Available online at www.sciencedirect.com

ScienceDirect

Current Opinion in Microbiology

An update on the current understanding of the infant skin microbiome and research challenges

Iliana R Serghiou[1,2,*], Mark A Webber[1,3,†] and Lindsay J Hall[1,2,3,4,‡]

Multiple factors contribute to establishment of skin microbial communities in early life, with perturbations in these ecosystems impacting health. This review provides an update on methods used to profile the skin microbiome and how this is helping enhance our understanding of infant skin microbial communities, including factors that influence composition and disease risk. We also provide insights into new interventional studies and treatments in this area. However, it is apparent that there are still research bottlenecks that include overreliance on high-income countries for skin microbiome 'surveys', many studies still focus solely on the bacterial microbiota, and also technical issues related to the lower microbial biomass of skin sites. These points link to pertinent open-research questions, such as how the whole infant skin microbiome interacts and how microbial-associated functions shape infant skin health and immunity.

Addresses
[1] Quadram Institute Bioscience, Norwich Research Park, Norwich, Norfolk NR4 7UQ, UK
[2] School of Biological Sciences, University of East Anglia, Norwich Research Park, Norwich, Norfolk NR4 7TJ, UK
[3] Norwich Medical School, University of East Anglia, Norwich Research Park, Norwich, Norfolk NR4 7TJ, UK
[4] Intestinal Microbiome, School of Life Sciences, ZIEL – Institute for Food & Health, Technical University of Munich, Freising, Germany

Corresponding authors: Serghiou, Iliana R (iliana.serghiou2@quadram.ac.uk), Webber, Mark A (mark.webber@quadram.ac.uk), Hall, Lindsay J (lindsay.hall@quadram.ac.uk)
[*] ORCID: 0000-0002-0699-5892
[†] ORCID: 0000-0001-8938-5709
[‡] ORCID: 0000-0001-9169-7592

Current Opinion in Microbiology 2023, **75**:102364

This review comes from a themed issue on **Microbiota**

Edited by **Christopher Stewart** and **Maria Carmen Collado**

Available online xxxx

https://doi.org/10.1016/j.mib.2023.102364

Where the infant skin microbiome field currently stands

The human skin microbiome is organised into microbial communities at different body sites [1]. These communities include bacteria, archaea, viruses and fungi, and participate in the host's skin physiological functions and immunity, and overall skin health [1–3]. The infant skin bacteriome has been studied in various projects in the last 20 years and has been found to typically consist of members of the phyla *Bacillota*, *Actinomycetota*, *Pseudomonadota* and *Bacteroidota* [4]. As well as the bacteriome, the infant mycobiome has been found to contain *Malassezia*, *Candida*, *Cladosporium*, *Alternaria*, *Rhodotorula*, *Fusarium*, *Cryptococcus*, *Exophiala*, *Aspergillus and Nigrospora* [5–8]. Directly after birth, coagulase-negative staphylococci species (CoNS) (*Staphylococcus epidermidis* and *Staphylococcus capitis*) dominate the neonatal skin [9,10] along with *Lactobacillus iners*; not long after, these microbes decrease in abundance, which allows gradual colonisation by *Acinetobacter*, *Streptococcus*, *Veillonella*, *Bifidobacterium* and *Enhydrobacter* species [4]. Preterm neonates have been shown to have a more varied skin microbiome and exhibit more *Staphylococcus*, *Raoultella*, *Klebsiella*, *Serratia*, *Streptococcus*, *Enterococcus* and *Enterobacter* [10]. *Streptococcus* species particularly appear to be more abundant in infancy, and decrease with age [11–13]. Perturbations in these communities, particularly early in life, have been associated with dermal conditions, including staphylococcal-scalded skin syndrome (SSSS), atopic dermatitis (AD), diaper dermatitis (DD) and tinea capitis (TC) [1,4,5,7,14–17].

Most recent research has adopted higher-resolution methods to defining the skin microbiome. This has largely confirmed previous studies in terms of species present (with AD the most-studied skin disease), although there has been more of a focus on detailed interactions between factors that affect the infant skin microbiome, mainly in high-income countries (HICs) [1–3,5,15,18,19]. Delivery mode, antibiotic exposure, breastfeeding and neonatal skin structure and function are factors that have been shown to influence initial skin community establishment [2,4,20]. Longer term, the environment, skincare cosmetics, diet, age and gender also impact the composition of the skin microbiome [2,3]. The skin microbiome community make-up appears to be largely defined by age, and only transiently

influenced by factors such as drug use and cleaning and moisturising practices [4]. Recently, Zioutis et al. [21] found that community assembly was driven primarily by ecological drift, suggesting occurrence of stochastic processes. Other recent popular research topics include skin disease microbiome profiling [4,5,14–17], investigation of understudied microbial communities [4,5,22], combined studies using metagenomics, metabolomics and culturomics [5,23–25] and probiotic interventions [19,26–28].

Given the recent increase in knowledge, the aim of this review was to provide an update on the current infant skin microbiome research. We identified 33 research papers and eight reviews published since 2021, which we focus on in this paper (Table S1).

Factors affecting the infant skin microbiome

There are many factors that affect the infant skin microbiome, and more recent studies have focussed on how some of these influence skin microbiome establishment, function and disease [4–6,9,10,18,20–24,29–32].

Delivery mode influences skin microbial colonisation, which in turn affects skin barrier function [4,5]. A recent investigation tested the impact of vaginal delivery (VD) in water on the infant skin (bacterial) microbiome [4]. The authors identified a higher abundance of *Streptococcus* on the skin of infants born by elective caesarean section (CS) and VD in water, compared with normal VD [4]. Rapin et al. [4] further distinguished between elective and emergency CS, and while they found no significant difference in bacterial skin diversity, they did observe higher *Lactobacillus* abundance in emergency compared with elective CS (likely due to initial labour-associated exposure to the vaginal microbiota) [4]. Dry skin was also observed in all infants born through elective CS, which was associated with higher *Streptococcus* abundance [4]. Mycobiome-focused studies have also shown *Candida albicans* and *Rhodotorula* species in higher abundance on the skin of VD infants, while *Aspergillus* was in higher abundance in CS infants [5,6]. The pregnancy and birthing process (whether vaginally or CS delivery), can encounter complications, which may lead to the use of antibiotics. Antibiotic exposure in infants has been shown to reduce skin microbial diversity, although this appears to be transient followed by recovery, and then increasing diversity seen over time, despite exposure [9,30]. More recently, it appears that antibiotic use in pregnancy leads to colonisation of the infant skin with genitourinary tract-associated pathogens (*Ureaplasma* and *Gardnerella*) [23].

To prevent CS-associated conditions (e.g. AD), interventions have been trialled, such as vaginal seeding [20,29]. This exposes CS-delivered infants to the maternal (vaginal) microbiome that is 'bypassed' during CS delivery, although it does not account for important vertical transfer of maternal gut microbes [20,29]. However, there is concern regarding infection transmission from the mothers' vaginal microbiome to the neonate, for example, transfer of group-B *Streptococcus*, but screening steps have been put in place [20,29]. Currently, there are five vaginal seeding randomised placebo-controlled trials in infants investigating how this process correlates with immunity and health outcomes in infants (Table S2). To date, one clinical trial (ID: NCT03567707) does not appear to have published any data, however, the other four clinical trials (ID: NCT03298334, ID: NCT03809390, ID: ChiCTR2000031326 and ID: ACTRN12618000339257) have conducted associated studies, some showing that vaginal seeding can partially 'restore' microbiota profiles in CS babies and normalise neurodevelopment [20,29,33–35]. However, two associated studies demonstrated that vaginal seeding had no significant impacts on gut microbiota composition, growth, anthropometry or allergy risks during the first few months to two years of life [36,37].

Other maternal factors, such as the mothers' breastmilk and food allergies, have been associated with infant skin microbiome changes [4,18]. Mother food allergies have been associated with higher levels of *Prevotella* and *Alloprevotella* on infant skin [4], and breastfeeding has been associated with transfer of transient microbes (*Prevotellaceae*) to the infant skin, which was limited to the typical period of breastfeeding [4]. These transient microbes could have important implications in community establishment and health, however, further investigation into this is required. There have also been differing opinions as to whether breastmilk has an effect on the infant skin microbiome composition, allergic disease and AD in infants [18,21], however, further studies are needed in this area.

The maternal and infant 'environment' also appears to influence skin community composition. For example, the presence of dogs during pregnancy is associated with higher representations of *Betaproteobacteriales* and *Ralstonia* on the infant skin [4]. Longer-term hospital stays, including in neonatal intensive care units, predispose for carriage of potential pathogens on the skin of preterm infants, and show differences between countries. For example, *Mycobacterium tuberculosis* and *Mycobacteroides abscessus* were found on the skin of neonates in a hospital in India [31], *Streptococcus* was identified on neonates in a hospital in Sweden [4,31], and bacterial colonisation with Gram negatives *Klebsiella pneumoniae* and *Serratia marcescens* appeared to be common in neonates born in South African hospitals [32]. Another study identified similarities between the preterm skin microbiome and the environment of the infant's incubator/

isolator and air swabs, although they concluded that the skin microbiome swabs clustered separately from incubator/isolator and control swabs [10].

Cleansing practices are common in hospitals around the world, and many frequently use chlorhexidine gluconate to cleanse the skin of neonates, which has been shown to be effective for skin antisepsis and reducing bacterial colonisation [22,32]. These antisepsis products can be harsh on the neonatal skin, therefore emollient application may be necessary to improve skin condition, which has previously been shown to increase Gram-positive *Staphylococcus aureus* colonisation [32]. Capone et al. [24] claims to be the first study to evaluate the impact of commercialised baby skincare products on the infant skin microbiome; they showed that routine emollient use in infants increased their skin microbiome richness, ceramide and free fatty acid levels, which plays an important role in skin barrier integrity. In contrast, other studies have shown no associations between emollient use and skin bacterial composition [4]. This demonstrates the need for more in-depth investigations into the effects of emollient use on infant skin composition and health.

Other less-studied factors impacting the infant skin microbiome include genetics and gender. Genetics, specifically filaggrin (gene) functional deficiency, has shown no association with the skin microbiome, despite it being responsible for impaired skin barrier function and a major risk factor for AD [4]. There have also been few studies comparing the impact of gender on the infant skin microbiome, and have shown contrasting results: some identifying no significant effect [6], whereas others have shown a significant difference in the first week of birth, specifically in the groin area, but the reasons were unclear [30].

Infant skin disease microbiome profiling

SSSS, AD, DD and TC are common neonatal skin diseases [1,4,5,7,14–17], however, the majority of recent studies have focused on AD and DD. Skin microbiome profiling of infant AD has shown altered microbiome community composition, with *S. aureus* identified as the main bacterial driver, whilst others have shown the reverse [1,15,16], or no specific bacterial taxa associated with AD [4]. There appears to be a mixed consensus on the main causative agent of AD, which needs to be clarified through further investigation. Furthermore, both lesional and non-lesional skin of AD-afflicted infants have shown a slower temporal development of the skin microbiome than healthy infants [16]. DD has been studied in relation to the bacteriome and mycobiome, with *Candida* and *S. aureus* directly correlating with disease severity [5,17]. TC is caused by pathogenic fungi *Microsporum canis*, which has been correlated with an increase in abundance of *Cutibacterium* and *Corynebacterium*, and reduced *Streptococcus* [7].

Understudied infant skin microbiome communities

The infant skin bacteriome is better studied than the mycobiome, virome and archaeome, allowing bacteriome culture collections to be developed, such as the Skin Microbial Genome Collection (SMGC) and Skin Bacteria Culture Collection (SBCC) [38]. These collections identified a novel skin-abundant bacterial genus *Candidatus pellibacterium* in adults and infants. More recently, research has provided more insight into the infant skin fungal communities [5,39]. *C. albicans* has been shown more abundant in areas with skin-to-skin contact, whereas *Cladosporium* and *Alternaria* were more abundant in less-occluded areas [5]. Saheb Kashaf et al. [38] also recently identified three novel *Malassezia* species (*Malassezia auris*, *Malassezia palmae* and *Malassezia rara*) in adults and infants.

There is a lack of infant skin virome research, and current work is focused on disease outcomes in neonates, such as the herpes simplex virus 2 [39]. Viruses identified in adults and infants have been classified to the order *Caudovirales*, and families *Siphoviridae* and *Myoviridae* [38]. The toe web appears to be a site that is abundant in viruses, and novel jumbo phages have been identified here [38]. Archaeome research and its role in the skin microbiome is completely lacking across the lifespan; *Thaumarchaeota* is currently the main archaeal genus identified on human skin, with no specific genera relating to infant skin [3].

Research on early-life skin microbial community assembly using metagenome-assembled genomes (MAGs) is currently very limited, however, an Early-Life Skin Genomes catalogue has recently been developed for infants aged 2–3 months and 12 months [40]. This catalogue comprises of 9194 bacterial genomes from 1029 species, 206 fungal genomes from 13 species and 39 viral sequences [40]. Top genera identified from bacteria, fungi and viruses were *Streptococcus*, *Corynebacterium*, *Neisseria*, *Bifidobacterium*, *Prevotella*, *Malassezia*, *torque teno virus* and *gammapapillomavirus* [40].

Metagenomic, metabolomic and culturomic integrative studies

In recent years, more integrative approaches are being used to study the infant skin microbiome and its function, using combinations of metabolomics, culturomics and metagenomics [5,23–25,38,41,42]. This has allowed a coexistence of three distinct metabolite–microbe clusters to be identified: the first was dominated by *Cutibacterium* linked to hydrophobic elements of the skin barrier, the second associated the *Staphylococcus* genus

with amino acids relevant to water holding capacity and pH regulation of the skin surface and the third was characterised by *Streptococcus* associated with amino acid and sugar abundance [41]. Furthermore, Saheb Kashaf et al. [38] used an integrative approach of culturomics and metagenomics to identify members and functions of the human skin microbiome, and led to the development of the SMGC and SBCC from infant and adult skin. These integrative studies will have implications for identifying potential strains for probiotic interventions to treat skin disease and maintain skin health.

Probiotic interventions

Probiotic interventions, mostly using *Lactobacillus* and *Bifidobacterium* spp., and *Lacticaseibacillus rhamnosus* GG, have shown promising results in treating AD in infants [26–28]. After probiotic treatment with *L. rhamnosus* GG, higher levels of *Prevotella*, *Veillonella* and *Ralstonia* and lower levels of *Stenotrophomonas* and *Microbacterium* were identified. Certain skin and gut microbiota (*Acinetobacter* spp., *Haemophilus haemolyticus*, *Bacteroides ovatus*, *Schaalia odontolytica* and *Actinomyces graevenitzi*) have also been identified as potential candidates for probiotic treatment of AD and food allergies [19]. There are multiple clinical trials for skin probiotic interventions in infants currently being conducted, or that were completed within the last two years (Table S3); which will assess the potential of probiotics for treatment of skin disease.

Technical research limitations

Although there continues to be an increase in infant skin microbiome research, several technical and study design limitations may be impacting the associations and conclusions drawn. For example, most longitudinal and RCT studies have focused on multiple timepoints closely clustered temporally, rather than taking a longer-term outlook into infancy [1,2,4,5,9,10,14–17,21,23,24,27,28,30,31,41]. Other infant skin microbiome studies have been limited due to either low microbial taxonomic resolution and/or lack of microbial functional information, given the frequent use of targeted gene region sequencing methods [43]. The way skin samples are collected further impacts the resolution and robustness of infant skin microbiome studies; while research has identified that the deeper layers of skin tissue hold stable viable bacterial populations compared with the skin surface [44], the Manos [15] review revealed multiple studies that used skin scrapings (that can access these deeper tissues), resulted in reduced DNA quantity and quality that was not adequate for 16S rRNA gene sequencing, and resulted in elevated host DNA contamination [15]. Furthermore, skin scrapings are invasive to infants causing neonatal skin trauma. Also, although groups have used commercialised DNA extraction methods (some with slight alterations) to study the infant skin microbiome, these are not optimised for skin. The skin is a low-biomass niche [45] and has microbial components, such as the mycobiome, that are particularly difficult to lyse, which affect DNA quantity and quality, thus sequencing outcomes. For example, Teufel et al. [17] identified an issue of internal-transcribed spacer sequencing (used to profile fungal communities) not yielding enough reads for analysis. Furthermore, even with rigorous controls in place, low-biomass niches are also at a high risk of contamination [25,42]. Thus, new methods and approaches optimised for study of the skin microbiome are required to address these technical limitations and improve infant skin microbiome research.

Unmet research questions

There is a pressing need for more longitudinal (following infants from birth into infancy) and higher-resolution infant skin microbiome studies. Shotgun metagenomic sequencing will provide higher resolution over 16S rRNA gene sequencing, allowing species and strain-level profiling as well as functional information to be obtained [43]. However, to date, there are very few skin microbiome studies that utilise shotgun metagenomics [5,9,13,30,46]. A consideration for these types of studies is the ability to extract enough high-quality DNA, but ongoing studies in this area are addressing this need [13]. Profiling using shotgun metagenomics will enable researchers to robustly study the infant skin microbiome, including the mycobiome, virome and archaeome, which are significantly understudied in infants when compared with the bacteriome.

Research on how the whole microbiome (viruses, fungi, bacteria and archaea) interacts and functions as a community, and how this is associated with skin health or disease, is also lacking [5]. Moreover, although there has been a research focus on infant skin microbiome in relation to certain skin diseases [4,5,7,14–18,21], as of yet, no one has been able to distinguish between microbiome-driven and microbiome-independent cases. This is a crucial missing research gap that needs to be addressed for improved treatment interventions [4]. Clinical studies have used culturomic and viromic methods to diagnose skin disease in independent cases and examine certain factors such as the effects of cleansing and moisturising products on skin bacterial colonisation [14,22,32,39]. However, to improve the robustness of these studies, multiple techniques such as culturomics, viromics and metabolomics with metagenomics, should be more widely employed, as currently these are few and far-between [7,25,38,41]. These multi-omics studies would help to identify perturbation-associated microbiota changes and fully understand their functional role in infant skin health and immunity, before and after birth, which is lacking. This would also accelerate development of improved maintenance, preventative and treatment options that will improve standard of care of full-term and preterm neonates, therefore optimising

their long-term health. Interventions include oral and topical probiotic use, development of live biotherapeutics products and improved skin transplantation and wound dressing techniques, some of which are already underway [14,26].

Currently, the vast majority of infant skin microbiome studies have only focused on a few HICs, and skin health maintenance, prevention and treatment interventions would be significantly benefitted by diversifying the cohorts that are sampled to a wider geographical and socio-economic reach. This would also help establish a baseline microbiome composition for a healthy infant skin microbiome, the influence of factors modulating the skin microbiota and how skin conditions are linked to microbial compositional changes. Certain practices, such as kangaroo mother care (KMC) and breastfeeding, are known to improve neonatal health outcomes, and their practice is advised globally by the World Health Organisation's updated 2022 recommendations [47]. Shah, Govindarajan, Rangaiah et al. [31] revealed that the presence of *M. tuberculosis* and *M. abscessus* on Indian neonates diminished with KMC, demonstrating its importance in neonatal health outcomes. Other practices worldwide may also influence seeding of the infant skin microbiota and should be explored further to understand the effects that practices have on birth outcomes and neonatal microbiomes, which could have lasting health implications [48].

Conclusions

Infant skin microbiome research over the last two years has focused on the bacteriome and investigated a more detailed interaction of certain factors that affect it. Infant skin exposed to these factors and afflicted with skin disease (mainly AD) has been assessed and profiled (mainly in HICs), which has led to initial investigations of probiotic skin health interventions. There are clear focused research bottlenecks, which have left open questions on how the whole infant skin microbiome interacts and functions in infant skin health and immunity, before and after birth. These could be addressed by profiling cohorts across the globe, and overcoming technical limitations, which include lack of integrative approaches used, overuse of targeted gene sequencing and unoptimised skin collection and DNA extraction methods used. This would improve neonatal skin health interventions and optimise their long-term health.

CRediT authorship contribution statement

Iliana R Serghiou: Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Project administration. **Lindsay J Hall:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Project administration. **Mark A Webber:** Conceptualization, Methodology, Investigation, Writing – original draft, Writing – review & editing, Project administration.

Data availability

No data were used for the research described in the article.

Declaration of Competing Interest

The authors declare no conflict of interest.

Acknowledgements

I.R.S. is funded by a Biotechnology and Biological Sciences Research Council (BBSRC) CTP studentship with Unilever (BB/T508974/1). L.J.H. is supported by Wellcome Trust Investigator Awards 100974/C/13/Z and 220876/Z/20/Z; and a BBSRC Institute Strategic Programme, Gut Microbes and Health BB/R012490/1, and its constituent projects BBS/E/F/000PR10353 and BBS/E/F/000PR10356. M.A.W. is supported by project Grant (BB/T014644/1) from the Biotechnology and Biological Sciences Research Council and BBSRC Institute Strategic Programmes Microbes in the Food Chain BB/R012504/1 and its constituent project BBS/E/F/000PR10349.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.mib.2023.102364.

References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- • of special interest

1. Townsend EC, Kalan LR: **The dynamic balance of the skin microbiome across the lifespan**. *Biochem Soc Trans* 2023, **51**:71-86.

2. Dwyer LR, Scharschmidt TC: **Early life host-microbe interactions in skin**. *Cell Host Microbe* 2022, **30**:684-695.

3. Skowron K, *et al.*: **Human skin microbiome: impact of intrinsic and extrinsic factors on skin microbiota**. *Microorganisms* 2021, **9**:543.

4. • Rapin A, *et al.*: **The skin microbiome in the first year of life and its association with atopic dermatitis**. *Allergy* 2023, **7**:1949-1963.
Early-life microbial colonization of the skin may modulate the immune system and impact the development of AD and allergic diseases later in life. The authors show that skin microbiome composition during infancy is defined by age, transiently influenced by delivery mode as well as environmental, parental factors and breastfeeding. They also identify an association between the microbiome, skin barrier integrity and the onset of AD. This is the largest longitudinal study assessing the skin microbiome in the first year of life and the first to investigate the impact of delivery mode while considering VD in water and distinguishing between elective and emergency CS.

5. Nguyen UT, Kalan LR: **Forgotten fungi: the importance of the skin mycobiome**. *Curr Opin Microbiol* 2022, **70**:102235.

6. Wang YR, *et al.*: **Infant mode of delivery shapes the skin mycobiome of prepubescent children**. *Microbiol Spectr* 2022, **10**:e0226722.

7. Tao R, *et al.*: **Altered skin fungal and bacterial community compositions in tinea capitis**. *Mycoses* 2022, **65**:834-840.

8. Shah PA, *et al*.: **Exploring the skin mycobiome in very preterm babies during the early neonatal period in a Neonatal Intensive Care Unit of India**. *Trop Doct* 2022, **52**:362-364.

9. • Hellmann KT, *et al*.: **Viability-resolved metagenomics reveals antagonistic colonization dynamics of Staphylococcus epidermidis strains on preterm infant skin**. *mSphere* 2021, **6**:e0053821.

The skin is a habitat for microbes that commonly infect preterm infants, but the use of sequencing for fine-scale study of the infant skin microbial communities has been limited by technical barriers. Using a photoreactive dye that eliminates DNA from nonviable microbes, and shotgun metagenomics to sequence the remaining DNA, the authors resolve skin species and strains from preterm skins swabs. CoNS species, *Staphylococcus epidermidis* and *Staphylococcus capitis*, dominated the neonatal skin. Two strains of *Staphylococcus epidermidis* showed an antagonistic relationship on the skin. The authors show the feasibility of gaining detailed information about strain colonization dynamics from this difficult-to-sequence body site of preterm infants, which might be used to guide novel approaches to prevent infections.

10. Schoch JJ, *et al*.: **Skin microbiome sampling in the preterm neonate**. *Pediatr Dermatol* 2023, **40**:129-131.

11. Capone KA, *et al*.: **Diversity of the human skin microbiome early in life**. *J Investig Dermatol* 2011, **131**:2026-2032.

12. Zhu T, *et al*.: **Age and mothers: potent influences of children's skin microbiota**. *J Investig Dermatol* 2019, **139**:2497-2505.e6.

13. • Serghiou IR, *et al*.: **An efficient method for high molecular weight bacterial DNA extraction suitable for shotgun metagenomics from skin swabs**. *Microb Genom* 2023, **9**, https://doi.org/10.1099/mgen.0.001058.

The relatively low bacterial biomass of skin, in comparison to other areas such as the gut microbiome, makes obtaining sufficient DNA for shotgun metagenomic sequencing challenging. Shotgun metagenomic sequencing is needed for taxonomic resolution and functional information in order to study community compositions and functional capabilities of the skin microbiome. The authors optimised a DNA extraction method that produces enough DNA from skin swabs, suitable for shotgun metagenomics, and demonstrated it can be used to effectively characterise the skin microbiota. This method will allow future studies to identify taxonomic and functional changes in the skin microbiota, which is needed to develop interventions to improve and maintain skin health.

14. McKeown KE, Baker RB: **Staphylococcal scalded skin syndrome, identification, and wound care: a case report series**. *Adv Neonatal Care* 2022, **22**:325-332.

15. Manos J: **The human microbiome in disease and pathology**. *APMIS* 2022, **130**:690-705.

16. Olesen CM, *et al*.: **Altered maturation of the skin microbiome in infants with atopic dermatitis**. *Acta Derm Venereol* 2022, **102**:adv00817.

17. Teufel A, *et al*.: **Characterization of the microbiome in the infant diapered area: insights from healthy and damaged skin**. *Exp Dermatol* 2021, **30**:1409-1417.

18. Gołębiewski M, *et al*.: **Mother's milk microbiome shaping fecal and skin microbiota in infants with food allergy and atopic dermatitis: a pilot analysis**. *Nutrients* (10) 2021, **13**:3600.

19. Łoś-Rycharska E, *et al*.: **A combined analysis of gut and skin microbiota in infants with food allergy and atopic dermatitis: a pilot study**. *Nutrients* (5) 2021, **13**:1682.

20. Hourigan SK, Dominguez-Bello MG, Mueller NT: **Can maternal-child microbial seeding interventions improve the health of infants delivered by cesarean section?** *Cell Host Microbe* 2022, **30**:607-611.

21. Zioutis C, *et al*.: **Ecological processes shaping microbiomes of extremely low birthweight infants**. *Front Microbiol* 2022, **13**:812136.

22. Sharma A, *et al*.: **Aqueous chlorhexidine 1% versus 2% for neonatal skin antisepsis: a randomised non-inferiority trial**. *Arch Dis Child — Fetal Neonatal Ed* 2021, **106**:643-648.

23. Orchanian SB, *et al*.: **Multiomic analyses of nascent preterm infant microbiomes differentiation suggest opportunities for targeted intervention**. *Adv Biol* 2022, **6**:e2101313.

24. • Capone KA, *et al*.: **A randomized clinical study on the effects of emollient use on the developing infant skin microbiome and metabolome**. *Exp Dermatol* 2023, **32**:75-77.

There is limited information available on the effects of skin care products on the skin microbiome of healthy individuals. The authors are the first to study the impact of baby skin care products on the infant skin microbiome. The routine use of an appropriately formulated emollient in infants increases their skin microbiome richness, ceramide levels and free fatty acids that play an important role in skin barrier integrity.

25. Mishra A, *et al*.: **Microbial exposure during early human development primes fetal immune cells**. *Cell* 2021, **184**:3394-3409.e20.

26. Andrade PDSMAd, *et al*.: **Efficacy of probiotics in children and adolescents with atopic dermatitis: a randomized, double-blind, placebo-controlled study**. *Front Nutr* 2022, **8**:833666.

27. Pan H, Su J: **Association of probiotics with atopic dermatitis among infant: a meta-analysis of randomized controlled trials**. *Oxid Med Cell Longev* 2022, **2022**:5080190.

28. Carucci L, *et al*.: **Therapeutic effects elicited by the probiotic *Lacticaseibacillus rhamnosus* GG in children with atopic dermatitis. The results of the ProPAD trial**. *Pediatr Allergy Immunol* 2022, **33**:e13836.

29. • Song SJ, *et al*.: **Naturalization of the microbiota developmental trajectory of cesarean-born neonates after vaginal seeding**. *Med* 2021, **2**:951-964.e5.

Cesarean section-born babies show altered microbiota development in relation to babies born vaginally, which can have immunological implications. The authors present the first statistically powered longitudinal study to determine the effect of restoring exposure to maternal vaginal fluids after cesarean section birth. Microbiota trajectories of exposed cesarean section-born babies aligned more closely with that of vaginally born babies. The majority of amplicon sequence variants from maternal vaginal microbiomes on the day of birth were shared with other maternal sites, in contrast to non-pregnant women from the Human Microbiome Projec t study. The results of this observational study prompt urgent randomized clinical trials to test whether microbial restoration reduces the increased disease risk associated with cesarean section birth and the underlying mechanisms. It also provides evidence of the plur-ipotential nature of maternal vaginal fluids to provide pioneer bacterial colonizers for the newborn body sites.

30. Xu Y, *et al*.: **Antibiotic exposure prevents acquisition of beneficial metabolic functions in the preterm infant gut microbiome**. *Microbiome* 2022, **10**:103.

31. • Shah PA, *et al*.: **Mycobacterium species on the cutaneous microbiome of very preterm neonates**. *J Trop Pedia* (2) 2022, **68**:fmac020.

Disruption to the neonatal skin microbiome could lead to pathological disease. There is a need to understand the neonatal skin microbiome of very preterm neonates admitted to the neonatal intensive care unit at a tertiary healthcare setting before and after kangaroo mother care, using next-generation sequencing, which the authors investigated. The authors showed a relative abundance of *Mycobacterium tuberculosis* and *Mycobacteroides abscesses* on the skin microbiome of very preterm neonates before and after kangaroo mother care. The presence of these bacilli as commensals or as potential pathogens is alarming due to the risk of early exposure and incidence of tuberculosis from birth. These authors identify their findings to be the first established in such a setting.

32. Dramowski A, *et al*.: **Impact of 1% chlorhexidine gluconate bathing and emollient application on bacterial pathogen colonization dynamics in hospitalized preterm neonates — a pilot clinical trial**. *EClinicalMedicine* 2021, **37**:100946.

33. Zhou L, *et al*.: **Effects of vaginal microbiota transfer on the neurodevelopment and microbiome of cesarean-born infants: a blinded randomized controlled trial**. *Cell Host Microbe* 2023, **31**:1232-1247.e5.

34. Dominguez-Bello MG, *et al*.: **Partial restoration of the microbiota of cesarean-born infants via vaginal microbial transfer**. *Nat Med* 2016, **22**:250-253.

35. Mueller NT, *et al*.: **Maternal bacterial engraftment in multiple body sites of cesarean section born neonates after vaginal seeding — a Randomized Controlled Trial**. *mBio* 2023, **14**:e00491-23.

36. Liu Y, *et al*.: **Effects of vaginal seeding on gut microbiota, body mass index, and allergy risks in infants born through cesarean delivery: a randomized clinical trial**. *Am J Obstet Gynecol MFM* 2023, **5**:100793.

37. Wilson BC, *et al*.: **Oral administration of maternal vaginal microbes at birth to restore gut microbiome development in infants born by caesarean section: a pilot randomised placebo-controlled trial**. *eBioMedicine* 2021, **69**:103443.

38. • Saheb Kashaf S, *et al*.: **Integrating cultivation and metagenomics for a multi-kingdom view of skin microbiome diversity and functions**. *Nat Microbiol* 2022, **7**:169-179.
Previous metagenomic investigations into the role of the skin microbiome in health or disease have found that much of the sequenced data do not match reference genomes, making it difficult to interpret metagenomic datasets. The authors combined bacterial cultivation and metagenomic sequencing to assemble the SMGC, which comprises 622 prokaryotic species derived from 7 535 MAGs and 251 isolate genomes. This collection includes 174 newly identified bacterial species and 12 newly identified bacterial genera, including the abundant genus '*Candidatus pellibacterium*', which has been newly associated with the skin. The SMGC increased the characterized set of known skin bacteria by 26% and recovered 12 eukaryotic species, and assembled thousands of viral sequences, including newly identified clades of jumbo phages. This collection provides a comprehensive view of skin microbiome diversity.

39. Hayes CK, *et al*.: **Herpes simplex virus-2 variation contributes to neurovirulence during neonatal infection**. *J Infect Dis* 2022, **226**:1499-1509.

40. Shen Z, *et al*.: **A genome catalog of the early-life human skin microbiome**. *bioRxiv* 2023, https://doi.org/10.1101/2023.05.22.541509

41. • Roux PF, Oddos T, Stamatas G: **Deciphering the role of skin surface microbiome in skin health: an integrative multiomics approach reveals three distinct metabolite–microbe clusters**. *J Investig Dermatol* 2022, **142**:469-479.e5.
There is still much to learn about the role the microbiome plays in skin physiology. The authors employed an integrative methodology for microbiome and metabolome analysis of skin surface samples collected from healthy infants aged 3–6-months. Their integrative analyses delineated the coexistence of three distinct metabolite–microbe clusters.

42. Kennedy KM, *et al*.: **Questioning the fetal microbiome illustrates pitfalls of low-biomass microbial studies**. *Nature* 2023, **613**:639-649.

43. Sfriso R, *et al*.: **Revealing the secret life of skin — with the microbiome you never walk alone**. *Int J Cosmet Sci* 2020, **42**:116-126.

44. Acosta EM, *et al*.: **Bacterial DNA on the Skin Surface Overrepresents the Viable Skin Microbiome**. eLife Sciences Publications, Ltd; 2023.

45. Bjerre RD, *et al*.: **Effects of sampling strategy and DNA extraction on human skin microbiome investigations**. *Sci Rep* 2019, **9**:17287.

46. Fleming E, *et al*.: **Cultivation of common bacterial species and strains from human skin, oral, and gut microbiota**. *BMC Microbiol* 2021, **21**:278.

47. WHO: **WHO Recommendations for Care of the Preterm or Low Birth Weight Infant**. World Health Organization; 2022.

48. Nsereko E, *et al*.: **Consideration of cultural practices when characterizing the vaginal microbiota among African and African American women**. *Biol Res Nurs* 2021, **23**:91-99.