The skin's wide range of microbiota improves the immune system

Just as those in the gut, the microorganisms in the skin play an important role in improving the body's immune system. Mira Grönroos, community ecologist at the University of Helsinki, is studying the connections between the environment, microbiota and human health. She is interested in how spending time in the forest and connecting with nature affect the skin microbiota. Her aim is to find ways to improve the human immune system. This topic has not been studied much before.

Allergologist **Tari Haahtela** has made a special biodiversity hypothesis about human health: without exposure to nature and its microbes, our immune system dos not function as it should. If there is little or no interaction with nature, the immune system can't learn to distinguish between what is dangerous and what is not. The body goes into a state of stress, which results in low-grade inflammation. The immune system overreacting may lead to diseases.

Mira Grönroos is working as a post-doctoral researcher in a multidisciplinary NATUREWELL project (2019–2025) funded by the Research Council of Finland. The project, led by Docent **Riikka Puhakka**, aims to study the impact of outdoor recreation on the health and well-being of Finnish youth. In the project, Grönroos focuses on studying how outdoor recreation and activities affect the human microbiota.

"The youth participated in a variety of outdoor activities in nature. Microbial samples were taken from their skin before and after the activities. We are studying whether hiking in a forest or spending time in urban nature changes the microbiota of the youth. We are also looking for ways to encourage young people to go out in nature," Grönroos explains.

Grönroos is part of a research group led by **Aki Sinkkonen**, who works as a senior researcher at the Natural Resources Institute Finland (Luke). For the other studies in the group, researchers have been measuring interleukin and T-cell levels, for example. Cytokines, which are small proteins, function as messengers in the system controlling cellular functions in the body. These include interleukins, which increase or decrease inflammation. T cells help destroy pathogens living inside cells. B cells, on the other hand,


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are responsible for antibody-mediated immunity. The studies found that the levels of anti-inflammatory interleukin-10 proteins increased after microbial exposure.

Changes in how daycare-age children's immune systems function

According to Grönroos, the immune system and microbes are in constant interaction.

"The results so far are very encouraging, and now we're studying the intensity of the natural exposure required. Spending time in nature also has many other wellbeing benefits that make the forest a good place to be. One way to increase microbial contact while enjoying nature is to eat snacks without washing or sanitising hands first," says Grönroos.

Sinkkonen's research group has been carrying out intervention studies, where the researchers' intervention in the phenomenon under study is an integral part of the method. One study increased the interaction between daycare children and natural microbiota. The study followed daycare children between the ages of three and five in ten daycare centres in Lahti and Tampere for a month.

"The yard of the daycare centre was made greener to increase the children's contact with natural materials. In another study, material containing microbiota was added to the sand in the yard," Sinkkonen says.

The studies showed, for the first time in the world, that the children's immune system regulation changed while they were in contact with the diverse microbiota of natural materials.

The microbiota collected from sand, skin and gut was sequenced. The study examined how the microbiota changed between the test group and control group. In the study, the gene region of 16S ribosomal RNA (16S rRNA) was sequenced and the bioinformatics was carried out with the resources of Finnish ELIXIR Node, CSC – IT Center for Science. The 16S gene regions have remained unchanged for millions of years of bacterial evolution, which is why they can be used to identify different species.

The samples taken from the children's skin helped identify the composition of the bacterial community, i.e. the metagenome. The relative amount of more than

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Natural exposure and microbial diversity have also been used commercially. Olli Laitinen, molecular virologist at Tampere University, and Aki Sinkkonen, then a senior researcher, co-founded Uute Scientific. In 2020, the company started producing an extract in Lohja, Finland, containing thousands of microbes extracted from forest soil. There are already more than 40 products in the form of powder. Together with their colleagues, Sinkkonen, Laitinen and Grönroos have patented the method in Europe and the United States.


Uute design


Mira Grönroos

30 bacterial genera increased on the children's skin. The increase in the amount of immune-boosting gammaproteobacteria was connected to a change in interleukin-17A, which is associated with the development of allergies and immune-mediated diseases.

"Efficient sequencing methods and the data they generate are vital for studying microbial diversity and its impacts. Cultivation methods alone aren't enough for studying things like this," Grönroos says.

Next-generation sequencing technology enables the simultaneous sequencing of millions or even billions of DNA segments in a sample. Sinkkonen's research group has also started random sequencing, or shotgun sequencing as it's called.

"This method gives us more detailed information about the taxonomic profile of the entire microbiome and its functionalities, such as genes and metabolic pathways," Sinkkonen says.

Mira Grönroos's research is multidisciplinary, and now also includes a social and pedagogical perspective. The aim is to promote interaction with nature. The previous studies conducted with daycare children already showed that children love playing with natural materials. A recently started project at Tampere University studies children's view on microbes.

"Microbes are made visible through both science and art. I'm in charge of the part about science. The children can decide what they want to take a sample of. They also get to follow the progression of the samples in the laboratory via video messages. Then I'll present the results of the sequencing to the children."

21.10.2024 | Ari Turunen

MORE INFORMATION:

University of Helsinki
https://www.helsinki.fi/en/researchgroups/nature-based-solutions

Natural Resources Institute Finland
https://www.luke.fi/en/projects/biwe

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