



Letter to the editor

מכתב למערכת

Introducing IS.ME: The Israeli Skin Microbiome Experience

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ת ק צ י ר

העור הוא האבר האפיתליאלי הגדול ביותר בגוף האדם. אבר זה מספק שטח מגע גדול ביותר בין המאכסן לבין כל הגורמים הסביבתיים המקיפים אותו. העור משמש גורם ההגנה הראשון בפני כל אתגר פיזי, כימי או ביולוגי. התיישבות החיידקים בעור מוכרת זה זמן רב כגורם אתילוגי במחלות עור שונות, וכן כגורם מרכזי בהתפתחות התגובה החיסונית ובשמירת ההומאוסטזיס של העור. מחקרים רבים שעסקו במיזם המיקרוביום האנושי הצביעו על מצבים שונים של המיקרוביום של העור, שבהם הוא ממלא תפקיד חשוב במניעת מחלות ובשמירת תקינות העור. אולם רוב המחקרים הללו היו מוגבלים לקבוצות של עד מאה פרטים, ולכן לא היו מסוגלים להקיף את כל המשתנים הצפויים באוכלוסיות גדולות. מיזמים עם אוכלוסיות אזרחיות גדולות הראו כי בשל יכולתם להגיע לאוכלוסיות גדולות הם יכולים לשמש במה מתאימה לפיתוח המאגר הגדול ביותר בעולם של מיקרוביום של העור. מאמר זה מתאר מיזם שמטרתו היא (1) פיתוח תוכנית חינוכית עבור תלמידי תיכון ואוכלוסיות אזרחיות אחרות שבמסגרתה ייאספו דגימות של המיקרוביום העורי מאוכלוסיות מגוונות, המייצגות את כל סוגי האוכלוסייה הבריאה. במה זו תשמש מרכז לנוער ולאזרחים שוחרי מדע; (2) הכנת ספריות מדגימות המיקרוביום העורי מ-100 אלף ישראלים המייצגים את כל הקבוצות האתניות ומכל רקע גיאוגרפי, מוצא, גיל ומגדר הקיימים באוכלוסייה בישראל; (3) שיתוף הקהילה המדעית הבינלאומית ומתן אפשרות לאנשי מדע להשתמש שימוש מרבי במאגר ידע זה. הפוטנציאל הטמון במיזם ימומש באמצעות פרסומים מדעיים, כנסים ועבודות משותפות. שיטות ותוצאות צפויים: איסוף הדגימות ועיבודן יתבצעו בשיטות המקובלות ולפי פרוטוקולים שהופעלו בפרויקט המיקרוביום האנושי העולמי. למטרה זאת תפותח מערכת דינמית, ידידותית למשתמש ופתוחה לכל משתמש חיצוני, כך שתעודד שיתוף ושימוש הדדי בנתונים עם כל גורם בינלאומי. אנו מצפים כי תוצאות מפעל זה יחשפו את כל הגורמים הפועלים באוכלוסיות שונות בעולם ומשפיעים על המיקרוביום של העור הנורמלי, ועל ידי כך יעזרו למקד את הגורמים הקשורים בסביבה האקולוגית והגיאוגרפית – רקע אתני, משקל, גיל ומגדר – המשפיעים על המיקרוביום הנורמלי של העור.

מילות מפתח:

מיקרוביום עורי
מדע-אזרחי
חינוך מדעי
מאגר מידע

ABSTRACT

IS.ME will be an initiative to characterize systematically the microbial taxonomic diversity and related biological processes of human skin in Israel and beyond. Datasets of such a scale may serve as a baseline for subsequent skin microbiome studies. Through educational outreach activities, we aim to approach over 100,000 individuals and collect relevant biological and clinical data to establish the largest database of human skin microbiome. This database will enable our group to address previously unexplored scientific hypotheses, including but not limited to, correlations between skin, aging, lifestyle, microorganisms, medication, drugs, ethnicity, allergies, chronic illnesses, twins and others. Additionally, both our biobank and datasets can be used to leverage further studies, thereby placing our project at the epicenter of the multitude of potential future skin microbiome studies.

Keywords:

Skin microbiome
Citizen science
Scientific education
Database

Recent technological and scientific advances have facilitated exploration of the diversity of human microbiome. Microbial flora of the skin has been of great interest as it contributes to both health and diseases. Traditional cutaneous microbiology has focused on *Staphylococcus epidermidis*, *Staphylococcus aureus* and *Propionibacterium acnes*, yet expanding experimental techniques have shown that healthy skin is a habitat for a milieu of other microorganisms, including varied species in the *Staphylococcus* genus, *Micrococcus luteus*, *Corynebacterium spp.*, *Streptococcus mitis*, *Malassezia globosa*, *Malassezia restricta* and others (Grice, Kong et al., 2009; Oh, Byrd et al., 2014; Oh, Byrd et al., 2016). Importantly, bio-topography of the body affects the human microbiome, as well as its virome (Hannigan, Meisel et al., 2015), metabolome (Bousslimani, Porto et al., 2015), and antimicrobial peptide expression (Falconer, Ikram et al., 2001; Gläser, Harder et al., 2005; Köten, Simanski et al., 2009; Wittersheim, Cordes et al., 2013). Hence there are clearly strong determinants of biogeographical distribution that affect microbial, chemical and immunological profiles across the skin. These determinants, whether biotic or abiotic, must be unmasked and their mechanisms fully understood in order to improve skin care in health and disease.

To date, large-scale microbiome projects largely address questions exclusively related to the gut microbiome and oral microbiome due to the efficiency of sample collection and wealth of knowledge currently available regarding these body sites. The skin, which serves as the primary barrier and interface between the body's integral systems and the outside world, has been a focus of several smaller studies which have enabled skin-based forensics and have elucidated spatial, temporal and disease phenomena of the skin microbiome (Costello, Lauber et al., 2009; Fierer, Lauber et al., 2010; Oh, Byrd et al., 2016). However, large-scale studies are needed to validate the aforementioned approaches, as well as to empower predictive algorithms with wide-scale applicability. An example of the magnitude of large-scale microbiome projects can be found in the works of the American Gut Project (Debelius, Vázquez-Baeza et al., 2016) and DayTwo (Zeevi, Korem et al., 2015). Each has leveraged their data troves to create clinical tests, diagnostic tools and personalized health plans for their participant populations. In addition to creating a physical barrier, the skin serves as the largest epithelial surface for interactions with microorganisms and can serve as a window into the on-goings of the human body (Gallo, 2017). It therefore has tremendous diagnostic potential, and its importance in immune-training is immense.

Creation of a nationwide skin microbiome biobank alongside massive data collection regarding lifestyle, environment

and personal history will significantly enhance the power of international skin microbiome research endeavors, informing both research hypotheses and conclusions and enabling machine learning or artificial intelligence methodologies. Specifically, a focus on ethnicity, geography, age-groups and households, integrated with other personal and environmental data, will help to uncover the driving factors behind skin microbiome composition.

IS.ME, or the Israeli Skin Microbiome Experience, is an innovative initiative which aims to engage the broader public in skin microbiome research. Our team consists of Prof. Zvi Bentwich, Dr. Oded Keynan and Michael Brandwein. Our groundbreaking approach aims to develop an educational curriculum to engage high school students in microbiome research and involve them in sample collection and microbiome analysis. Through a strategic partnership with the Davidson Institute of Science Education (www.davidson.weizmann.ac.il), which will provide pedagogical training to local high school teachers, we will train tomorrow's microbiome scientists and provide them with crucial hands-on molecular biology experiences.

Additionally, we will develop an interactive and dynamic web-based platform to bridge clinical scientists and professional microbiome researchers' additional strategic partnerships with the Department of Dermatology at Soroka Hospital, led by Prof. Alex Zvulonov, and the Sial Research Center, led by Prof. Pesach Schwartzman have been established to guide us through clinical and ethical considerations of the project. Once cultivated this bank will serve two crucial purposes: Firstly, it will enable research into the collective Israeli skin microbiome in health and disease. Secondly, it will provide us with the necessary critical mass to launch our project internationally.

Our project is innovative in its effort to *engage high school students as citizen scientists*, as well as their family members and their broader community. High school students will receive specialized theoretical and practical training in microbiome research and will serve as the project's ambassadors. This involvement is crucial for the scalability of the project and serves the greater purpose of educating today's youth in cutting edge microbiome research. Additionally, the project is innovative as we intend to *establish the world's first open-access skin microbiome biobank and database*.

We will use these resources to further our research into skin diseases, including atopic dermatitis, psoriasis and Darier's disease in addition to our research into the healthy skin microbiome and the skin microbiome of other systemic or chronic illnesses such as inflammatory bowels disease, chronic fatigue syndrome and CIPA (congenital insensitivity to pain with

anhidrosis). The final breakthrough in our approach is the *open-access nature of the database*, whereby both citizen scientists and professional researchers not affiliated with our group will be able to explore our datasets and use them to empower their own research endeavors.

It is our hope that this multifaceted endeavor, integrating a vast array of disciplines, proves to be a valuable scientific and educational tool for academia, education systems, clinical settings and the public at large. More information about IS.ME can be found at IS.MEproject.com.

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