Original article

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PROPIONIBACTERIUM ACNES PHYLOGENETIC TYPE III IS ASSOCIATED WITH PROGRESSIVE MACULAR HYPOMELANOSIS

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Progressive macular hypomelanosis (PMH) is a skin disorder that is characterized by hypopigmented macules and usually seen in young adults. The skin microbiota, in particular the bacterium *Propionibacterium acnes,* is suggested to play a role.

Here, we compared the *P. acnes* population of 24 PMH lesions from eight patients with corresponding nonlesional skin of the patients and matching control samples from eight healthy individuals using an unbiased, culture-independent next-generation sequencing approach. We also compared the *P. acnes* population before and after treatment with a combination of lymecycline and benzoylperoxide.

We found an association of one subtype of *P. acnes,* type III, with PMH. This type was predominant in all PMH lesions (73.9% of reads in average) but only detected as a minor proportion in matching control samples of healthy individuals (14.2% of reads in average). Strikingly, successful PMH treatment is able to alter the composition of the *P. acnes* population by substantially diminishing the proportion of *P. acnes* type III.

Our study suggests that *P. acnes* type III may play a role in the formation of PMH. Furthermore, it sheds light on substantial differences in the *P. acnes* phylotype distribution between the upper and lower back and abdomen in healthy individuals.

Keywords: progressive macular hypomelanosis, *Propionibacterium acnes, Cutibacterium acnes,* next-generation sequencing, subtype III, skin microbiota, single locus sequencing type, phylotype

Abbreviations: PMH, progressive macular hypomelanosis; SLST, single-locus sequencing typing; ST, sequence type; NGS, next-generation sequencing; BPO, benzoylperoxide

Introduction

Progressive macular hypomelanosis (PMH) is characterized by symmetric nonscaly hypopigmented skin areas that are predominantly visible in the sebaceous areas of the trunk. In the lower back and abdomen, discrete lesions are distinguished while they are more confluent on the upper trunk. There is no inflammation, pain, or itching associated with PMH, but the disease can have a major psychosocial effect on patients. PMH appears to be more frequent in young women, and although the disorder has a worldwide distribution, it is most often identified in dark-skinned populations [1–3].

Several treatment modalities are used against PMH including topical benzoylperoxide 5% (BPO) and clindamycin 1% alone or in combination with ultraviolet A (UVA) or narrow band ultraviolet B (UVB) irradiation [4–7], oral lymecycline in combination with topical BPO 5% for 3 months [8], and low-dose isotretinoin for 1 month [9]; however, the ideal treatment is not yet defined.

The etiology of PMH is not known; however, several studies indicate that the Gram-positive anaerobic bacterium *Propionibacterium acnes* may play a pivotal role [10, 11]. Biopsy specimens from PMH lesions contained *P. acnes* in pilosebaceous ducts in contrast to biopsies

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from healthy skin [11], real-time PCR showed a significant predominance of *P. acnes* in lesional skin as compared to nonlesional skin [10], and red fluorescence was detected in lesions when subjected to Woods light [11]. Finally, antibacterial treatment effective against *P. acnes* leads to repigmentation [4, 8]. It is not known how *P. acnes* could induce hypopigmentation. Using microscopy, a decrease in melanin production and a change in the distribution of melanosomes with a resultant decrease in epidermal melanin was shown in PMH lesions [12, 13].

Based on multilocus sequence typing (MLST) and single-locus sequence typing (SLST) schemes and complete genome sequencing, the population of *P. acnes* has been shown to consist of several phylogenetic subtypes commonly designated IA1, IA2, IB, IC, II, and III [14–21]. A previous study based on bacterial cultivation has indicated that certain subtypes of *P. acnes* may be associated with PMH: an abundance of a specific but unidentified type of *P. acnes* was observed in PMH lesions that is different from *P. acnes* types isolated from acne lesions [22]. Recently, we cultured *P. acnes* isolates belonging to the otherwise uncommon type III from lesions of PMH patients and sequenced their genomes [23], and a very recent study revealed an abundance of *P. acnes* type III in bacterial cultures from lesional skin in 14 of 34 PMH patients [24].

In the present study, the type distribution of the entire population of *P. acnes* in affected and unaffected skin areas of PMH patients, including samples after treatment, and matching control samples was determined using a culture-independent next-generation sequencing (NGS)-based SLST approach. Results show a strong association of *P. acnes* type III with disease.

Materials and methods

Patient and control cohort, treatment regimen

Eight patients with PMH were recruited by voluntary consent in a private dermatology practice in Aalborg, Denmark. The patients were all clinically examined by a specialist in dermatology (H.B. Lomholt), and PMH was diagnosed based on the finding of clinically characteristic lesions, patient history, and a lack of *Malassezia* in microscopic inspections. All patients were female between 18 and 31 years of age (mean, 23.5 years) (see *Supplementary Table S1* online). Five of the patients were treated in a 3-month course with oral lymecycline (300 mg, daily) combined with a daily wash using a 5% BPO washing gel, and one patient used only the 5% BPO wash (see *Supplementary Table S2* online). As controls, eight healthy volunteers were recruited among students at the University of Aarhus, Denmark. They were all female between 24 and 31 years of age (mean, 26.5 years). Information regarding the study participants and treatment is summarized in *Supplementary Tables S1 and S2* online.

Sampling sites and procedure

Samples were taken in all patients from three lesional areas including the lower, middle, or upper back (depending on the position of the PMH lesions) and the abdomen, and additional samples were taken from patients in unaffected adjacent skin areas. One patient had no lesions on the abdomen and was sampled from all three positions on the back. Six of the patients were additionally sampled after treatment from the same areas as the pretreatment sample. Samples from the lower and upper back, and abdomen were taken from the eight healthy controls. In addition, samples from the forehead and the buccal cavity were taken from patients *(Fig. S1)*. Samples for NGS-based SLST were obtained by swabbing the skin firmly for 20 s with a sterile cotton swab moistened in sampling buffer (0.1% detergent [Triton X-100] in 0.075 M phosphate buffer, pH 7.9) [25]. DNA was extracted from all collected samples, and SLST fragment amplification was performed as described previously [20]. The amplicons were then subjected to next-generation sequencing (NGS) using the pyrosequencing technology. Subsequent bioinformatics analysis included quality control and sequence read assignment to the STs of the SLST scheme (http://medbac.dk/slst/pacnes), resulting in a high-resolution phylotype analysis of the *P. acnes* population in each sample.

Samples for bacterial cultivation were taken with a sterile charcoal swab moistened in sampling buffer firmly scrubbed on the skin for 20 s. From each patient, two swabs were obtained from lesional skin on the back and abdomen, respectively, and, in addition, two swabs from adjacent nonlesional skin. For a semiquantitative estimation of the number of bacteria, the primary charcoal cotton swabs were streaked on tryptone-yeast-glucose (TYG) agar plates and incubated for 120 h in an anaerobic chamber (Forma Scientific Anaerobic System model 1024).

Next-generation sequencing-based single-locus sequence typing (NGS-based SLST)

Cotton swab samples from both patients and healthy controls were transferred to 1.5-ml Eppendorf tubes, and bacterial DNA was isolated and purified using PowerLyzer® PowerSoil® DNA Isolation Kit (MO BIO, Carlsbad, CA, United States) according to the manufacturer's instruction. The isolated DNA was then subjected to amplification by PCR as described previously [20]. All primer sequences are given in *Supplementary Table S3* online. All PCR reactions were made by mixture of 5 µl DNA sample, 2.5 µl AccuPrime PCR Buffer II (Invitrogen), 1.5 µl of forward primer, 1.5 µl of reverse primer (10 µM), 0.15 µl AccuPrime Taq DNA Polymerase High Fidelity (Invitrogen), and 14.35 µl PCR-grade water into a total volume of 25 µl. All samples were amplified by an initial denaturation for 2 min at 94 °C, followed by 35 cycles of 20 s of denaturation at 94 °C, 30 s at 55 °C for annealing, and 60 s of extension at 68 °C, ending with a 5-minute step of ex-

tension at 68 °C. Three PCRs per sample were performed and verified on an agarose gel, pooled together, and purified using a NucleoSpin Extract Kit (Macherey-Nagel). The concentration of purified DNA samples was measured with a NanoDrop 2000 spectrophotometer (Thermo Scientific). The amplicons were pooled in batches of 20 and sequenced unidirectionally from the forward primer using Roche GS FLX+ pyrosequencing technology either at Institute of Microbiology and Genetics, Georg-August University Göttingen, Göttingen, Germany or at Eurofins Genomics, Ebersberg, Germany. The data were then processed using the PyroNoise implementation in Mothur v. 1.36.1 [26]. All sequences have been deposited at NCBI with the project number PRJNA347641. The sequence reads were aligned to all the known STs in the SLST database (http://medbac.dk/slst/pacnes) using BLASTn [27] and assigned an individual ST based on a best-hit model with a cut-off value of 99.5%; anything below this threshold or reads with two or more identical best hits were discarded as unassigned reads.

Sanger sequencing-based SLST of bacterial isolates

SLST typing of *P. acnes* isolates has been described previously [20]. In brief, the sampled charcoal cotton swabs were streaked on tryptone-yeast-glucose (TYG) agar plates and incubated for 72 h in an anaerobic chamber (Forma Scientific Anaerobic System model 1024). This primary culture was then examined; up to 10 random single colonies resembling *P. acnes* were selected and individually subcultivated on new TYG agar plates for 72 h under anaerobic conditions. After growth, the *P. acnes* isolates were harvested and subjected to DNA extraction by a boiling procedure at 100 °C for 10 min in 0.5 ml Eppendorf PCR tubes containing 300 µl PCR-grade water. A PCR was carried out with the SLST primers (see *Supplementary Table S3* online) as follows: 2 µl of the crude DNA extract was mixed with 1 µl of each forward and reverse primer (10 µM), 10 µl 5´-PRIME Hotmastermix (5 PRIME, Hamburg, Germany), and 11 µl of PCR-grade water. PCR conditions were as follows: initial denaturation of 40 s at 96 °C followed by 35 cycles of 35 s of denaturation at 96 °C, 40 s of annealing at 55 °C, and 40 s of extension at 72 °C, followed by a finale 7-minute extension step at 72 °C. The resulting PCR products were run on a 1% agarose gel to ensure quality and were then sequenced at GATC Biotech AG (Konstanz, Germany) with the forward and reverse SLST primers. The sequences were assembled and trimmed to the known SLST fragment size (484 bp) using MEGA v.6.06 [28]. Finally, the resulting sequences were assigned to STs using the SLST database (http://medbac.dk/slst/pacnes).

Statistical analysis

The proportions of *P. acnes* type III were compared between mean values of the three lesional sites in patients

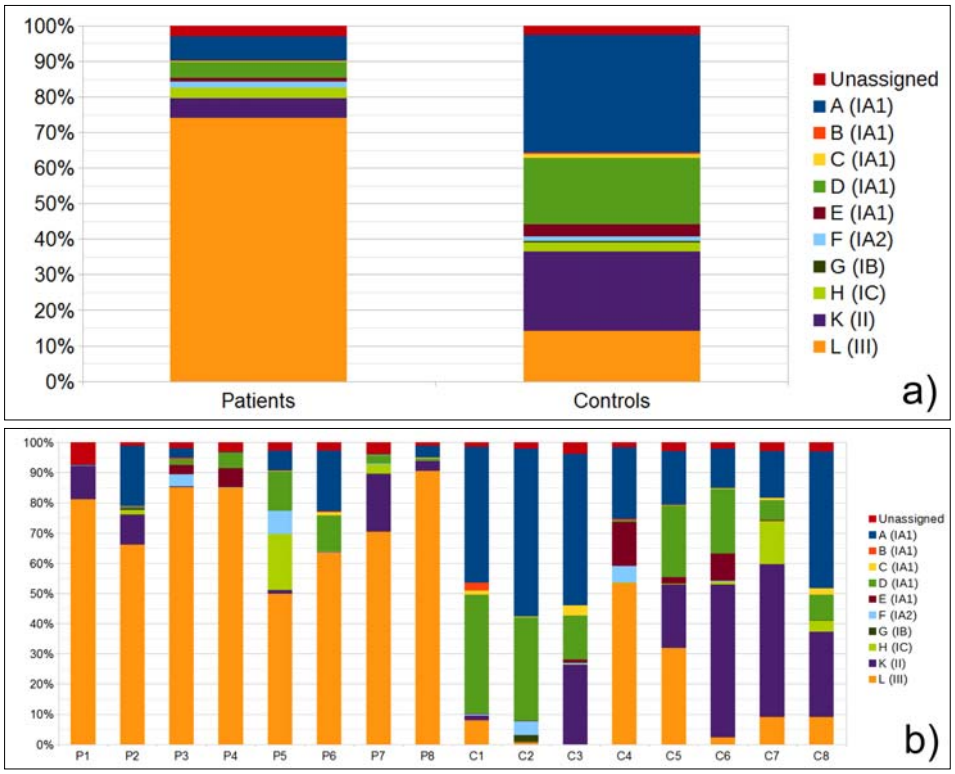

Fig. 1. Comparison of *P. acnes* ST distribution in PMH samples and controls based on next-generation sequencing data. a) Average of *P. acnes* ST proportions in patient versus controls samples. b) Each column represents ST proportions as an average of the three sampling sites (upper back, lower back, and abdomen). Data are given for eight patients, P1 to P8, and eight controls, C1 to C8. Each ST (A to L) is given a color as indicated, and the corresponding *P. acnes* subtype is given in brackets

and corresponding sites in controls using the unpaired Wilcoxon rank sum test/Mann–Whitney *U* test. Lesional sites in patients before and after treatment were compared using the paired Wilcoxon signed rank test.

Ethics statement

The study protocol was approved by the Ethics Committee of Region North, Denmark (document N-20120050), and the study was conducted according to the principles of the declaration of Helsinki. Written informed consent was obtained from all study participants.

Results

Type III P. acnes *predominates in PMH samples*

SLST amplicons from 96 samples were selected for pyrosequencing. In average, 7911 sequence reads per sample were obtained and 97% of the reads could be assigned to a *P. acnes* sequence type (ST) (see *Supplementary Table S4* online). In the whole data set, the SLST scheme distinguished 90 different STs of *P. acnes*.

The results of the *P. acnes* ST distribution in PMH lesions from eight patients and eight matching healthy controls are shown in *(Fig. 1a,b)*. A clear distinction was found when comparing PMH lesional samples to matching controls: *P. acnes* type III (the corresponding ST is designated "L") was the dominating phylotype in PMH lesions *(Fig. 1a)*; on average, 73.9% of the reads belonged to this type. In contrast, in the matching control samples, only 14.2% of the reads could be assigned to *P. acnes* type III (p value 7.8×10^{-5}). Instead, control samples contained a higher proportion of type IA1 (STs "A" to "E") strains (56.8%) and type II (ST "K") strains (22.3%), while these were found in much lower proportions in PMH lesions: type IA1 (12.8%) and type II (5.6%). Individual variation among the patients and controls was observed: the proportion of type III in the total *P. acnes* population varied between 50% and 91% in PMH lesions and between 0% and 53% in control samples *(Fig. 1b)*.

We wanted to confirm these findings with a culture-dependent technique: swab samples taken from PMH lesions and healthy controls were cultivated anaerobically. Up to 10 *P. acnes* colonies per sample were randomly selected from the agar plates; for each isolate, the classical SLST assignment by Sanger sequencing of the PCR-amplified SLST fragment was carried out. In average, 39.6% of the *P. acnes* colonies were type III in lesion samples, in contrast to only 12.5 % in controls (see *Supplementary Fig. S2* online).

P. acnes *type III in PMH patients is enriched in PMH regions and adjacent skin areas but is rarely found at other body sites*

A recent study [29] suggested that the phylotype distribution of *P. acnes* is relatively uniform and stable throughout the body. Thus, we wanted to investigate if PMH patients are also predominantly colonized by *P. acnes* type III at different body sites other than the PMH lesions. Samples from different locations including the lower and upper back, the forehead and the buccal mucosa were analyzed from patients and controls.

Type III was rarely detected on the forehead or in the buccal mucosa of patients *(Fig. 2a)*. Most patients had a mixture of different *P. acnes* types on the forehead, in particular, strains of the phylotypes IA2, IC, and II. Only one

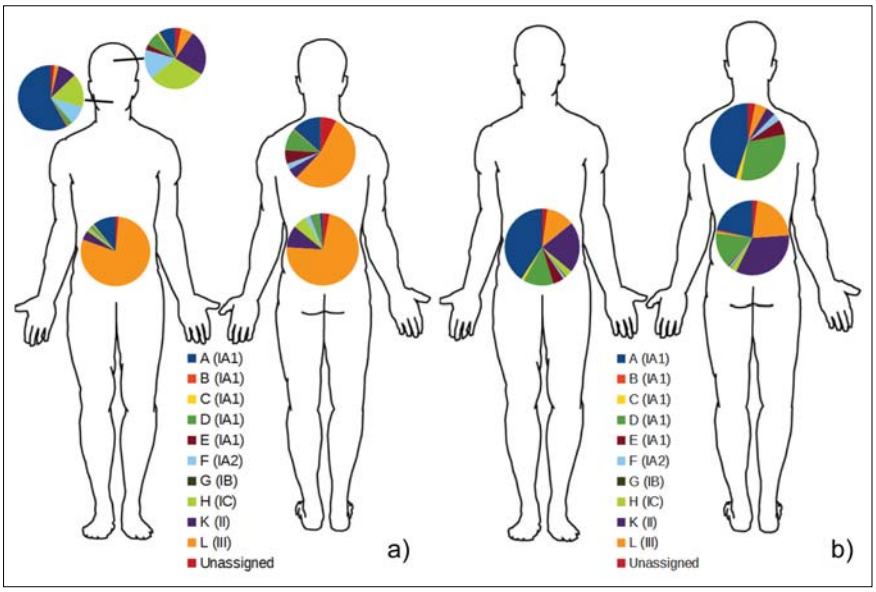

Fig. 2. Average *P. acnes* ST distribution shown for different body sites in patients and controls. a) *P. acnes* ST distribution in patient PMH lesions on lower back, upper back, and abdomen, and unaffected skin on the forehead and buccal mucosa. b) ST distribution in controls at sites corresponding to patient lesions on lower back, upper back, and abdomen. Each ST (A to L) is given a color as indicated, and the corresponding *P. acnes* subtype is given in brackets

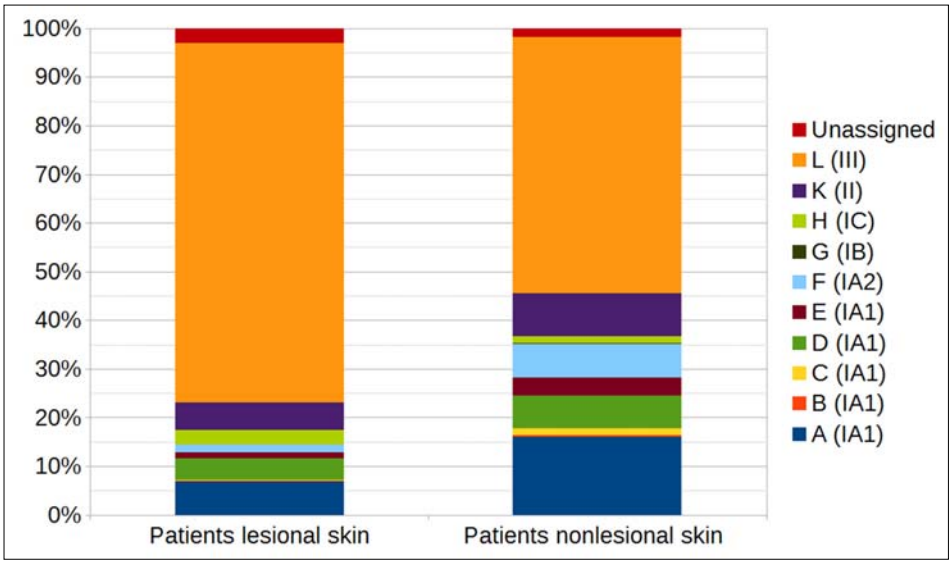

Fig. 3. Comparison of average *P. acnes* ST distribution in PMH patients in lesional versus nonlesional skin based on next-generation sequencing data. Each ST (A to L) is given a color as indicated, and the corresponding *P. acnes* phylobtype is given in brackets

patient was found to have a significant proportion of type III *P. acnes* on the forehead. On the buccal mucosa, type IA1 was predominant in most patients.

Looking at the *P. acnes* phylotype distribution of patients on nonlesional skin sites, a dominance of type III strains was detected, albeit at a lesser extent than on lesional skin, 53% versus 74%, respectively *(Fig. 3)*.

Healthy individuals were analyzed as well. Interestingly, in average, we could detect a larger proportion of type III strains (21.7%) on the lower back skin compared to the upper back skin (5.0%), indicating that the lower back is the preferred habitat for type III strains *(Fig. 2b)*. The dominant *P. acnes* type on the lower back skin of healthy controls was type II (33.5%), a type that was rarely detected on the upper back (4.0%). The dominating type of the upper back and the abdomen was type IA1 (44.7% and 40.6%, respectively).

PMH treatment alters the P. acnes *population and diminishes the proportion of type III strains*

Next, we wanted to investigate how the treatment of PMH with a combination of lymecycline and BPO might alter

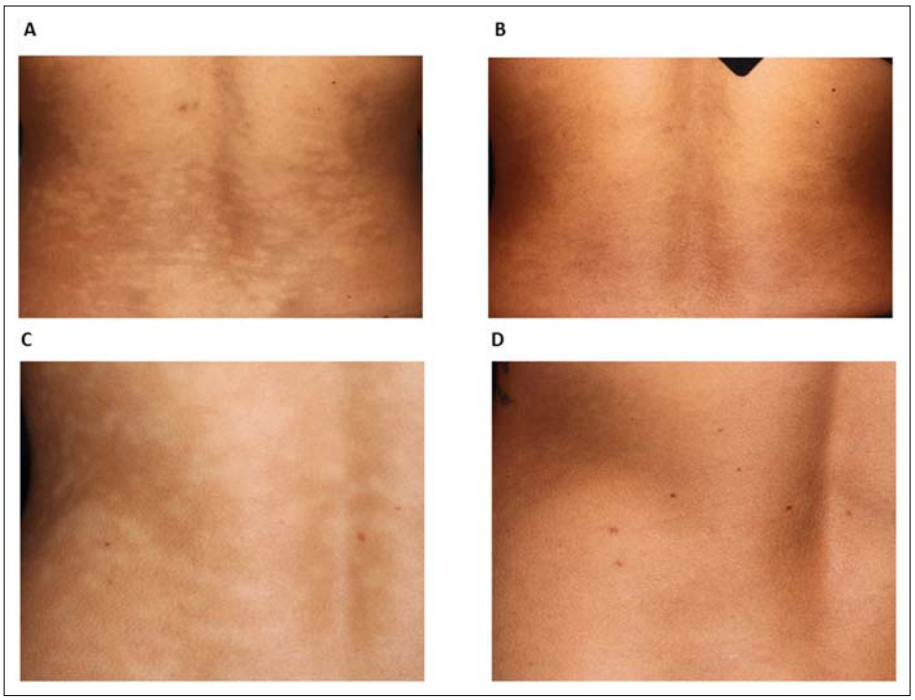

Fig. 4. Clinical PMH treatment responses. Lesional skin on the back before and after treatment with lymecycline 300 mg and BPO daily washes for 3 months shown for patient P2 (A and B) and patient P4 (C and D)

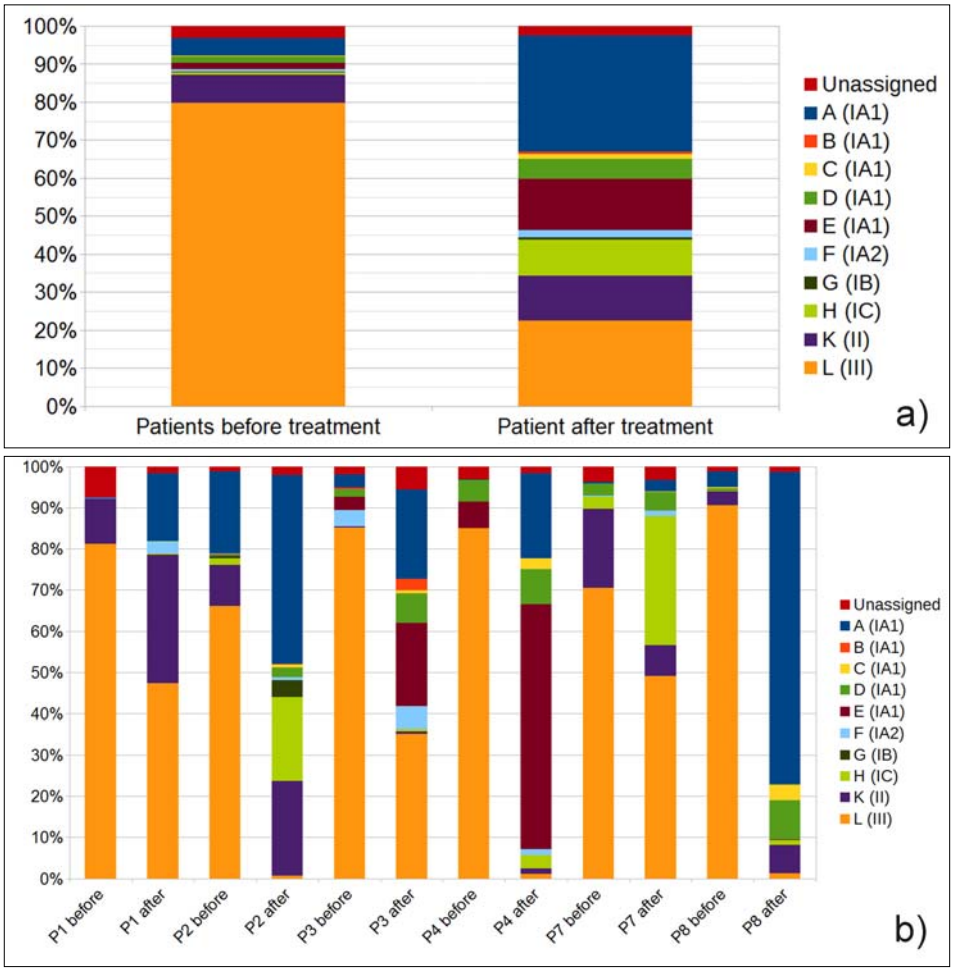

Fig. 5. Comparison of *P. acnes* ST distribution in PMH patients before and after treatment based on next-generation sequencing data. a) Average *P. acnes* ST proportions in patient samples before and after treatment. b) Each column represents ST proportions as an average of the three sampling sites (upper back, lower back, and abdomen). Data are given for six patients before and after treatment. Each ST type A to L is given a color as indicated, and the corresponding *P. acnes* subtype is given in brackets

the *P. acnes* type distribution. Six patients were treated for 3 months, and samples were taken before and after treatment from the same skin location. Information about the treatment regimen and the response for each patient is

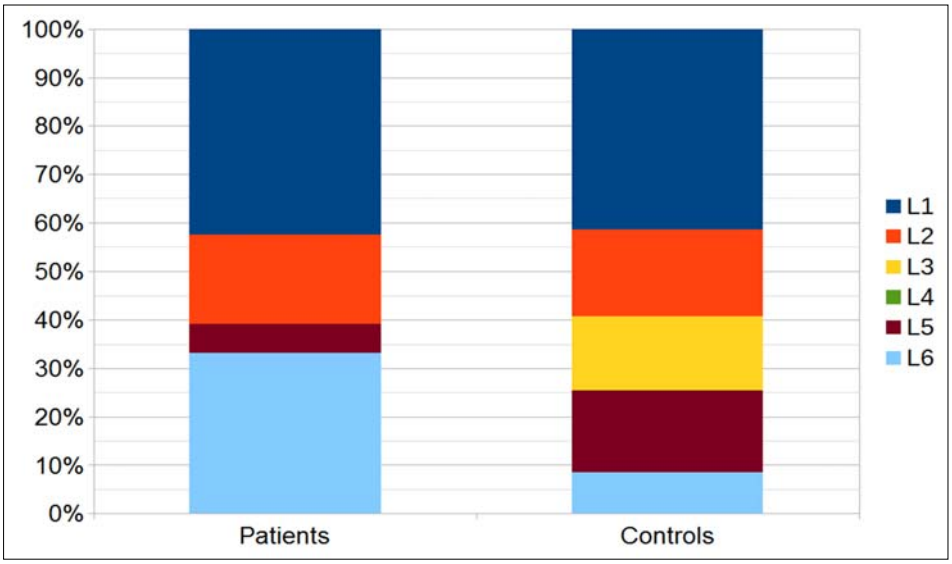

Fig. 6. Comparison of average ST distribution among *P. acnes* subtype III strains in PMH patients versus controls based on next-generation sequencing data. Each type III ST (L1 to L6) is given a color as indicated

given in *Supplementary Table S2* online. Representative images of the back skin of two patients who responded well to the treatment are shown *(Fig. 4)*.

We could detect a striking reduction of the proportion of type III *P. acnes* from an average of 80% before treatment to 22% after treatment ($p = 0.015$) *(Fig. 5a)*. In all six patients, the type III proportion was diminished after treatment in PMH-affected skin sites. In three patients (P2, P4, and P8), the type III population was almost completely eradicated after treatment *(Fig. 5b)*. Interestingly, these three patients showed a particular good response to the treatment with almost no remaining PMH lesions. The type distribution after treatment resembled in average the one detected in controls samples *(Fig. 1b)*. In contrast, in patients with a less good treatment response, a substantial type III population could be still detected *(Fig. 5b)*.

Existence of a specific type III linage associated with PMH lesions?

Since type III strains were also detected, albeit fewer, in healthy samples, in particular on the lower back skin, we wanted to investigate if PMH-associated type III strains belong to a specific lineage that is different from health-associated type III strains. Our SLST scheme can differentiate six STs within the type III lineage. The analyses showed that PMH-associated type III *P. acnes* belong predominantly to the STs L1 (56%) and L6 (25%); the latter ST was detected at lower rates among health-associated type III *P. acnes* (9%) *(Fig. 6)*. Overall, our data do not reveal a clear-cut difference between the type III populations of healthy and PMH-affected individuals.

Discussion

We report the hitherto most detailed data on the distribution of *P. acnes* subtypes on multiple skin sites on eight PMH patients and eight healthy controls, using a highly discriminative NGS-based SLST approach. The study revealed an association of one particular type of *P. acnes,* the phylotype III, with the skin disorder progressive macular hypomelanosis. Moreover, an indication that subtype III is involved in the PMH disease pathogenesis was revealed by the comparison of patient samples before and after treatment: therapy with lymecycline and BPO, both highly active against *P. acnes,* led to a diminished proportion of type III, which was paralleled by the disappearance of clinical PMH lesions.

The applied NGS-based SLST approach gave an average of 7911 reads per sample with 97% of reads assigned to known *P. acnes* STs. This provided a robust basis for a high-resolution estimate of the type distribution in each sample. Though this technique is regarded as less biased than culture-dependent techniques, a PCR bias due to disproportional amplification of certain sequences cannot be ruled out. Therefore, up to 10 randomly selected colonies were cultured from samples and analyzed by traditional Sanger sequencing for comparison. Importantly, the dominance of type III strains in PMH lesions as compared to controls was consistent in both techniques.

P. acnes subtype III was first reported as a new phylogenetic type in 2008 based on four strains isolated from spinal intervertebral disc material [17]. In addition, subtype III isolates were recently detected in surgically excised lumbar disc herniations from 5 of 24 patients [30]. Subtype III bacterial cells differ from other *P. acnes* types in showing a long filamentous morphology reminiscent of *Propionibacterium propionicum*. Subtype III differs also in biochemical tests, matrix-assisted laser desorption–ionization time-of-flight mass spectrometry (MALDI-TOF MS) spectra, and genetic markers; thus, it was recently proposed as a new subspecies with the name *P. acnes* subsp. *elongatum* [31]. This subtype has rarely been cultured from healthy controls, opportunistic infections, or acne patients [14, 16, 18, 32]. In contrast, the present study showed a striking predominance of subtype III in PMH lesional samples from the lower, middle, and upper back, and abdomen. This corroborates the previous finding of a unique, unidentified *P. acnes* type in PMH patients [22], and the recent report that type III strains were cultured from lesions of 14 of 34 PMH patients [24].

The NGS-based SLST approach provided no data on the presence of other bacterial species or the total bacterial numbers but only on the proportional distribution of *P. acnes* subtypes. Previous studies have found a highly significant increase in *P. acnes* numbers in PMH lesions [11, 24]. In accordance, we could also confirm that *P. acnes* is more abundant in lesions compared to nonlesional skin: a semiquantitative analysis revealed that all PMH samples from patients had a higher colony-forming unit count as compared to adjacent nonlesional skin (data not shown). As in other studies, no *Malassezia* fungus was detected and only few bacteria of other species, mainly *Staphylococcus epidermidis*, were found.

Our study revealed a high proportion (74%) of *P. acnes* type III in lesional skin and also a relatively high proportion (53%) of type III isolates in adjacent nonlesional skin of the patients. In contrast, Barnard et al. cultured *P. acnes* from nonlesional skin in only one of 34 patient samples, indicative of low *P. acnes* numbers in nonlesional skin. Therefore, the type distribution at normal skin sites could not be assessed in their study [24]. In addition, the difference may reflect different sampling and sample processing approaches in the two studies. Barnard et al. cultivated bacteria from a homogenized 4-mm punch skin biopsy sample, whereas we used surface skin swabs from a circular area of approximately 1.5 cm in diameter. We noticed that it is difficult to completely separate lesions from adjacent nonlesional skin sites as lesions may be small and plenty and not well defined. This may explain the relatively high proportion of type III strains in nonlesional skin of patients in the present study. Normal controls harbored only a minor proportion of *P. acnes* type III on corresponding skin sites.

The SLST scheme can distinguish six different STs among type III strains and four of these were detected in PMH lesions with no clear differences in their relative proportions in patients and controls. Interestingly, a regional difference in prevalent type III clones was suggested, based on comparisons of PMH isolates from Europe and Brazil [24].

The mechanism leading to macular hypomelanosis is not known, but ultrastructural studies have shown less melanized and aggregated melanosomes instead of single mature melanosomes transferred from melanocytes to keratinocytes [12]. The association with *P. acnes* type III suggests that a type III-specific factor could be involved. Comprehensive comparison of type III genomes to *P. acnes* genomes of other subtypes has identified several genomic regions specific to type III genomes encoding functions such as type II secretion system, ABC transporter, inositol transport/modification, gyrase, integrase, transposase, oligopeptide transport, and processing of sugars/amino acids [24, 33, 34]. In addition, some genes are absent from type III genomes but present in all other types including hyaluronate lyase, magnesium-chelatase, iron transporter, bacteriocin, 3-isopropylmalate dehydrogenase, maltose transporter, and periplasmic binding protein. It has to be investigated in the future if and which factors of *P. acnes* type III are important in PMH pathogenesis.

At present, there is a major interest in defining the normal human skin microbiome as it is considered important for maintaining healthy skin. Several metagenomic studies have described the skin microbiome on species level, but it has become increasingly clear that subtypes within species may play important roles. Most previous *P. acnes* studies have shown a predominance of type IA1 followed by type II and IB among skin isolates derived from the face or upper back [14, 16, 18]. The present study is the most detailed study on *P. acnes* subtype distribution on different body sites. It was shown that subtype III is not normally dominant in skin areas of healthy skin; it was rarely found on the face and in the oral cavity. On healthy skin, type III is more frequent at the lower back and abdomen, together with type II, relative to other body sites.

The present study has some limitations. The number of patients and controls is low, even though many samples were analyzed from each person. In general, nonlesional skin was sampled lateral to the lesional area and, therefore, not on exactly corresponding skin areas. After treatment, faint residual lesions in three patients were detectable, even though the clinical response was satisfactory. We do not know if the bacteria most important in the disease process reside on the skin or in the follicles and the surface swab technique employed may have missed bacteria residing in follicles. Furthermore, detailed data on the total number of bacteria at each site and the presence and proportions of other microorganisms besides *P. acnes* were not obtained in this study.

In conclusion, the present study showed that *P. acnes* phylotype III is associated with PMH lesions and, therefore, may play a role in the disease pathogenesis. In the normal human microbiome, *P. acnes* subtype III appears to constitute only a minor portion, mainly residing on the lower back and abdomen, among the *P. acnes* population. The findings open for future studies of specific type III traits to further define the role of the bacterium and increase our understanding of the PMH disease pathogenesis.

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Authors' contributions

H.B.L. conceived the study idea, obtained ethical approval, included and treated the patients, and collected all bacterial samples from patients and controls. R.L.W. prepared samples for Sanger and next-generation sequencing. R.LW., C.F.P.S., and A.J. analyzed the sequencing data. R.L.W., H.B.L., and H.B. interpreted the data and prepared the draft article. All authors read, corrected, and approved the article.

Competing interests

The authors state no conflict of interest.

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Supplementary material

Table S1. Data on eight patients (P) and eight controls (C) included in the study

	Sex	Age		Sex	Age
P1	Female	19	C1	Female	28
P2	Female	24	C2	Female	31
P3	Female	18	C3	Female	27
P4	Female	22	C4	Female	26
P5	Female	24	C5	Female	25
P6	Female	31	C6	Female	25
P7	Female	29	C7	Female	26
P8	Female	21	C8	Female	24

Table S2. Treatment and treatment responses in six PMH patients treated with benzoylperoxide (BPO) daily washes and/or peroral lymecycline (LC) 300 mg once daily for three months

Patient no.	Treatment	Outcome
P1	BPO, LC	Good response with a few residual lesions
P2	BPO, LC	Good response
P3	Irregular BPO, no LC	Improved with residual lesions
P4	BPO, LC	Good response
P7	Irregular BPO, irregular LC	Good response with a few residual lesions
P8	BPO, LC	Good response

Table S3. Primers used in this study

Primers for NGS-based SLST	
SLST_PA_REV	5′-CCTATCCCCTGTGTGCCTTGGCAGTCTCAG-CCGGCTGGCAAATGAGGCAT-3′
SLST_PA_MID1	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAG-ACGAGTGCGT-CAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID2	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAG-ACGCTCGACA-CAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID3	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGAGACGCACTCCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID4	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGAGCACTGTAGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID5	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGATCAGACACGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID6	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGATATCGCGAGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID7	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCGTGTCTCTACAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID8	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCTCGCGTGTCCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID10	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTCTCTATGCGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID11	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTGATACGTCTCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID13	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCATAGTAGTGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID14	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCGAGAGATACCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID15	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGATACGACGTACAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID16	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTCACGTACTACAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID17	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCGTCTAGTACCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID18	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTCTACGTAGCCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID19	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTGTACTACTCCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID20	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGACGACTACAGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID21	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGCGTAGACTAGCAGCGGCGCTGCTAAGAACTT-3
SLST_PA_MID22	5′-CCATCTCATCCCTGCGTGTCTCCGACTCAGTACGAGTATGCAGCGGCGCTGCTAAGAACTT-3
Primers for Sanger-sequencing-based SLST	
Sanger_SLST_for	5′-CGCCATCAAGGCACCAACAA-3′
Sanger_SLST_rev	5′-ATATCGGCCCGTATTTGGGC-3′

Table S4. Next-generation sequencing data: numbers of sequence reads and ST assignment in 96 samples

Patient	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P2	P2	P2	P2	P2	P2	P2	P2	P2	P3	P3	P3	P3
Sampling spot	LB	LB	UB	UB	ABD	F	M	2-LB	2-UB	2-UB	2-ABD	LB	LB	MB	ABD	F	2-LB	2-MB	2-ABD	2-A	LB	LB	UB	UB
Number of reads	6661	10951	3840	5336	10036	14883	781	3938	5059	690	6379	4974	4383	9758	3189	7728	3760	3046	2485	185	10144	7440	2064	5196
Number of assigned reads	6341	10762	3175	5250	9992	14715	760	3872	5002	685	6245	4928	4330	9697	3127	7641	3665	2972	2450	184	10023	7315	1999	5121
% unassigned reads	4.80	1.73	17.32	1.61	0.44	1.13	2.69	1.68	1.13	0.72	2.10	0.92	1.21	0.63	1.94	1.13	2.53	2.43	1.41	0.54	1.19	1.68	3.15	1.44
Unassigned	320	189	665	86	44	168	21	66	57	5	134	46	53	61	62	87	95	74	35	1	121	125	65	75
A1	12	19	4	261	19	809	461	123	384	141	2398	16	749	86	1846	96	1535	1435	1200	4	132	1385	127	737
A2	0	0	0	0	0	22	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
A4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
A5	0	0	0	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	6
A6	0	0	0	0	0	0	0	0	1	0	2	0	2	0	1	1	3	2	19	0	2	3	0	5
A7	0	0	0	4	0	6	1	0	2	0	0	0	0	0	20	0	0	6	0	0	0	0	0	0
A8	0	0	0	0	0	2	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0
A9	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	0	0
A10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A11	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0
A12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A13	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
A14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0
A16	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
A17	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	1
A18	0	2	0	3	0	0	1	0	1	0	9	0	1	0	4	0	0	0	0	0	0	8	0	0
A19	0	0	0	0	0	0	2	1	0	0	2	0	0	0	0	0	1	1	0	0	1	0	0	0
A20	0	0	0	0	0	0	2	0	0	0	3	0	0	0	2	0	1	0	0	0	0	0	0	1
A21	0	0	0	0	0	0	0	0	4	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0
A22	0	0	0	0	0	0	2	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
A23	0	0	0	0	0	0	0	0	15	0	2	0	0	0	2	0	0	1	0	0	0	2	0	0
B1	0	2	1	0	3	0	0	0	0	0	0	0	11	0	0	0	0	18	0	0	15	61	20	102
C1	0	0	0	0	1	476	1	2	1	0	3	0	6	0	11	0	7	17	26	0	0	470	1	137
C2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1
C3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
C4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1	0	0

Table S4. *(cont'd)*

Patient	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P2	P2	P2	P2	P2	P2	P2	P2	P2	P3	P3	P3	P3
Sampling spot	LB	LB	UB	UB	ABD	F	M	2-LB	2-UB	2-UB	2-ABD	LB	LB	MB	ABD	F	2-LB	2-MB	2-ABD	2-A	LB	LB	UB	UB
D1	0	0	0	0	0	1	12	0	4	0	12	0	64	8	13	4	83	113	29	0	63	289	91	504
D2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
D3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
E1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E3	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
E4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0
E7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	11	0	1	0	21	80	4	122
E8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E9	0	0	0	0	0	0	0	0	0	0	0	0	3	0	3	0	0	0	0	1	70	503	159	883
F1	0	3	0	4	1	2252	52	0	1	0	151	0	0	0	20	0	0	0	0	0	0	0	0	0
F2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F3	0	0	0	0	0	5	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0
F4	0	0	0	0	0	67	49	0	0	0	1	0	0	2	0	0	13	44	1	0	25	463	216	278
F5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
F6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0
F7	0	8	0	12	21	6897	33	8	33	0	365	0	0	0	0	0	0	0	0	0	0	0	0	0
F8	0	0	0	0	0	1	18	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	1	1
F9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G1	0	0	0	0	0	0	0	0	0	0	0	0	26	7	50	0	169	140	84	0	0	0	0	1
H1	0	0	0	22	0	4158	1	18	21	0	1	0	161	3	155	90	718	633	518	0	0	1	1	14
H2	0	0	0	0	0	5	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
H3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
H4	0	0	0	0	0	0	0	0	0	0	0	0	14	0	0	0	0	0	0	0	0	0	0	0
H5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
K1	37	7	38	3	0	0	2	0	0	0	0	4	410	60	425	6623	554	400	386	114	1	187	1	39
K2	30	5	72	20	10	0	2	0	14	1	7	0	28	1	2	148	74	21	17	7	69	0	0	0
K3	0	0	19	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0
K4	0	0	0	0	0	0	63	0	0	26	0	0	0	0	0	0	0	0	0	0	0	0	0	17

Table S4. *(cont'd)*

Patient	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P1	P2	P2	P2	P2	P2	P2	P2	P2	P2	P3	P3	P3	P3
Sampling spot	LB	LB	UB	UB	ABD	F	M	2-LB	2-UB	2-UB	2-ABD	LB	LB	MB	ABD	F	2-LB	2-MB	2-ABD	2-A	LB	LB	UB	UB
K5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	0	0	0	0	0	0
K6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0
K7	0	0	0	2	0	0	0	0	0	14	0	0	10	0	0	47	0	0	0	1	0	1	0	0
K8	800	300	620	2758	54	3	17	121	4503	472	61	0	117	19	490	623	442	109	167	57	0	9	0	0
K9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
K10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0
K13	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L1	5288	10375	2191	2002	9822	7	33	11	4	31	3177	0	2715	9503	57	0	5	23	0	0	0	0	25	3
12	149	38	145	136	56	0	0	3587	9	0	38	0	2	1	14	0	20	7	0	0	0	0	1	0
L3	0	0	14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L5	25	2	71	6	4	0	0	1	0	0	0	4907	6	5	0	0	21	0	0	0	0	0	1	21
L6	0	1	0	14	1	1	7	0	0	0	5	1	4	2	0	0	0	0	0	0	9623	3839	1349	2245

Table S4. *(cont'd)*

Patient	P3	P3	P3	P3	P3	P4	P4	P4	P4	P4	P4	P4	P4	P4-2	P5	P5	P5	P5	P5	P6	P6	P6	P6	P6
Sampling spot	ABD	F	2-LB	2-UB	2-ABD	LB	LB	MB	UB	F	2-LB	2-UB	2-UB	2-UB-2	LB	LB	ABD	CH	F	LB	LB	UB	ABD	F
Number of reads	11989	7710	11831	16240	14294	11453	5424	16143	9719	5933	4381	3373	4487	8107	668	1858	12708	6808	14254	6239	4225	7404	13528	12788
Number of assigned reads	11816	7493	11443	14467	13916	11273	5296	15702	9234	5858	4288	3316	4418	8035	643	1816	12527	6613	13176	6111	4158	7122	13245	12196
% unassigned reads	1.44	2.81	3.28	10.92	2.64	1.57	2.36	2.73	4.99	1.26	2.12	1.69	1.54	0.89	3.74	2.26	1.42	2.86	7.56	2.05	1.59	3.81	2.09	4.63
Unassigned	173	217	388	1773	378	180	128	441	485	75	93	57	69	72	25	42	181	195	1078	128	67	282	283	592
A1	266	908	5007	626	2666	37	1287	28	7	559	2601	29	1802	104	6	184	29	1262	324	397	967	3463	908	1883
A2	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	0	0
A3	0	0	0	0	0	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
A4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A5	0	0	0	0	0	0	0	0	0	0	1	0	3	0	0	0	0	0	0	0	0	2	8	1
A6	1	2	16	0	7	0	0	0	0	0	3	0	11	0	0	1	0	3	0	1	3	19	3	0
A7	0	1	2	1	1	0	9	0	0	0	0	1	3	0	0	0	0	1	3	0	0	4	4	0
A8	0	0	2	1	1	0	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	2	0	2
A9	0	0	1	0	1	0	0	0	0	0	1	0	3	0	0	0	0	0	0	0	0	0	0	0
A10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A11	0	0	0	0	2	0	0	0	0	0	2	0	0	2	0	0	0	0	0	1	1	0	0	0
A12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
A14	0	0	0	0	0	0	0	0	0	0	0	0	25	0	0	0	0	0	0	0	0	0	0	0
A15	0	0	1	0	0	0	0	0	0	0	5	0	0	0	0	0	0	0	0	1	1	0	0	0
A16	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A17	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0
A18	1	9	3	0	3	0	7	0	0	0	1	1	2	3	0	0	0	12	0	1	1	2	2	3
A19	2	1	0	0	2	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0
A20	0	1	1	0	1	0	0	0	0	0	6	0	0	0	0	0	0	0	0	1	0	12	1	0
A21	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
A22	0	0	1	0	1	0	0	0	0	0	0	0	0	0	0	0	0	6	0	1	0	0	0	0
A23	0	0	2	0	3	0	1	0	0	0	1	0	0	0	0	0	0	1	0	0	0	0	0	0
B1	7	41	187	1019	65	0	0	1	0	0	0	0	3	0	1	0	0	4	0	0	1	20	89	2
C1	19	35	174	47	29	0	13	1	1	10	22	5	10	1	1	0	2	42	154	0	5	25	330	244
C2	0	0	0	0	0	0	0	0	0	0	313	0	216	8	0	0	0	0	0	0	0	0	0	0
C3	0	0	1	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	18	0	0

Table S4. *(cont'd)*

Patient	P3	P3	P3	P3	P3	P4	P4	P4	P4	P4	P4	P4	P4	P4-2	P5	P5	P5	P5	P5	P6	P6	P6	P6	P6
Sampling spot	ABD	F	2-LB	2-UB	2-ABD	LB	LB	MB	UB	F	2-LB	2-UB	2-UB	2-UB-2	LB	LB	ABD	CH	F	LB	LB	UB	ABD	F
C4	0	0	2	22	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0
D1	40	32	1148	1711	177	28	269	99	1432	121	88	464	416	818	105	618	9	1583	424	475	285	1603	918	4209
D2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
D3	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0
E1	0	0	0	1	0	0	0	0	21	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E3	0	0	2	27	2	3	1	0	3	1	13	103	42	177	0	0	0	0	0	0	1	0	0	0
E4	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E5	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E7	38	38	115	849	65	93	544	221	1617	128	308	2705	1137	6920	0	0	0	0	0	0	4	0	0	0
E8	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0
E9	16	1359	1785	5413	772	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F1	0	0	1	0	1	0	1	0	0	0	22	0	0	0	0	1	0	0	11	0	0	0	0	0
F2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F4	134	790	337	882	1062	28	1532	0	2	1122	163	3	426	2	121	408	20	326	1708	2	261	13	25	603
F5	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F6	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F8	10	40	2	0	0	3	10	0	0	6	0	0	0	0	0	1	0	0	47	0	5	0	0	1
F9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F10	0	1	1	0	86	0	8	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
G1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0
H1	10	14	12	2	213	0	0	0	0	3861	415	2	105	0	272	123	576	659	9462	0	59	11	0	5195
H2	0	0	0	0	0	0	0	0	0	6	1	0	0	0	0	0	0	0	13	0	0	0	0	3
H3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	5
H4	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	1	1	1	1	0	0	0	0	0
H5	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	4	0	0	0	0	21
K1	9	3	20	0	75	0	4	0	0	4	16	0	11	0	15	126	51	72	389	0	176	0	3	0
K2	0	788	20	7	87	0	0	0	0	12	58	0	23	0	0	1	0	2	631	0	0	0	1	0
K3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table S4. *(cont'd)*

Patient	P3	P3	P3	P3	P3	P4	P4	P4	P4	P4	P4	P4	P4	P4-2	P5	P5	P5	P5	P5	P6	P6	P6	P6	P6
Sampling spot	ABD	F	2-LB	2-UB	2-ABD	LB	LB	MB	UB	F	2-LB	2-UB	2-UB	2-UB-2	LB	LB	ABD	CH	F	LB	LB	UB	ABD	F
K4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
K5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0
K7	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0
K8	4	97	6	0	41	8	0	0	0	0	100	0	11	0	0	0	0	0	0	0	0	0	0	0
K9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K11	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0
K13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L1	17	2	31	393	68	4	19	16	36	0	57	0	38	0	116	348	11721	2628	1	5217	2372	1661	10929	23
12	0	0	0	1	0	0	0	1	0	0	81	0	71	0	0	0	8	0	0	3	2	0	1	0
L3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L5	2	0	7	3	2	1	2	6	4	0	0	1	0	0	1	2	107	9	0	7	13	260	6	0
L6	11240	3330	2554	3459	8482	11051	1582	15328	6109	23	5	2	55	0	1	1	3	1	1	2	0	4	12	0

Table S4. *(cont'd)*

Patient	P6	P7	P7	P7	P7	P7	P7	P7	P7-2	P7-2	P8	P8	P8	P8	P8	P8-2	P8-2	P8-2	C1	C1	C1	C1	C2	C2
Sampling spot	M	LB	LB	MB	ABD	M	2-LB	2-LB	2-MB	2-ABD	LB	LB	ABD	F	M	2-LB	2-UB	2-ABD	LB	LB	UB	ABD	LB	LB
Number of reads	2655	4321	290	10068	8766	3223	1864	5707	9899	13630	7437	5757	10330	8430	1366	3912	10423	2636	11079	14191	9044	13576	9422	9230
Number of assigned reads	2612	3943	285	9934	8671	3179	1811	5627	9314	13499	7364	5667	10194	8187	1348	3860	10240	2609	10891	13926	8920	13378	9225	9033
% unassigned reads	1.62	8.75	1.72	1.33	1.08	1.37	2.84	1.40	5.91	0.96	0.98	1.56	1.32	2.88	1.32	1.33	1.76	1.02	1.70	1.87	1.37	1.46	2.09	2.13
Unassigned	43	378	5	134	95	44	53	80	585	131	73	90	136	243	18	52	183	27	188	265	124	198	197	197
A1	1757	2	0	53	45	687	78	1592	38	469	78	2702	680	1291	1130	2770	8093	2023	5468	12157	247	10963	2877	4718
A2	0	0	0	0	0	0	0	0	0	1	1	2	0	4	0	1	4	6	0	4	1	0	0	2
A3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	19	33	57	7	0	2
A4	0	0	0	0	0	0	0	1	0	2	0	0	0	0	0	0	5	0	0	2	3	1	0	0
A5	0	0	0	0	0	0	1	0	0	3	0	2	0	0	0	1	1	0	1	4	0	0	32	12
A6	3	0	0	0	0	0	0	4	0	7	0	6	7	13	0	4	18	1	27	25	0	9	12	5
A7	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	7	13	0	2	17	0	18	9	10
A8	0	0	0	0	0	0	0	4	0	0	0	0	0	2	0	0	3	4	1	1	0	2	3	1
A9	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	3	0	1	8	0
A10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A11	4	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	0	1	2	3	0	1	2	0
A12	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2
A13	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	1	0	1	0	0	2	1	0
A14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A15	25	0	0	0	0	0	0	0	0	0	0	2	0	0	0	0	2	0	2	0	0	4	0	0
A16	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	3	1	0	1	0	4	0	5
A17	0	0	0	0	0	0	0	0	0	2	0	5	1	0	0	0	1	0	4	4	0	0	1	0
A18	1	0	0	0	0	2	0	2	0	6	0	5	2	13	1	4	15	1	18	30	0	31	9	4
A19	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	5	0	2	0	2
A20	4	0	0	2	0	0	0	0	0	0	0	1	0	0	1	1	5	0	1	24	0	4	2	3
A21	2	0	0	0	0	0	0	0	0	0	0	0	0	1	0	1	20	1	1	27	0	1	0	1
A22	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	1	0	0	1	0	3	2	10
A23	1	0	0	0	0	0	0	0	0	0	0	1	0	2	0	0	18	1	4	17	0	1	3	20
B1	0	0	0	1	0	6	4	0	0	14	2	17	4	6	34	2	0	0	763	44	82	12	1	3
C1	0	12	0	0	0	0	1	9	4	31	6	224	42	75	0	175	371	89	62	63	8	415	14	23
C2	0	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0
C3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	0	1	1	0	13	0	1
C4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table S4. *(cont'd)*

Patient	P6	P7	P7	P7	P7	P7	P7	P7	P7-2	P7-2	P8	P8	P8	P8	P8	P8-2	P8-2	P8-2	C1	C1	C1	C1	C2	C2
Sampling spot	M	LB	LB	MB	ABD	M	2-LB	2-LB	2-MB	2-ABD	LB	LB	ABD	F	M	2-LB	2-UB	2-ABD	LB	LB	UB	ABD	LB	LB
D1	77	355	1	1	31	171	131	963	492	212	3	418	118	1324	0	486	665	251	1644	1057	8501	1332	5384	3034
D2	0	0	0	0	5	0	0	1	0	0	0	0	0	1	0	0	0	0	1	0	3	0	2	2
D3	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	2	4	0	29	1
E1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0
E3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	2	0
E4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E7	0	0	0	0	0	8	0	0	0	0	0	1	0	0	0	8	45	0	1	7	0	10	10	38
E8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E9	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
F1	0	0	0	1	0	14	4	0	0	0	0	0	0	9	0	0	0	0	120	45	0	82	304	109
F2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F4	111	11	0	3	32	384	34	522	51	197	0	3	1	0	13	3	6	0	7	5	0	1	261	380
F5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
F7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F8	0	0	0	0	0	7	0	8	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F10	0	0	0	0	0	0	0	0	1	0	0	9	0	0	0	0	0	0	0	1	0	0	3	1
G1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	190	486
H1	192	300	3	39	158	1765	391	2263	6553	931	0	65	32	772	54	61	102	17	0	4	0	0	23	8
H2	0	0	0	0	0	0	0	5	3	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
H3	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0
H4	0	0	0	0	0	0	0	0	0	0	0	1	0	66	0	0	5	0	0	0	0	0	0	0
H5	0	0	0	0	0	4	0	9	2	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0
K1	60	2342	0	33	2	49	10	212	2156	9	4	14	34	35	38	178	396	163	148	270	12	352	8	7
K2	0	124	0	0	7	2	2	2	0	21	452	242	30	3969	21	89	319	11	1	1	0	18	8	0
K3	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K4	0	0	0	0	0	0	0	0	0	0	0	55	0	32	0	0	0	0	0	0	0	0	0	0

Table S4. *(cont'd)*

Patient	P6	P7	P7	P7	P7	P7	P7	P7	P7-2	P7-2	P8	P8	P8	P8	P8	P8-2	P8-2	P8-2	C1	C1	C1	C1	C2	C2
Sampling spot	M	LB	LB	MB	ABD	M	2-LB	2-LB	2-MB	2-ABD	LB	LB	ABD	F	M	2-LB	2-UB	2-ABD	LB	LB	UB	ABD	LB	LB
K5	0	0	1	0	0	0	0	0	4	0	0	1	0	344	0	0	4	0	0	0	0	0	0	0
K6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K7	0	1	0	6	0	25	0	0	0	0	0	0	0	0	0	0	0	0	2	0	0	3	0	13
K8	348	1	0	0	0	0	0	0	0	0	1	11	0	7	47	1	6	1	10	3	0	9	3	35
K9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K11	0	1	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0
K12	0	0	0	0	0	0	0	0	0	0	0	1	0	4	0	0	0	8	0	1	0	2	0	0
K13	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L1	24	765	273	9760	8360	53	1146	26	7	11578	0	0	1	208	0	0	0	11	2513	3	0	5	0	1
12	1	0	1	4	2	0	0	0	0	0	6795	1874	9241	3	7	66	109	19	1	57	0	69	22	93
L3	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L5	0	25	4	1	1	0	5	0	0	5	1	1	1	0	0	0	0	0	9	0	0	0	0	0
L6	0	0	1	28	28	1	3	0	1	10	21	0	0	0	0	0	0	0	52	4	1	0	0	0

Table S4. *(cont'd)*

Patient	C2	C2	C3	C3	C3	C3	C4	C4	C4	C4	C5	C5	C5	C6	C6	C6	C6	C7	C7	C7	C8	C8	C8	C8
Sampling spot	UB	ABD	LB	LB	UB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD
Number of reads	10716	11233	13394	8265	19242	16172	12935	5910	13972	4298	7483	4560	14148	13528	3374	12825	6836	9334	4230	5383	5438	7202	16129	11094
Number of assigned reads	10559	10936	12988	7949	17996	15895	12806	5843	13558	4250	7313	4494	13645	13391	3303	12406	6710	9060	4083	5236	5267	7065	15614	10816
% unassigned reads	1.47	2.64	3.03	3.82	6.48	1.71	1.00	1.13	2.96	1.12	2.27	1.45	3.56	1.01	2.10	3.27	1.84	2.94	3.48	2.73	3.14	1.90	3.19	2.51
Unassigned	157	297	406	316	1246	277	129	67	414	48	170	66	503	137	71	419	126	274	147	147	171	137	515	278
A1	9314	5265	2052	2611	8947	14187	282	1235	5191	1353	2035	892	1101	446	805	690	2054	1094	704	1033	1633	1755	13979	2008
A2	0	1	0	0	0	0	0	0	0	0	2	0	0	0	0	0	1	0	0	1	0	0	2	5
A3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
A4	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A5	4	0	3	0	1	2	0	15	7	1	1	0	1	0	1	0	0	0	0	0	1	0	2	0
A6	12	13	6	6	17	10	1	5	8	3	16	3	0	0	2	1	19	6	2	0	3	3	8	0
A7	4	25	2	1	6	30	0	2	5	0	0	0	1	0	1	6	3	2	2	1	3	3	12	1
A8	9	5	0	0	0	9	0	0	0	2	3	1	0	0	0	6	0	2	0	0	4	0	12	0
A9	1	1	0	2	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3	0
A10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A11	1	0	1	0	0	2	0	0	0	0	1	0	0	0	0	1	1	0	0	0	0	1	0	0
A12	1	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	1	0	0	0	0	0
A13	1	0	0	0	0	1	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0
A14	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
A15	1	10	0	1	1	4	0	6	0	0	0	0	1	0	0	0	0	0	0	0	0	1	2	2
A16	5	0	0	0	0	14	0	0	0	0	3	2	0	0	0	0	0	0	0	0	1	0	2	1
A17	1	1	1	2	2	3	0	0	1	0	0	0	0	0	2	0	0	0	0	0	3	0	0	1
A18	42	8	7	15	4	20	1	1	9	2	1	5	0	0	0	0	4	1	4	3	5	1	10	5
A19	0	0	0	2	0	3	0	0	0	0	0	0	1	0	0	0	0	1	0	0	0	1	10	1
A20	3	1	1	0	0	5	0	0	3	0	1	0	0	0	1	1	2	1	0	3	1	0	5	0
A21	0	0	0	1	0	22	0	0	2	0	1	0	0	2	0	4	1	0	0	1	0	0	1	0
A22	0	4	0	6	15	0	0	1	2	0	9	0	0	0	0	0	1	0	3	0	0	0	1	0
A23	14	6	0	4	5	6	0	0	17	0	1	0	1	0	0	0	1	1	1	0	0	2	12	1
B1	7	2	7	0	0	1	2	9	103	9	1	0	23	0	0	0	0	0	0	0	0	0	28	8
C1	55	35	12	73	1425	377	3	16	9	5	20	42	29	0	7	6	51	124	16	1	77	334	482	215
C2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
C3	1	1	0	1	0	0	0	1	1	0	2	1	1	0	2	0	0	0	0	0	0	0	3	1
C4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Table S4. *(cont'd)*

Patient	C2	C2	C3	C3	C3	C3	C4	C4	C4	C4	C5	C5	C5	C6	C6	C6	C6	C7	C7	C7	C8	C8	C8	C8
Sampling spot	UB	ABD	LB	LB	UB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD
D1	813	4237	668	2640	6895	505	10	2	0	60	1761	1571	3364	95	447	6424	914	1101	553	69	586	785	55	1567
D2	0	1	0	0	3	0	0	0	0	0	0	1	0	0	0	0	0	2	0	0	0	0	0	0
D3	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	4	0	0	0	0	0	2
E1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E2	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E3	0	0	1	4	67	1	3	36	36	38	4	1	6	2	16	29	2	0	1	0	0	0	0	2
E4	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E6	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0
E7	16	21	1	45	440	108	197	1324	1886	1175	119	53	363	44	639	2697	356	26	30	23	0	0	1	3
E8	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	8	0	0	0	0	0	0	0	0
E9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	2
F1	33	106	48	135	1	3	3	20	0	4	1	0	0	0	0	0	25	0	0	1	0	0	0	0
F2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F4	30	609	1	3	160	3	0	82	2086	0	0	0	0	0	15	4	31	0	0	0	0	1	0	15
F5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F6	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F9	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
F10	0	42	0	0	0	0	0	0	244	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
G1	145	388	6	2	0	12	0	9	0	0	0	11	0	0	0	0	0	0	0	0	10	2	0	0
H1	0	0	8	13	0	48	1	17	2	6	40	22	20	14	12	3	207	1490	300	622	158	292	20	923
H2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	3
H3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0
H4	0	16	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	9	13	53	0	0	0	0
H5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	2	0	0	0	1
K1	0	2	3	10	1	204	1	10	0	0	416	300	56	9	17	12	649	106	1075	1920	1860	2450	259	3862
K2	0	0	4620	172	2	77	0	0	0	0	683	393	3790	12671	1184	2497	1646	4063	995	1060	34	40	8	64
K3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K4	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	0	26	0	0	0	52	53	431	30

Table S4. *(cont'd)*

Patient	C2	C2	C3	C3	C3	C3	C4	C4	C4	C4	C5	C5	C5	C6	C6	C6	C6	C7	C7	C7	C8	C8	C8	C8
Sampling spot	UB	ABD	LB	LB	UB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD	LB	LB	ABD	LB	LB	UB	ABD
K5	0	0	1	2	0	0	0	26	0	6	0	3	0	0	0	0	1	1	12	2	0	1	0	0
K6	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	1	0	0	0
K7	0	0	0	0	0	0	8	8	0	2	0	0	0	0	0	0	0	0	0	0	2	2	0	9
K8	2	20	5527	2164	2	225	0	16	0	6	10	1	3	32	29	12	296	19	22	35	48	84	13	874
K9	0	0	2	0	0	1	0	0	0	0	0	0	2	1	0	0	0	1	0	0	0	0	0	0
K10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
K11	0	0	1	0	0	0	0	0	0	0	0	0	0	1	0	1	0	0	1	1	0	0	0	0
K12	0	5	0	0	0	0	0	0	0	0	1	0	0	1	0	0	0	1	7	8	0	0	0	0
K13	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	6	0	0	0	0	0
K14	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1	0	0	0	0
L1	24	1	3	31	2	5	12275	2992	3930	1572	357	188	875	71	116	0	126	35	32	105	0	0	0	0
12	19	109	0	1	0	1	3	1	0	1	27	26	11	0	0	0	0	20	89	158	48	17	1	26
L3	0	0	0	0	0	0	0	0	0	0	1688	891	3859	0	0	0	0	576	208	128	0	0	0	0
L4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
L5	0	0	0	0	0	0	2	3	9	0	108	87	88	0	1	0	283	1	0	0	737	1235	251	1182
L6	0	0	2	1	0	0	13	2	6	4	1	0	48	1	4	0	5	371	4	5	0	2	0	1

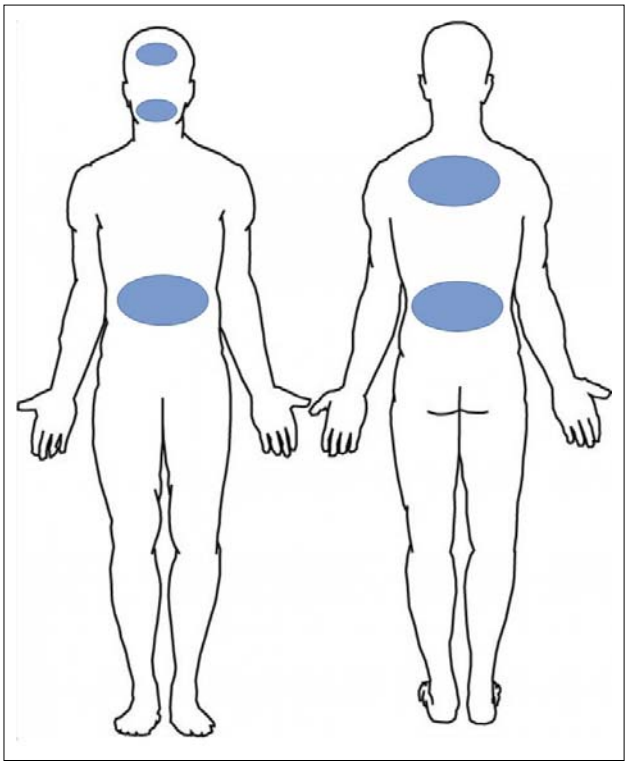

Fig. S1. Sampling sites in patients and controls. Patients were sampled from lesional skin on lower back, upper back, and abdomen and adjacent non-affected skin. In addition, unaffected skin of the forehead and buccal mucosa were sampled. After treatment and in healthy controls samples were obtained from areas corresponding to lesions

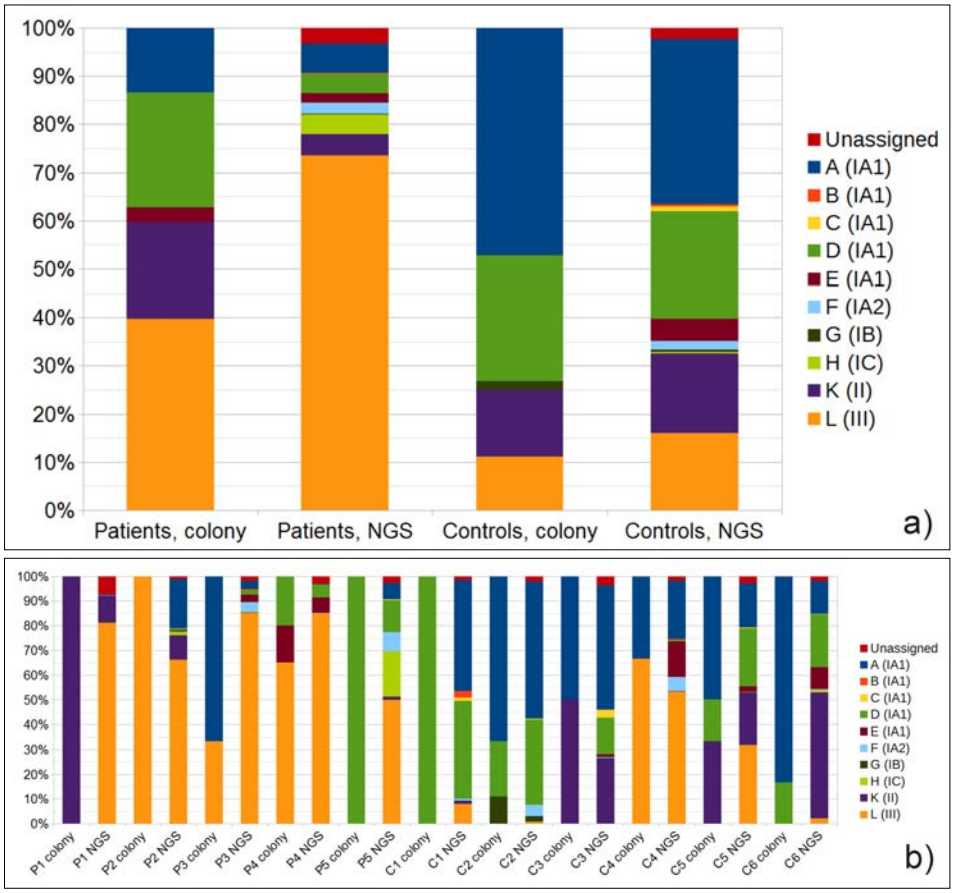

Fig. S2. Comparison of two methods of *P. acnes* ST distribution analysis: cultivation and subsequent SLST of up to 10 colonies per lesion versus next-generation sequencing (NGS)-based SLST. a) Average ST proportions in patient and control samples analysed by culture versus NGS. b) Culture versus NGS determination of ST proportions shown for individual patients and controls. Each ST type A to L is given a color as indicated, and the corresponding *P. acnes* subtype is given in brackets