million tons of it ends up in the sea every year.

Turtles were some of the first creatures ever observed consuming plastic, with reports of bags being found in their stomachs stretching back to the 1980s. A new study published in the journal *Nature* has attempted to quantify the harm that plastic is having on the turtle population of eastern Australia.

In their research, a team led by Dr Britta Denise Hardesty from the Commonwealth Scientific and Industrial Research Organisation examined data from nearly 1,000 dead turtles to understand the role plastic played in their deaths. They found that the youngest turtles appeared to be most susceptible to plastic pollution.

Just over half of the post-hatchling individuals had ingested plastic, and around a quarter of the slightly older juveniles were affected, compared to around 15 per cent of adults.

While the number of plastic pieces in the reptiles' guts varied wildly from one to over 300, the scientists were able to deduce that turtles have a 50 per cent probability of death after consuming 14 pieces.

The Independent

## Bad? Not quite



Agriculture that appears to be more eco-friendly but uses more land may actually have greater environmental costs per unit of food than "high-yield" farming that uses less land, according to a new study.

There is mounting evidence that the best way to meet rising food demand while conserving biodiversity is to wring as much food as sustainably possible from the land we farm, so that more natural habitats can be "spared the plough". However, this involves intensive farming techniques thought to create disproportionate levels of pollution, water scarcity and soil erosion. Now, a study published recently in the journal *Nature Sustainability* shows this is not necessarily the case.

Scientists have put together measures for some of the major "externalities" — such as greenhouse gas emission, fertiliser and water use — generated by high and low-yield farming systems, and compared the environmental costs of producing a given amount of food in different ways.

Previous research compared these costs by land area. As high-yield farming needs less land to produce the same quantity of food, the study's authors say this approach overestimates its environmental impact.

However, the team behind the study led by scientists from the University of Cambridge and involving researchers from the University of Sheffield in the UK, cautions that if higher yields are simply used to increase profit or lower prices, they will only accelerate the extinction crisis we are already seeing.

The study analysed information from hundreds of investigations into four vast food sectors, accounting for large percentages of the global output for each product — Asian paddy rice (90 per cent), European wheat (33 per cent), Latin American beef (23 per cent), and European dairy (53 per cent). Examples of high-yield strategies include enhanced pasture systems and livestock breeds in beef production, use of chemical fertiliser on crops, and keeping dairy cows indoors for longer.

The scientists found data to be limited, and say more research is urgently needed on the environmental cost of different farming systems. Nevertheless, results suggest many high-yield systems are less ecologically damaging and, crucially, use much less land. The study authors say that high-yield farming must be combined with mechanisms that limit agricultural expansion if they are to have any environmental benefit. These could include strict land-use zoning and restructured rural subsidies.

The Independent

# Shortening recovery route

**UK parents describe how funding child brain tumour testing opened door to less toxic treatment**



Alex with mother Anthea

ALEX MATTHEWS-KING

A mother whose four-year-old son has just completed 10 months of targeted chemotherapy for an aggressive brain tumour has called for every child to have access to testing that can help minimise the risk of life-long kidney damage and hearing loss. Alex Hobbs had his last session of chemotherapy a week ago but he would have had three more gruelling months ahead if genomic testing of his cancer's unique DNA markers had not flagged him as eligible for a clinical trial.

The Europe-wide study is trying to establish whether a bespoke chemotherapy regime for medul-

loblastoma, the most common cancerous brain tumour in children, can cause fewer side effects without impacting survival, and Alex was its first UK participant.

For Alex's parents, Anthea and David, this began with an "impossible choice" between the uncertainties of the trial and wanting to give Alex the best chance of a healthy life. Anthea told *The Independent* that it would have been unimaginably worse to have options taken off the table because of a lack of funding or by living in the wrong part of the country.

The first time Anthea and David noticed anything was wrong was a Friday in September 2017 when Alex

began to lose his balance. "We noticed he was stumbling like he was a little bit drunk, and his eye was turning in like a squint," says Anthea. "We'd say, 'Come on Alex, what are you doing with your eyes? You're being silly', and he'd correct it. We thought there's definitely something not right here, but I thought he had an inner ear infection."

As it didn't seem urgent Anthea booked to see the GP first thing on Monday morning. "The GP pretty much saved his life at that point," Anthea says. "It was a big tumour and he was going downhill pretty quickly."

Alex was sent straight to the local hospital and diagnosed in two hours.

They were "blue lighted" to Great Ormond Street Hospital in London on the following Tuesday morning and on Friday Alex had eight and a half hours of surgery to remove his tumour. Anthea describes that week as "incredible, but just horrendous". Even though the tumour was removed in its entirety there was a lot of treatment ahead.

However the road could have been much longer if the hospital had not just become part of the SIOP PNET 5 trial, which has been running in Europe since 2014 and is recruiting 360 participants. "This trial is providing the ability to give children treatment that is tailored to their tumour and signals a great step forward in brain cancer management," says Dr Antony Michalski, paediatric oncologist at Gosh and chief investigator in the UK for the SIOP PNET 5 trial. "Working with our European colleagues, we are able to reduce treatment for children with lower-risk tumours as well as researching ways of improving outcomes for children with standard-risk disease."

Genomic medicine is the practice of analysing the suite of human DNA markers and mutations and their effects on health and disease. In cancer, as cells multiply, the tumours collect a host of mutations that can make them harder to treat or more likely to spread. Over the last two decades doctors treating medulloblastoma have built up a panel of these "biomarkers", which Alex's tumour was checked against. These key genes can give clues on whether the tumour is likely to have left cells in the body that could cause a relapse, and how they might respond to treatment.

Patients at low or standard risk are eligible for the trial and 10 years from now it will assess differences in kidney function, hearing loss and nerve damage between the two groups of patients given either the usual treatment, or treatment tailored to their biomarkers. However, the primary measure of whether this tailored treatment is effective is survival.

All the evidence suggests the only difference should be that patients given tailored treatment have fewer long-term side effects. But this can only be proven for certain with the clinical trial and this requires patients like Alex, and parents like Anthea and David to accept some degree of uncertainty. "We had the weekend to decide. The consultant came to talk to us on Friday and said Alex has been deemed as standard risk," Anthea says. "He said: 'We have this clinical trial, here is some information, and we need you to tell us by Monday because he needs to start treatment.'"

The options were explained and

the likely side effects of the 48-week standard chemotherapy were set out against 36-week tailored chemotherapy he would receive if he was selected for that part of the trial. But the final decision had to come from Anthea and David. "It's cold, but it has to be," Anthea says. "You're kind of damned if you do, damned if you don't. You want him to have the maximum he can have, because with this cancer if it comes back it's very hard to treat."

"But with chemo, the longer you go on the more your body can't tolerate it. So they've tried to switch out some of the chemo that has an effect on your kidneys and your hearing, and swap in ones they still know are effective. There isn't an effect on the survival rate, apparently. But it's so hard to know when it's the beginning of a trial."

As chemotherapy can be brutal and could have a lasting effect on Alex's life, they decided to participate. "Any research that can help us get closer to a cure, while reducing the long-term effects, has got to be worth it for Alex and for future generations," Anthea said.

As the chemotherapy progressed the medical team had to make changes to the regime — a drug called vincristine had to be omitted in a few cycles because it was damaging the nerves in his hands and feet.

Alex also has some kidney damage, and if he had been on the longer standard course of treatment there would have been more treatment choices to make.

When *The Independent* spoke to Anthea on Thursday, one week after his final chemotherapy session, Alex was playing on the trampoline. He had already been out on his scooter to help pick up his sister from school and his mum remarked on the way he has taken the last year in his stride.

"Adults have a choice (in the treatment they want), this is kids and we have to make that choice for them. That's impossible in itself, but to then to be faced with not being in the right area, not having funding — I couldn't even imagine that." Currently the The Brain Tumour Charity is funding testing for medulloblastoma biomarkers at a cost of £2,200 per child and will do so for at least two years. Alongside York-based Oscar's Paediatric Brain Tumour Charity, the charity is also supporting UK children to join the PNET 5 trial as well.

Marie Hughes, who co-founded Oscar's six months after losing her son, said, "We saw first-hand how the treatments used to fight brain tumours had a devastating effects on Oscar's body and mind."

The Independent