



ORIGINAL ARTICLE

Phenotypic and molecular characterization of *Staphylococcus aureus* isolates conducted in nares of psoriatic patients attending a public hospital in Argentina



Carina A. Boncompain^a, Cristian A. Suárez^{a,b}, Mario Squeff^c, Valeria Belluzo^c, Gustavo Piccirilli^c, Ana Molteni^c, Ramón A. Fernández Bussy^{c,*}, Héctor R. Morbidoni^{a,d,*}

^a Laboratorio de Microbiología Molecular, Facultad de Ciencias Médicas, Universidad Nacional de Rosario, Santa Fe 3100, Rosario, Argentina

^b Consejo Nacional de Investigaciones Científicas y Tecnológicas, CONICET, Argentina

^c Cátedra de Dermatología, Facultad de Ciencias Médicas, Universidad Nacional de Rosario, Santa Fe 3100, Rosario, Argentina

^d Consejo de Investigaciones, Universidad Nacional de Rosario, Maipú 1065, Rosario, Argentina

Received 4 April 2021; accepted 14 February 2022

Available online 25 June 2022

KEYWORDS

Staphylococcus aureus;
Nasal carriage;
Psoriasis;
Strain specificity;
Antibiotic resistance

Abstract Although *Staphylococcus aureus* increases its relative abundance in psoriasis when compared with the microbiome of healthy subjects, it is not the most important microorganism underlying this disease. However, there is scant data on the role and molecular features of *S. aureus* strains in psoriasis; therefore, the aim of this study was to evaluate nasal carriage of this microorganism, its phenotypic and molecular characteristics as well as the impact of host factors on its carriage in psoriatic patients. The presence of *S. aureus* was analyzed in nasal swabs from 46 healthy volunteers and 50 psoriatic patients by conventional microbiology techniques. Nasal carriage of *S. aureus* was higher in psoriatic patients than in the control group (37.24% vs 22.98%, respectively), being associated to sex (male), age (adults) and severity of the disease (more frequent in moderate and severe cases). Determination of antibiotic resistance detected 12% of β -lactam resistant isolates, with variable accompanying resistance to macrolides, aminoglycosides and fluoroquinolones. No resistance to rifampicin, vancomycin, mupirocin or trimethoprim/sulfamethoxazole was found.

* Corresponding authors.

E-mail addresses: fbussy@gmail.com (R.A. Fernández Bussy), morbiatny@yahoo.com (H.R. Morbidoni).

A preliminary molecular characterization of the isolates was performed by PCR amplification of virulence genes. Molecular characterization of the strains did not reveal a predominant strain in psoriatic patients. Although we established host factors related to increased carriage of *S. aureus* in psoriatic patients, we could not establish the predominance of one type of strain. Genomic and transcriptomic analysis of the isolated strains would be necessary to address this point.

© 2022 Asociación Argentina de Microbiología. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

PALABRAS CLAVE

Staphylococcus aureus;
Portación nasal;
Psoriasis;
Especificidad de cepa;
Resistencia a antibióticos

Caracterización fenotípica y molecular de aislamientos de *Staphylococcus aureus* portados en narinas de pacientes con psoriasis que concurren a un hospital público en Argentina

Resumen A pesar de que *Staphylococcus aureus* incrementa su abundancia relativa en la psoriasis cuando se compara con el microbioma de personas sanas, no es el microorganismo más importante subyacente a la enfermedad. Sin embargo, existen pocos datos sobre el papel y las características moleculares de las cepas de *S. aureus* en pacientes con psoriasis. Nuestro objetivo fue evaluar la portación nasal de este microorganismo, sus características fenotípicas y moleculares, y el impacto de factores del hospedador sobre dicha portación en estos pacientes. Se analizó la presencia de *S. aureus* en hisopados nasales de 46 voluntarios sanos y 50 pacientes con psoriasis mediante técnicas microbiológicas convencionales. Se encontró mayor portación en pacientes con psoriasis que en el grupo control (37,24% vs. 22,98%, respectivamente) y esta estuvo asociada al sexo (masculino), la edad (adultos) y la gravedad de la enfermedad (más frecuente en casos moderados a graves). El 12% de los aislamientos de *S. aureus* mostraron resistencia a betalactámicos, con resistencia acompañante a macrólidos, aminoglucósidos y fluoroquinolonas en grado variable. No se encontró resistencia a rifampicina, vancomicina, mupirocina o trimetoprima/sulfametoxazol.

Se realizó una caracterización molecular preliminar de los aislamientos por amplificación de genes de virulencia mediante PCR. Si bien se identificaron factores relacionados con el hospedador que incrementan la portación nasal de *S. aureus* en pacientes con psoriasis, la caracterización molecular de las cepas no reveló ninguna característica genotípica predominante asociada a esta afección. Se necesitan más estudios genómicos y transcriptómicos para profundizar en esta caracterización.

© 2022 Asociación Argentina de Microbiología. Publicado por Elsevier España, S.L.U. Este es un artículo Open Access bajo la licencia CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Introduction

Psoriasis (PS) is a chronic inflammatory skin disease that affects 1–3% of the world population irrespective of age or sex, causing a significant impact on the social and working life of psoriatic patients because of the clinical lesions caused by the disease²⁴. Current understanding of its etiology indicates that psoriasis is multi-factorial in origin, with patient genetics, lifestyle and diet contributing to its development and clinical manifestations. From the skin cell biology perspective, an increase in Th7 response has been shown as a key factor in the inflammation process as well as in the proliferation of keratinocytes. For several years the role of microorganisms in the onset and severity of this disease and other chronic inflammatory diseases such as atopic dermatitis (AD) has been discussed. Highly discriminative techniques such as transcriptomic and nucleic acid deep sequencing along with powerful bioinformatics tools are now

producing information on the role of the skin microbiome in AD and PS³⁰. A recent report clearly showed differences between the skin microbiome of AD and PS patients, with *Staphylococcus aureus* being the most predominant bacteria present in the former; however, despite being at increased levels than in healthy volunteers, were less important in the global microbiome imbalance in PS⁵. However, so far, there is only one study on *S. aureus* strains specifically present in PS⁹.

S. aureus frequently colonizes human and animal bodies without signs of overt infection. It is a formidable and versatile pathogen capable of producing various exotoxins such as Panton-Valentine leukocidin (PVL) and enterotoxins, their expression along with that of other virulence traits is positively regulated by *agr* (accessory regulatory gene system). *agr* is a global regulator that controls the expression of many virulence factors present in *S. aureus*. It is known that a functional form of *agr* is associated with the

expression of toxins while the non-functional form is associated with the expression of adhesins. While genes related to colonization are under negative regulation by *agr*, by switching *agr* expression on/off, *S. aureus* changes its lifestyle from a colonizing-prone behavior to a loose, disseminated form³¹.

The increasing antibiotic resistance (especially against β -lactams) displayed by this pathogen is becoming a major problem in public health. A novel Penicillin Binding Protein (PBP) designated as PBP2A encoded by the *mecA* gene, was identified as conferring broad β -lactam antibiotic resistance²⁷. This gene is carried on a mobile genetic element (*Staphylococcal* cassette chromosome *mec*, *SCCmec*) containing two discrete regions, *mec* and *ccr* (cassette chromosome recombinase) linked by a region designated as J (Junkyard)²⁷. The classification of predominant circulating strains is often based on the analysis of *SCCmec*, *spa* type and the presence of genes encoding toxin and virulence factors⁶.

Although the role of *S. aureus* as a component of the unbalanced microbiome in AD and psoriasis has been studied, so far, there are no studies on whether a specific *S. aureus* genotype is predominant in psoriatic patients. As an initial step toward that goal, we herein report the isolation and characterization of *S. aureus* from a cohort of PS patients and a control group attending a public major hospital in Rosario, Argentina. Although preliminary, this is the first report on this subject in South America and will warrant future studies on the pathogen features responsible for the differences between fast evolving infections and diseases where *S. aureus* is chronically present.

Materials and methods

Study cohort

A convenience sample of fifty adult patients with plaque psoriasis (25 men and 25 women) treated at Hospital Provincial del Centenario, a public general hospital in Rosario, Argentina, were recruited. Moreover, 46 healthy volunteers (12 men and 34 women) attending the same hospital with no history of altered skin barrier were recruited for this case-control study. Exclusion conditions for the control group were: positive HIV screening test, cancer, or other immunosuppressive conditions, inflammatory skin conditions and antibiotic use within six months prior to sample collection. Patients were assessed via medical visits, interviews, and reviews of medical records by trained dermatologists from the Dermatology Service, Hospital Provincial del Centenario, who collected information on disease severity, comorbidities, and treatments. Samples were taken from October 2016 to October 2017. Personal and demographic data included age and sex. In the case of female volunteers, the use of oral contraceptives was not considered an exclusion factor in spite of reports indicating a possible link between persistent nasal carriage and hormonal contraceptives³⁴. Obesity has been proposed as a factor increasing *S. aureus* nasal carriage²⁵; however, none of the volunteers in our study was obese. The severity of the disease presentation was assessed based on the scores obtained for BSA (Body Surface Area), PASI (Psoriasis Area and Severity Index) and DLQI (Dermatology Life Quality Index). The

definition of moderate-to-severe disease was (PASI, BSA and DLQI > 10) and for mild psoriasis (PASI, BSA and DLQI $\leq$ 10)¹⁹. Healthy volunteers did not have a personal history of PS. This study was evaluated and approved by the Bioethics Committee from the Faculty of Biomedical Sciences, Rosario National University.

Specimen collection

Duplicate nasal swab samples were collected using individually packed, sterile cotton swabs. Study participants were asked to refrain from showering and using any substances on their skin (lotion, perfume, make-up, among others) for at least 24 h prior to sampling. Swabs were inserted in test tubes containing Stuart medium (Britania, Argentina) and taken to the microbiology lab within 2 h of sampling.

Microbiology and drug susceptibility techniques

Samples were spread on Chapman medium (Britania, Argentina) followed by incubation at 37°C for 48 h. Possible *S. aureus* isolates were confirmed by Gram stain and conventional confirmatory techniques (presence of catalase, ability to clog serum). The assessment of resistance to antibiotics was performed by disk diffusion protocols according to CLSI⁴. The antibiotics tested and concentration used were: cefoxitin (FOX, 30 μ g), ciprofloxacin (CIP, 5 μ g), erythromycin (ERY, 15 μ g), clindamycin (CLI, 2 μ g), rifampicin (RIF, 5 μ g), trimethoprim-sulfamethoxazole (TMP/SMX, 25 μ g), tobramycin (TOB, 10 μ g), gentamycin (GEN, 10 μ g), vancomycin (VAN, 30 μ g) and mupirocin (MUP, 200 μ g). In the latter two cases, the use of disks was only for the purpose of detecting susceptibility of high level resistance. For isolates that displayed resistance to ERY and susceptibility of intermediate resistance to CLI, testing for induction of inducible clindamycin resistance (ICR) was performed by disk diffusion using the D-zone test.

Molecular characterization of *S. aureus* isolates

Strain identity and their methicillin resistance was confirmed by multiplex PCR of 16S rRNA, *mecA* and *nuc* genes¹⁸. Template DNA from each isolate was obtained according to the MLST (MultiLocus Sequencing Typing) protocol as described in <https://pubmlst.org/organisms/staphylococcus-aureus/primers>. PCR amplification and analysis of chosen genes (see below) were done by standard protocols using the primers listed in Table S1. Determination of *agr* loci as type I, II, III and IV was performed by multiplex PCR^{8,9}. Detection of *ica*, *lukS/F-PV* and *sei* was carried out by using the primers described in the literature^{9,16,21}. In each case, appropriate positive controls strains (kindly provided by Dr. M. Mollerach, School of Pharmacy and Biochemistry, University of Buenos Aires) were included.

SCCmec typing was performed according to recommendations of the International Working Group on the Classification of the *Staphylococcus* Cassette Chromosome Elements (IWG-SCC, <http://www.sccmec.org>). *SCCmec* molecular typing

Table 1 Analysis of age, sex and nasal carriage in the groups under study.

	PS group	Control group
Average age (years)	47.39	38.06
Range (years)	59	49
Sex	25 male/25 female	12 male/34 female
<i>S. aureus</i> carriage	40% (20/50)	17.39% (8/46)

was assessed by determining *mec* (A, B, or C) and recombinase (*ccr*) combinations as described in Refs. 7, 12, 13, 15 (Table S1). Complex *ccr1*, *ccr2* and *ccr3* (*ccrAB*) were determined as described by Ito et al. (Table S1)¹². When needed, the presence of Tnp20 in class B *mec* was tested by using *IS1272* and *mecR1* primers (Table S1) followed by amplicon (2 kbp) purification²⁶. A diagnostic digestion with two single cutter restriction enzymes (*HindIII* and *XbaI*) was chosen to verify the insertion.

Phenotypic assays

Functionality of *agr* locus. In order to test the functionality of the *agr* operon, the evaluation of δ -hemolysin activity was made by cross-streak of the strains under assay with *S. aureus* RN4220 (a β -hemolysin producer) on Blood Agar Plates³³.

Production of biofilm. The ability to form biofilms of the strains under study was measured by a test tube adherence protocol at 37 °C on TSB supplemented with dextrose 1% (w/v) and visual inspection at 24, 48 and 72 h²³. *S. epidermidis* strain NRS101 and *S. aureus* strain Newman Δ *ica* were included as (+) and (–) controls respectively.

Statistical analysis

Statistical analysis was performed using RStudio Version 1.1.463. Odd ratio was determined using *epi.2by.2*

within the *epiR* package. Multivariate MCA (Multiple Correspondence Analysis) was obtained by FactoMineR and Factoextra packages (<https://cran.r-project.org/web/packages/factoextra/index.html>). V and Chi square test were calculated by the *catdes* function of the FactoMineR package. The adjusted ratio was calculated by the direct method, where the rate expected to be found in the populations under study – provided that all of them had the same composition according to the variable we wanted to adjust –, was calculated. A population designed as “standard”, whose segments corresponded to the factor we wanted to adjust and to which specific rates used for the same segments of the populations under study, were used. Therefore, a number of “expected” cases if the composition of each population was the same for each segment, was obtained. The adjusted rate was calculated as the ratio of expected cases by the total “standard” population²⁰. Group comparison was calculated by the Fisher test using Epi-info (v7.2). Images were edited using Inkscape version 0.92.5.

Results

Analysis of *S. aureus* nasal carriage

We determined the frequency at which *S. aureus* is carried in the nostrils of psoriatic patients compared to a healthy population. The age and sex distribution of PS and control groups as well as their nasal carriage findings are shown in Table 1. Carriage of *S. aureus* was statistically more often found in PS patients (20 out 50) than in the control group (8 out 46), with a *p* value of 0.024, an odd ratio of 3.12. Nasal carriage showed a significant difference when sex was considered, with a higher carriage in male for both groups (60% and 417%, for PS and CG, respectively) and in the different age groups (Table 2). Since age and sex are known variables linked to *S. aureus* carriage¹⁰, we used an adjusted ratio to discard the influence of those two variables; still, *S. aureus*

Table 2 *Staphylococcus aureus* carriage by age interval and sex in PS and control groups.

Group	Age groups ^a	Sex	Patient number	Total isolates	Prevalence ratio
PS	Y	M	5	4	4/5 (80%)
		F	5	2	2/5 (40%)
	A	M	4	4	4/4 (100%)
		F	5	1	1/5 (20%)
	S	M	16	7	7/16 (43.75%)
		F	15	2	2/15 (13.33%)
	Total	50	20	20/50 (40%)	
C	Y	M	4	1	1/4 (25%)
		F	10	1	1/10 (10%)
	A	M	2	1	1/2 (50%)
		F	11	0	0/11 (0%)
	S	M	6	3	3/6 (50%)
		F	13	2	2/13 (15.38%)
	Total	46	8	8/46 (17.4%)	

^a Where Y: 20–29 years, A: 30–39 and S: >40 years.

was more frequently isolated in PS patients (37.24%) than in healthy individuals (22.98%) (Fisher Test, $p < 0.05$).

Analysis of the relationship between categorical variables by Multiple Correspondence Analysis (MCA) revealed that carriage is more related to PS and male individuals, whereas the non-carriers are mainly associated with healthy and female individuals (Fig. 1A). Confidence ellipses ($p < 0.05$) around the categories (C and NC) of the variable carriage showed statistically significant differences. Correlation analysis of the variable carriage showed a significant link to the variable sex ($p = 2.15e^{-0.5}$) ($p = 1.49e^{-0.2}$) determined by the Chi square test. Moreover, the analysis of the v test parameter showed that male and PS categories were over-expressed for the carrier group (positive values), whereas female and CG categories were over-expressed for the non-carrier group (Fig. 1B). No correlation was observed for age groups and carriage, neither for PS nor CG groups (Chi square test, $p > 0.05$).

Patients (grouped upon dermatology evaluation using BSA, PASI and DLQI scores) undergoing a moderate to severe form of PS carried *S. aureus* more frequently than those having a mild form of the disease (58.33% vs 23.08% respectively; Fisher Test, $p < 0.05$) (Table 3). Further analysis showed that male patients with moderate to severe psoriasis showed a high nasal carriage (71.43%) while female patients in the equal severity group showed less nasal carriage (40%). The same analysis for groups suffering a mild form of the disease showed 45.45% and 6.67% nasal carriage respectively (Table 3). The statistical analysis of severity for each sex showed no difference (Fisher exact test. $p > 0.05$).

Antibiotic resistance in strains isolated from PS patients

We next addressed the profile of antibiotic resistance in both strains isolated from psoriatic patients and from the control

Table 3 Relationship between nasal carriage of *S. aureus* carriage and PS severity.

Nasal carriage	Sex	Severity	
		Mild	Moderate to severe
NC ^a	M	6	4
	F	14	6
MSSA	M	4	8
	F	0	2
MRSA	M	1	2
	F	1	2
Total	26	24	

^a NC = non-carriers.

group (Fig. 2A). Our findings showed that MRSA was more than twice higher in PS patients (30%) than in the control group (12.5%), followed by resistance to macrolides (35% vs 25% in each group). With regard to macrolide resistance, CLI resistance was always detected by the D-Test and in all cases, was inducible. Only one strain (PS group) was resistant to fluoroquinolones. All the strains were susceptible to RIF, TMP/SMX, MUP and VAN in agreement with our previous studies at the same hospital². Thus, based on our results, even though there were more MRSA strains in the PS group, the frequency of strains sensitive to all antibiotics is roughly the same (50%) for both groups, indicating that no significant difference in antibiotic resistance was present in both groups. Moreover, the influence of genre in *S. aureus* nasal carriage has only been observed in MSSA carriers as reported by us and others^{2,10}, whereas this influence has not been observed for MRSA carriage. The prevalence of MRSA in the PS group was 12% for both males and females, whereas for the

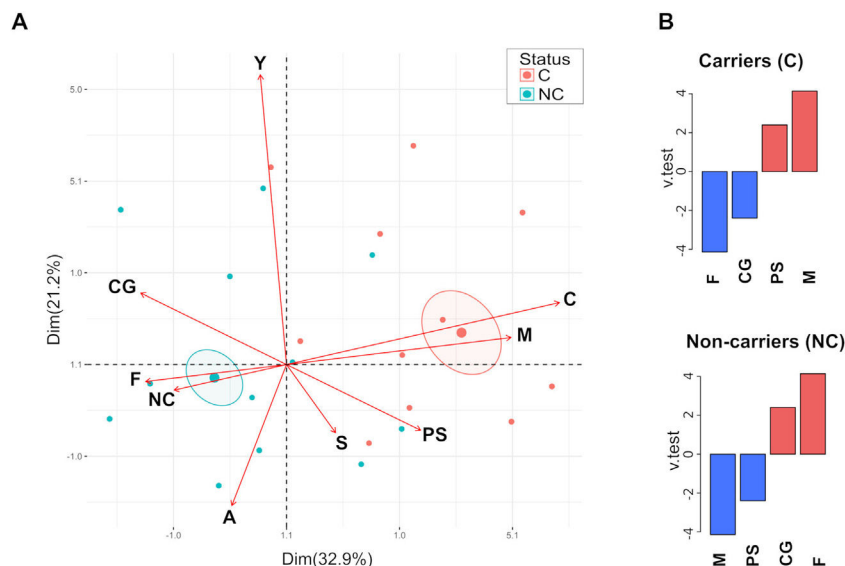


Figure 1 Multiple correspondence analysis. (A) Biplot graphic was generated by using FactoMineR and factoextra in RStudio. Variables analyzed are indicated by arrows; C = carrier, NC = non-carrier, M = male, F = female, Y = young, A = adult, S = senior, PS = psoriasis patients and CG = control group. Confidence ellipses were drawn around the mean of the carriage variable ($p < 0.05$). (B) Variable correlation was analyzed with the catdes function; down and over expressed variables (blue and red bar, respectively) were depicted for carriers and non-carrier groups.

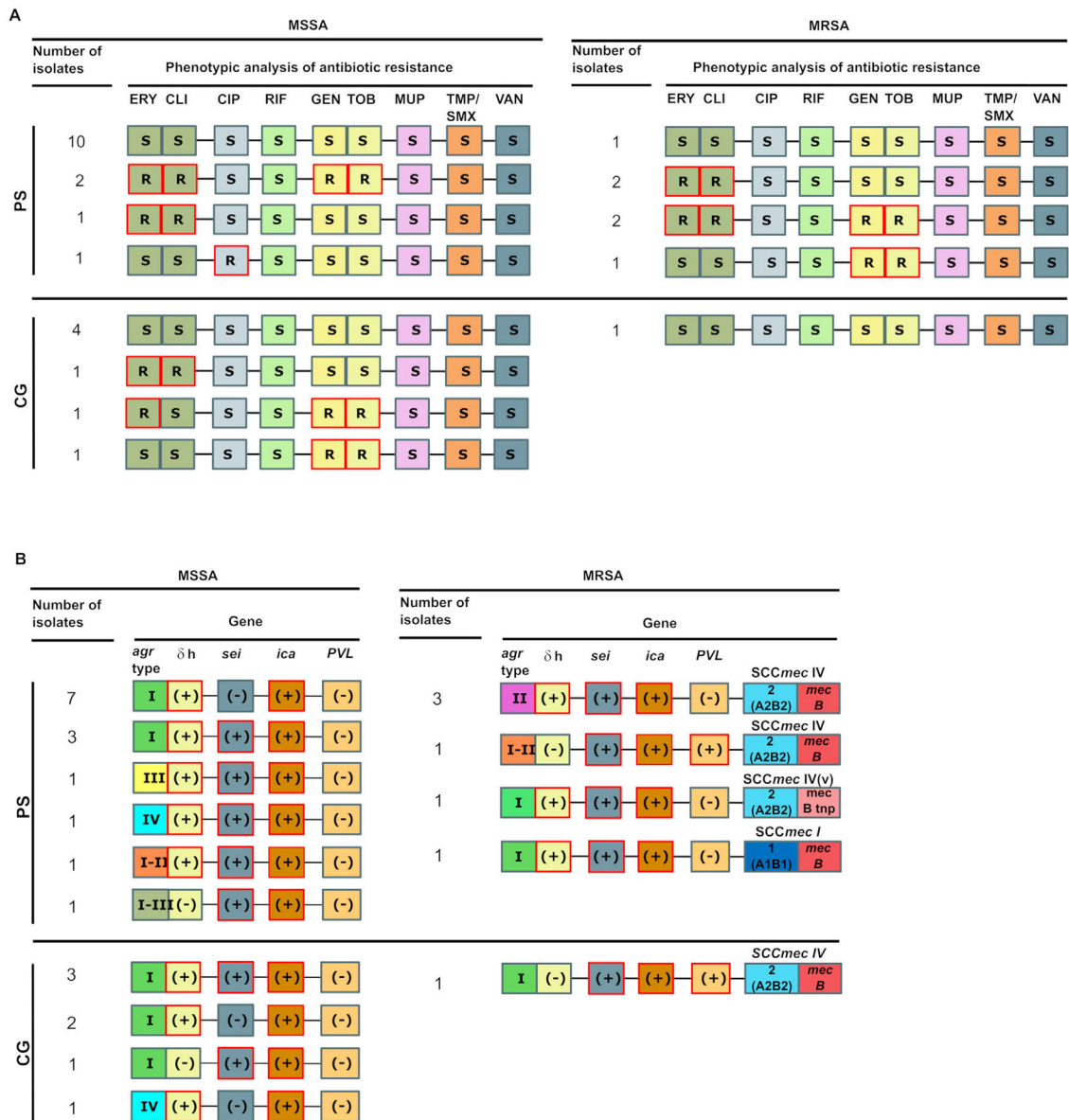


Figure 2 Schematic representation of antibiotic resistance profiles (A) and virulence genes (B) present in MRSA and MSSA isolated strains. (A) The phenotypic analysis of antibiotic resistance was carried out for MRSA and MSSA strains for each group; R and S represents resistant and susceptible, respectively. (B) The presence or absence of each feature are depicted by (+) and (-), respectively for each group. The *agr* type, δ -hemolysin activity, the presence of *ica*, *sei* and PVL genes and SCCmec type (for MRSA strains) are indicated.

control group only one MRSA strain was isolated. However, more work is necessary to address this issue (see Discussion).

Molecular characterization of *S. aureus* strains in PS patients

A full genomic typing of the *S. aureus* strain requires the detection of a large set of genes⁵ and even genome sequencing which is costly; thus, we identified the SCCmec type, the presence and expression of the *agr* locus – a global regulator of expression-, and the presence of genes relevant for virulence such as *ica*, *lukS/F-PV* and *sei* as an initial characterization of our isolates.

The typing of the SCCmec cassette in each MRSA strain showed that in the PS group five strains contained a recombinase type 2 (A2B2) and a type B *mec* gene, thus being classified as SCCmec type IV while the remaining isolate contained a recombinase type I (A1B1) and a type B *mec*, thus being classified as SCCmec type I (Fig. 2B). Of note, one of the five SCCmec type IV strains showed a *mecB* PCR product of a size larger than the expected (≈ 2000 bp versus 565 bp) due to the insertion of a genetic element related to transposase 20 (*tnp20*) as reported previously²⁶ (Fig. 3A). This was confirmed here by PCR amplification using *mecB* IS1272 and *mecR1* primers, and followed by digestion of the amplicon with *HindIII* and *XbaI*, obtaining the expected fragment sizes of 1210, 787, 129 pb and 1115 and 1015 pb, respectively

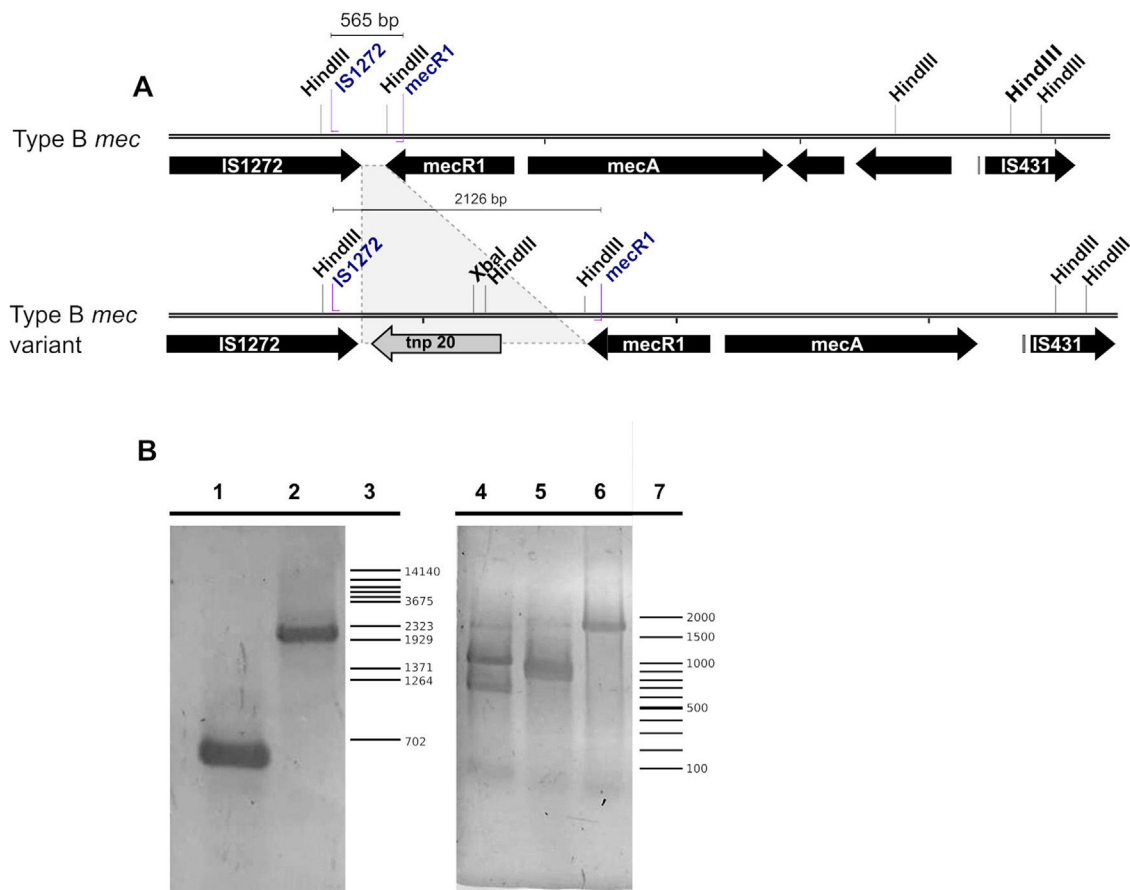


Figure 3 (A) Scheme of a typical SCCmec type IV class B element and a *tnp20* insertion variant. *HindIII* and *XbaI* restriction sites and primer hybridization sites are depicted. (B) Agarose gel of the *mecB* PCR product. Left gel, lane 1, *mecB* cassette; lane 2, *mecB::tnp20* variant; lane 3, λ /BstEII molecular weight marker. The gel on the right shows the amplicon digestion with *XbaI* (lane 4), *HindIII* (lane 5) or undigested (lane 6); lane 7, 100 bp molecular weight ladder.

(Table 1) (Fig. 3B). Only one MRSA strain from the control group was identified, which upon PCR analysis showed to contain a type 2 recombinase (A2B2) along with a class B *mec*, thus being also classified as SCCmec IV.

Sequence polymorphisms of *agr* locus yields four types (I–IV); our analysis showed that the *agr* type I loci is prevalent in the isolates of both PS and control groups (60% and 87.5%, respectively), which agrees with published reports on its frequency²⁸. Meanwhile, *agr* type II was detected only in three MRSA strain of the PS group, and a combination of two *agr* locus types I–II and I–III were only identified in strains isolated in the PS group. In most cases, *agr* was functional as judged by *agr* dependent δ -hemolysin activity (90% and 75% for PS and CG, respectively). Both the presence of *ica* and biofilm production was demonstrated in all the strains isolated from both groups. *lukS/F-PVL* was detected in only a single MRSA strain from each group (Fig. 2B).

Enterotoxins are superantigens that exacerbate the inflammatory response through polyclonal proliferation of T cells^{1,29}. The presence of *sei* (the most frequently isolated enterotoxin in strains of psoriatics patients⁹) was detected in both groups although with slightly different frequency (65% and 75%, for PS and CG groups, respectively) (Fig. 2B).

Discussion

The field of the microbiology of chronic inflammatory skin diseases is developing by the application of deep genomic sequencing, transcriptomics, metabolomics and bioinformatics. A recent example is the first detailed description of microbiome changes in AD and psoriasis as well as of global patterns of cutaneous gene expression in those patients⁵. While *Staphylococcus aureus* is the major species present in AD (with the consequent decrease in other beneficial species) and is associated to a specific skin transcriptomic signature of the host, psoriasis presents a weaker association between specific microorganisms and skin gene expression in this disease⁵. Moreover, comparable results were published by Statnikov et al., who showed that there are increases in the four major skin-associated genera (*Corynebacterium*, *Propionibacterium*, *Streptococcus* and *Staphylococcus*), both at the lesion sites and at unaffected sites in the counterpart of the body³⁰. This allowed these authors to propose “cutaneotypes” or clusters, of which cutaneotype 2 (*Firmicutes*–*Actinobacteria*) was enriched in lesions and healthy skin sites of psoriatic patients³⁰. However, although the weight of *S. aureus* in the psoriasis microbiome seems to be more diffuse than expected, the

use of genomic and transcriptomic tools has overlooked the identity of the “typical” (if any) *S. aureus* strain in psoriasis. Importantly, there are no reports on WGS for the analysis of *S. aureus* strains isolated from psoriatic patients. In order to start addressing this point, we analyzed the presence of *S. aureus* in nasal swabs of psoriatic and healthy patients. Our findings correlate with those of others -reviewed by Totte et al.³² – since we detected higher nasal carriage of this microorganism in psoriatic patients compared to the control group. Multivariate analysis showed that sex has a positive correlation with carriage in psoriatic patients, being males more frequently colonized than females). *S. aureus* carriage also correlated with the severity of the disease; contrary to what was described by Statnikov et al., who found that no specific taxa could be linked to all the degrees of severity³⁰. Differences in experimental design could explain the differences between the results of both groups.

The profile of antibiotic resistance of *S. aureus* strains isolated from PS patients and healthy individuals differed in that we found a higher proportion of MRSA carriers in the first group than in the control group (33.3% and 12.5% respectively). This result is in agreement with early reports¹⁴. Although neither group showed resistance to VAN, MUP, RIF or TMP/SMX, strains isolated from PS patients were more frequently resistant to macrolides than to fluoroquinolones.

A previous study by this group of *S. aureus* nasal carriage among health care workers at the same hospital attended by both PS and CG individuals yielded 24% MSSA and 6% MRSA² while a previous study at a different location in Argentina found 38% MSSA and 4% MRSA²². Other reports in the literature usually studied specific groups by age or occupation (i.e. patients and healthy individuals: medical students, health workers, community residents, young and senior individuals, to name a few) thus preventing direct extrapolation of our results^{3,17}; however, our findings show that the proportion of MRSA strains is clearly higher in patients suffering from psoriasis.

In summary, we have conducted a preliminary phenotypic and molecular characterization of *S. aureus* in patients suffering from psoriasis. More detailed studies addressing the molecular features (MLST, *spa* typing, toxin repertoire, resistance to methicillin) of clones present in psoriatic patients would be of value to provide a starting point to identify predominant (if any) circulating clones associated with this skin disease. A recent publication by Gregorio et al.¹¹ describing the whole genome sequencing of 190 CC30-MRSA strains circulating in Argentina provides a very well characterized framework for future work. Furthermore, a transcriptomics approach will be necessary to learn how *S. aureus* interacts with the host in this chronic skin disease. The strains isolated and reported herein would be very valuable to that end.

Conflict of interest

The authors declare that they have no conflicts of interest

Acknowledgements

Funding: This work was funded by Agencia Nacional de Promoción de la Investigación, el Desarrollo Tecnológico y la

Innovación (Agencia I+D+i), Argentina, through Grant PICT 3795-2017.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.ram.2022.02.008](https://doi.org/10.1016/j.ram.2022.02.008).

References

- Balci DD, Duran N, Ozer B, Gunesacar R, Onlen Y, Yenil JZ. High prevalence of *Staphylococcus aureus* cultivation and superantigen production in patients with psoriasis. *Eur J Dermatol*. 2009;19:238–42.
- Boncompain CA, Suárez CA, Morbidoni HR. *Staphylococcus aureus* nasal carriage in health care workers: first report from a major public hospital in Argentina. *Rev Argent Microbiol*. 2017;49.
- Chen B, Dai X, He B, Pan K, Li H, Liu X, Bao Y, Lao W, Wu X, Yao Y, Huang S. Differences in *Staphylococcus aureus* nasal carriage and molecular characteristics among community residents and healthcare workers at Sun Yat-Sen University, Guangzhou, Southern China. *BMC Infect Dis*. 2015;15.
- Cockerill FR. Performance standards for antimicrobial susceptibility testing; twenty-third informational supplement. Clinical and Laboratory Standards Institute; 2013.
- Fyhrrquist N, Muirhead G, Prast-Nielsen S, Jeanmougin M, Olah P, Skoog T, Jules-Clement G, Feld M, Barrientos-Somarribas M, Sinkko H, van den Bogaard EH, Zeeuwen PLJM, Rikken G, Schalkwijk J, Niehues H, Däubener W, Eller SK, Alexander H, Pennino D, Suomela S, Tessa I, Lybeck E, Baran AM, Darban H, Gangwar RS, Gerstel U, Jahn K, Karisola P, Yan L, Hansmann B, Katayama S, Meller S, Bylesjö M, Hupé P, Levi-Schaffer F, Greco D, Ranki A, Schröder JM, Barker J, Kere J, Tsoka S, Lauerma A, Soumelis V, Nestle FO, Homey B, Andersson B, Alenius H. Microbe-host interplay in atopic dermatitis and psoriasis. *Nat Commun*. 2019;10.
- Gardella N, Murzicato S, Di Gregorio S, Cuirolo A, Desse J, Crudo F, Gutkind G, Mollerach M. Prevalence and characterization of methicillin-resistant *Staphylococcus aureus* among healthy children in a city of Argentina. *Infect Genet Evol*. 2011;11:1066–71.
- Gardella N, von Specht M, Cuirolo A, Rosato A, Gutkind G, Mollerach M. Community-associated methicillin-resistant *Staphylococcus aureus*, eastern Argentina. *Diagn Microbiol Infect Dis*. 2008;62:343–7.
- Gilot P, Lina G, Cochard T, Poutrel B. Analysis of the genetic variability of genes encoding the RNA III-activating components Agr and TRAP in a population of *Staphylococcus aureus* strains isolated from cows with mastitis. *J Clin Microbiol*. 2002;40:4060–7.
- Göçmen JS, Şahiner N, Koçak M, Karahan ZC. PCR investigation of Panton-Valentine leukocidin, enterotoxin, exfoliative toxin, and *agr* genes in *Staphylococcus aureus* strains isolated from psoriasis patients. *Turkish J Med Sci*. 2015;45:1345–52.
- Gorwitz RJ, Kruszon-Moran D, McAllister SK, McQuillan G, McDougal LK, Fosheim GE, Jensen BJ, Killgore G, Tenover FC, Kuehnert MJ. Changes in the prevalence of nasal colonization with *Staphylococcus aureus* in the United States, 2001–2004. *J Infect Dis*. 2008;197:1226–34.
- Gregorio SD, Haim MS, Vielma Vallenilla J, Cohen V, Rago L, Gulone L, Aanensen DM, Argimón S, Mollerach M. Genomic epidemiology of CC30 methicillin-resistant *Staphylococcus aureus* strains from Argentina reveals four major clades with distinctive genetic features. *mSphere*. 2021;6.
- Ito T, Katayama Y, Asada K, Mori N, Tsutsumimoto K, Tienasitorn C, Hiramatsu K. Structural comparison of three types of staphylococcal cassette chromosome *mec* integrated in the

- chromosome in methicillin-resistant *Staphylococcus aureus*. Antimicrob Agents Chemother. 2001;45:1323–36.
13. Katayama Y, Ito T, Hiramatsu K. Genetic organization of the chromosome region surrounding *mecA* in clinical staphylococcal strains: role of IS431-mediated *mecI* deletion in expression of resistance in *mecA*-carrying, low-level methicillin-resistant *Staphylococcus haemolyticus*. Antimicrob Agents Chemother. 2001;45:1955–63.
14. Klein PA, Greene WH, Fuhrer J, Clark RAF. Prevalence of methicillin-resistant *Staphylococcus aureus* in outpatients with psoriasis, atopic dermatitis, or HIV infection. Arch Dermatol. 1997;133:1463–5.
15. Kondo Y, Ito T, Ma XX, Watanabe S, Kreiswirth BN, Etienne J, Hiramatsu K. Combination of multiplex PCRs for staphylococcal cassette chromosome *mec* type assignment: rapid identification system for *mec*, *ccr*, and major differences in junkyard regions. Antimicrob Agents Chemother. 2007;51:264–74.
16. Kumar JD, Negi YK, Gaur A, Khanna D. Detection of virulence genes in *Staphylococcus aureus* isolated from paper currency. Int J Infect Dis. 2009;13.
17. Legrand J, Temime L, Lawrence C, Herrmann JL, Boelle PY, Guillemot D. Occupational determinants of methicillin-resistant *Staphylococcus aureus* colonization among healthcare workers: a longitudinal study in a rehabilitation center. Infect Control Hosp Epidemiol. 2015;36:767–76.
18. Louie L, Goodfellow J, Mathieu P, Glatt A, Louie M, Simor AE. Rapid detection of methicillin-resistant staphylococci from blood culture bottles by using a multiplex PCR assay. J Clin Microbiol. 2002;40:2786–90.
19. Mrowietz U, Kragballe K, Reich K, Spuls P, Griffiths CEM, Nast A, Franke J, Antoniou C, Arenberger P, Balieva F, Bylaite M, Correia O, Daudén E, Gisondi P, Iversen L, Kemény L, Lahfa M, Nijsten T, Rantanen T, Reich A, Rosenbach T, Segaert S, Smith C, Talme T, Volc-Platzer B, Yawalkar N. Definition of treatment goals for moderate to severe psoriasis: a European consensus. Arch Dermatol Res. 2011;303:1–10.
20. Naing NN. Easy way to learn standardization: direct and indirect methods. Malays J Med Sci. 2000;7:10–5.
21. Nashev D, Toshkova K, Salasia SIO, Hassan AA, Lämmle C, Zschöck M. Distribution of virulence genes of *Staphylococcus aureus* isolated from stable nasal carriers. FEMS Microbiol Lett. 2004;233:45–52.
22. Nastri ML, Hecht P, Nastri N, Jewtuchowicz V, Cuesta A, Estrugo J, Gualtieri A, Sordelli DO, Rosa A. Nasal carriage of *Staphylococcus aureus* and *Candida* species in immunocompetent individuals. Acta Odontol Latinoam. 2012;25:324–9.
23. Neopane P, Nepal HP, Shrestha R, Uehara O, Abiko Y. *In vitro* biofilm formation by *Staphylococcus aureus* isolated from wounds of hospital-admitted patients and their association with antimicrobial resistance. Int J Gen Med. 2018;11:25–32.
24. Nestle FO, Kaplan DH, Barker J. Psoriasis. N Engl J Med. 2009;361:496–509.
25. Olsen K, Danielsen K, Wilsgaard T, Sangvik M, Sollid JUE, Thune I, Eggen AE, Simonsen GS, Furberg A-S. Obesity and *Staphylococcus aureus* nasal colonization among women and men in a general population. PLoS One. 2013;8:e63716.
26. Park C, Shin HH, Kwon EY, Choi SM, Kim SH, Sun HP, Choi JH, Yoo JH, Lee DG, Wan SS. Two variants of staphylococcal cassette chromosome *mec* type IVA in community-associated methicillin-resistant *Staphylococcus aureus* strains in South Korea. J Med Microbiol. 2009;58:1314–21.
27. Peacock SJ, Paterson GK. Mechanisms of methicillin resistance in *Staphylococcus aureus*. Annu Rev Biochem. 2015;84:577–601.
28. Singh R, Ray P. Quorum sensing-mediated regulation of staphylococcal virulence and antibiotic resistance. Future Microbiol. 2014;9:669–81.
29. Skov L, Baadsgaard O. Bacterial superantigens and inflammatory skin diseases. Clin Exp Dermatol. 2000;25:57–61.
30. Statnikov A, Alekseyenko AV, Li Z, Henaff M, Perez-Perez GI, Blaser MJ, Aliferis CF. Microbiomic signatures of psoriasis: feasibility and methodology comparison. Sci Rep. 2013;3.
31. Tan L, Li SR, Jiang B, Hu XM, Li S. Therapeutic targeting of the *Staphylococcus aureus* accessory gene regulator (*agr*) system. Front Microbiol. 2018;9.
32. Totté JEE, van der Feltz WT, Bode LGM, van Belkum A, van Zuuren EJ, Pasmans SGMA. A systematic review and meta-analysis on *Staphylococcus aureus* carriage in psoriasis, acne and rosacea. Eur J Clin Microbiol Infect Dis. 2016;35:1069–77.
33. Traber K, Lee E, Benson S, Corrigan R, Cantera M, Shopsin B, Novick R. *Agr* function in clinical *Staphylococcus aureus* isolates. Microbiology. 2008;154.
34. Zanger P, Nurjadi D, Gaile M, Gabrysch S, Kremsner PG. Hormonal contraceptive use and persistent *Staphylococcus aureus* nasal carriage. Clin Infect Dis. 2012;55:1625–32.