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Press release
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Microchimerism in humans: A puzzle for science
On the trail of foreign cells within us

Graz, 22 March 2022: A newly established international group of scientists has received a $5.34 million grant from the John Templeton Foundation to get to the bottom of the phenomenon of microchimerism. The international team is led by Thomas Kroneis (Medical University of Graz) and Amy Boddy (University of California—Santa Barbara). Frank Schildberg (University Hospital Bonn), Michael Eikmans (Leiden University Medical Center) and Henderson Cleaves (Tokyo Institute of Technology and Blue Marble Space Institute of Science) are its other members.

Microchimerism refers to when a person harbors cells from another individual (e.g., their mother) in addition to his/her own cells. In humans, an exchange of cells between mother and child during pregnancy is primarily responsible for this phenomenon. After traveling from one individual to another, these "foreign" microchimeric cells may remain alive and well in the new body for the rest of its life. As a consequence, we may all be chimeras and carry around cells from our ancestors and descendents.

The mystery of the chimera

Scientists would like to understand how these cells enter the body and whether they influence our physiology. It is known that microchimeric cells can differentiate into nearly all types of cells, including brain cells. Microchimerism seems to play a paradoxical role in our health. Some studies indicate it has benefits, for example it fosters regeneration of maternal tissue or adds immunological protection for the developing fetus. However, other studies have assigned microchimerism a role in the development of diseases, for example pregnancy complications such as preeclampsia or spontaneous miscarriage as well as cancer and autoimmune disease.

The new research team believes microchimerism is more widespread than previously thought, and that microchimeric cells take on an adaptive role in their hosts. These cells might have positive effects on mothers and their offspring, for example in the form of stem cells or key components and signals for the immune system. This mutually beneficial situation may not apply to all tissue since sometimes the "genetic" interests of the mother and her child do not match, which can lead to an increased susceptibility to disease.

A puzzle for science: Research challenges

"The analysis of very rare cells like microchimeric cells has always been a challenge for science. This is mainly because only a few clear markers are suitable for an uncomplicated analysis," reports Thomas Kroneis from the Division of Cell Biology, Histology and Embryology, who is the co-lead of the international consortium. The most commonly used

marker to detect microchimeric cells was the Y chromosome because it was supposed to be easy to analyze. "However, this was limited to the detection of male fetal cells in the mother's body. Analysis of mother-daughter samples was not possible, and it was also difficult to analyze maternal microchimerism—from the mother's cells to her offspring. During his dissertation, Thomas Kroneis dedicated himself to this problem, which he solved by using forensic DNA analysis of individual cells.

"To develop the right tools for our investigations, we will borrow from the molecular biology bag of tricks and adapt the latest techniques to serve our purposes, for example spatial histology." This is an approach that permits histologist Thomas Kroneis to characterize cells directly in tissue sections using hundreds of different RNA transcripts and draw conclusions from their location—for example to identify what type of cell the microchimeric cells are and to determine which immune cells are found in their proximity. "Spatial histology—the location-dependent characterization of cells in the context of tissue—is a method that brings analysis of individual cells into a relationship with their surroundings," explains Thomas Kroneis. "It is like a puzzle. The individual pieces are like cells—you can recognize details of a picture but not the context or complete picture even if you have already located the edge or corner pieces. The full picture and thus the content are revealed only when the puzzle pieces are in the right place. That means that for microchimeric cells too, the tissues in which they are found and the cells of the immune system that are nearby are also important."

The goal of the international consortium is to describe microchimeric cells, their distribution in tissue, how they got to be there and what influence they have on different tissue and the immune system. The research will help to reveal how the microchimeric cells interact with their target tissue to build up a tolerance for microchimerism during pregnancy as well as maintain it after birth. It will also explore whether this immune tolerance breaks down during certain diseases and if so, what the reasons for this are.

Research goals

The mission of this project is clear: to advance the understanding of the fundamentals of microchimerism. This is done by characterizing microchimeric cells, their environment and their interaction with the host’s immune system across different tissues and stages of development in humans and in mice. Following principles of the theory of evolution and systems biology, the team believes this approach provides a more profound understanding of the effects of microchimerism on mother and child. This project will boost the growing field of microchimerism research—not only in the form of generated data and analytical tools, but also by helping to organize the larger global research community, supporting junior researchers, preparing teaching materials and organizing exhibitions and lectures for the general public.

This project has the potential to lead to many new discoveries about the biology of mother-child interactions and to solve the mystery of the influence of this biology on our health and even the evolution of mammals. "We are highly motivated and can't wait to start working on the puzzle!" says Thomas Kroneis.

Facts and figures

Project:	We All Are Multitudes: the Microchimerism, Human Health and Evolution Project
Start date:	December 2021
Period:	33 months
Budget:	$5,339,698.40, $2,246,698.75 of which is for Med Uni Graz

Partners: Med Uni Graz/CBmed, University of California—Santa Barbara, Leiden University Medical Center, Blue Marble Space Institute of Science/Tokyo Technical University, University Hospital Bonn

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After receiving a diploma in technical chemistry in Graz, Kroneis earned his doctorate in the area of non-invasive prenatal diagnostics at Med Uni Graz in 2009. From 2014 to 2016 he was granted a Marie Skłodowska-Curie Fellowship at the Sahlgrenska Cancer Center in Gothenburg, Sweden. Back in Austria he completed his habilitation in cell biology, histology and embryology in 2018 and was appointed deputy head of the corresponding division at Med Uni Graz in October 2021. In 2019 he additionally joined CBmed GmbH, an applied biomarker research company where he heads the area of Total Quality Management since 2021.