Vitamin D and skin color revisited: Student exchange opens doors to research

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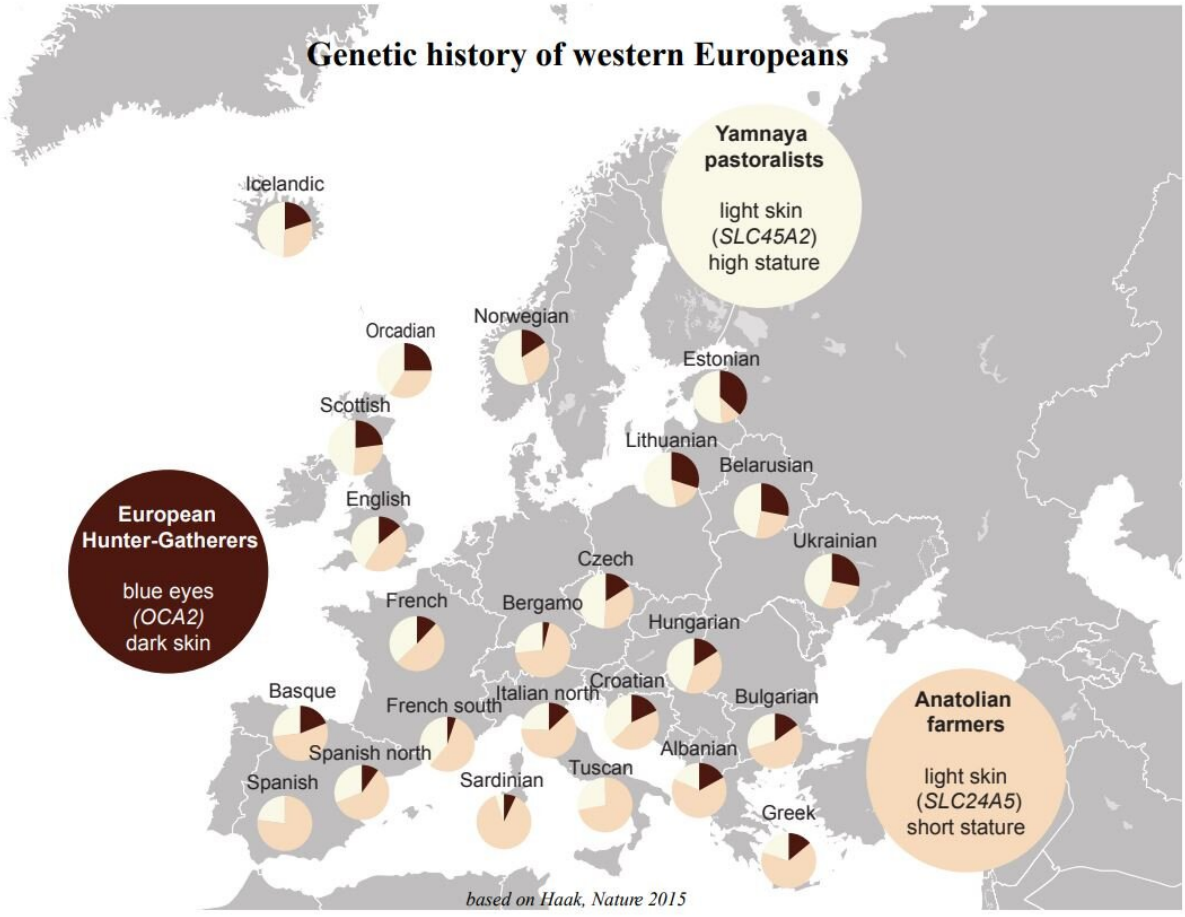

The map visualises the fact that present-day Europeans are the product of the Bronze Age collision of three ancestral tribes: indigenous European Hunter-Gatherers, Anatolian farmers originating from the area of present-day Turkey, and Yamnaya pastoralists originating from the Eurasian steppe. Anatolian farmers had a rather short body stature, brown eyes and light skin and settled mostly in southern Europe, whereas Yamnayas had high body

stature, brown eyes and light skin and settled in northern Europe. The indigenous European hunter-gatherers had dark skin and blue eyes. Pie charts indicate the respective percentages of these three founding populations in present Europeans. Credit: *Biochemical Pharmacology*

A recent review on vitamin D and evolution questions the traditional view of vitamin D as a driver of skin lightening in Europe and tracks down the development of its multiple functions. Authored by exchange student Andrea Hanel and Professor Carsten Carlberg, the review was published in *Biochemical Pharmacology*.

Hanel is so far the first student in Carlberg's group to have her Bachelor's thesis published in a scientific journal. "She took up the project with a lot of enthusiasm and agreed when I suggested aiming at a publication," says Carlberg, who is Professor of Biochemistry at UEF's Institute of Biomedicine in Kuopio.

Presenting a new angle on the topic, the article immediately got a good number of reads in ResearchGate. Carlberg has made it a point to encourage undergraduate students to publish, not just for visibility, but for career prospects. "Publications are what opens doors when applying for Ph.D. positions."

According to Carlberg, an exchange period lasting the whole academic year can offer hard-working students a good opportunity for a Master's or Bachelor's thesis project. For those interested in getting involved with his own Epigenomics of vitamin D research group , a natural first step is to take his lecture courses in Molecular Medicine and Genetics, Molecular Immunology, Cancer Biology, and Nutrigenomics.

These very courses became a turning point for the Czech-born Hanel.

Pursuing a Bachelor's degree in Nutritional Sciences at Justus Liebig University in Giessen, Germany, she originally came to UEF's Institute of Public Health and Clinical Nutrition for just a four-month Erasmus exchange. However, having come across Carlberg's courses, she became intrigued by the topics and was convinced she should stay longer in order to take part in all his lectures.

"Even though these courses were above my study level and outside the scope of my exchange, university staff both in Kuopio and in Giessen understood how passionate I felt, so they went out of their way to get me enrolled and to repeatedly extend my stay."

She says Carlberg opened a whole new dimension of understanding to her. "What resonated with me so strongly was the concept of epigenetic gene regulation in both health and disease—how our whole life including our lifestyle choices is recorded in our epigenome, the gatekeeper for gene activation. I knew I found what I had been looking for, a scientific basis for what I believe in—that our common diseases are at their core a lifestyle choice, and it is our own responsibility to care of ourselves to prevent or reverse them. As he describes in his new book Human Epigenetics: How Science Works, epigenetics provides a molecular explanation for this life philosophy."

Encouraged by a fellow student, Hanel asked Carlberg for a Bachelor's thesis project. "I didn't have any lab skills, so he presented me with the idea of a review article. Lacking background, I felt a lot of pressure about publishing a paper, but I wanted to be worth the investment my favorite professor was willing to make in me," Hanel recalls.

The first vitamin D receptor was in a boneless fish

In their review article "Vitamin D and evolution: Pharmacologic implications," Hanel and Carlberg demonstrate that the pleiotropy of

vitamin D signaling has an evolutionary origin, the understanding of which will allow a better use of the pharmacological potential of vitamin D and its derivatives. They point out that even though vitamin D is best known for its role in bone health, its immune regulatory function developed even earlier than its role in calcium homeostasis. Moreover, its original and likely still central function is to regulate genes involved in energy metabolism.

"In fact, the first known species to express a vitamin D receptor resembling that in humans was a boneless fish, sea lamprey, which is the common ancestor of all vertebrates. The first function of vitamin D simply had to be other than the regulation of bone metabolism," Hanel says.

For a long time, Europeans were dark-skinned

In addition, the review questions the common hypothesis that modern humans had to develop a lighter skin in order to secure sufficient vitamin D synthesis after migrating from Africa to higher latitudes where there's less sun exposure. Instead, genome-wide studies of ancient bones show that the original European hunter-gatherer population kept their dark skin, but developed blue eyes. More importantly, genetic adaptation led to increased concentrations of the vitamin D precursor in their skin, so less sunlight was needed to produce sufficient amounts of vitamin D.

Gene variants for lighter skin were brought to western Europe far later by Anatolian farmers and by Yamnaya pastoralists from the northern Caucasus. Present European populations descend from these three ancient populations in varying proportions, which explains the variation of skin pigmentation, body stature and many other traits.

According to Carlberg and Hanel, vitamin D responsiveness may also

have played a role in adapting to reduced sun exposure, a higher sensitivity to vitamin D being an asset. However, the genetic basis of vitamin D responsiveness is so far not well known. Carlberg says it can be hypothesized that the Yamnayas were high responders to vitamin D, whereas the European hunter-gatherers and the Anatolian farmers were mid and low responders, respectively. "High responsiveness to vitamin D may have provided the Yamnayas a more robust immune system needed to survive the cold dark winters of northern Europe."

A good review offers something new

Hanel describes Carlberg as an outstandingly motivating teacher and supervisor. "He told me a good review doesn't just sum up what is already known but offers something new by combining information in an innovative way. He always created space for discussions, and even though my different ideas and hypotheses were not always realistic, each explanation deepened my understanding and brought me closer to my findings."

An internship in Carlberg's research group enables her to continue with another review focusing on the role of vitamin D in the immune system. She is also applying for the Master's Degree Programme in Biomedicine in Kuopio.

"Vitamin D is across many countries the nutrient that people lack most, and yet it's essential to our health in so many ways. The importance of this topic supported by the science of epigenomics is my driving force, and I feel honored to work on it with a leading scientist in the field."

"At the moment, I'm living my dream. I'm so grateful to everyone who has made it possible for me to take up lectures that changed my life, and on top of it even get involved in research," Hanel says.

Those studying and working with her in Kuopio can't have missed her enthusiasm: sitting in the front row in class asking questions, knocking on Carlberg's door with more questions, and working seven days a week. "I thought my dedication could come off as annoying, but instead, many people have told me they have found it inspiring and are sincerely happy how things have worked out for me."

"I am overwhelmed by the support and hope that my story can inspire also others to follow their passion and to try their wings."

More information: Andrea Hanel et al. Vitamin D and evolution: Pharmacologic implications, *Biochemical Pharmacology* (2019). DOI: 10.1016/j.bcp.2019.07.024

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