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β-papillomaviruses and psoriasis: an intra-patient comparison of human papillomaviruses carriage in skin and hair

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Summary

Background—Human papillomaviruses (HPVs) of the beta genus (β-PV), especially HPV5 and HPV36, are proposed to play a pathogenic role in psoriasis, but many previous studies have failed to control for potential confounders, including treatment.

Objectives—To re-examine the relationship between β-PV and psoriasis addressing limitations present in previous studies and analyse intra-patient concordance for carriage of HPV.

Methods—Plucked eyebrow hairs and forearm skin scrapes were collected from 20 newly diagnosed, previously untreated adult patients with psoriasis and 23 normal controls. A combination of type-specific and degenerate polymerase chain reaction methods was used to achieve comprehensive HPV DNA detection.

Results—The prevalence of HPV in hair and skin from psoriasis patients was higher than in controls (83·3% vs. 46·7%, respectively, $P < 0{\cdot}03$ corrected for age and clustering). HPV5 or HPV36 were not over-represented. The profile of diverse β-PV types was comparable in the two groups. Intra-patient concordance for HPV DNA at separate sites was high ($P < 0{\cdot}00001$).

Conclusions—Our data do not support a specific causal role for HPV5 or HPV36 in psoriasis, but suggest that psoriatic skin may be more permissive for viral presence than normal skin. High intra-patient concordance for specific HPV types at separate sites, together with the ubiquity of HPV DNA in normal human skin, suggests that an individual becomes colonized with a particular β-PV profile presumably to the exclusion of other types. To what extent this HPV profile is then causal in the subsequent development of hyperproliferative skin disease is unknown.

Keywords

β-human papillomaviruses; epidermodysplasia verruciformis; hair; psoriasis; skin cancer

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Conflicts of interest
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Beta-papillomaviruses (β-PV) are a human papillomavirus (HPV) genus originally believed to be associated exclusively with the cutaneous lesions and skin malignancies of patients with epidermodysplasia verruciformis (EV). However, improved methods for detecting HPV DNA increasingly support a ubiquitous presence for β-PVs in normal human skin and hair follicles.1-4 Proteins encoded by the *EVER1* and *EVER2* genes5 may be involved in intrinsic immunity against these papillomaviruses, restricting productive and clinically apparent β-PV infections in normal keratinocytes.6

A high prevalence of β-PV DNA has been reported in psoriatic skin, especially HPV5 and HPV36. HPV5 is linked to the development of skin cancer in EV patients.7,8 Serological studies have also demonstrated increased HPV5 antibodies in patients with psoriasis, supporting a productive rather than a latent infection with HPV5.7,9 On this evidence it is suggested that psoriatic skin may be specifically permissive for β-PV infection thus providing a reservoir for EV-associated HPV within the normal population.7 It is also proposed that HPV antigens may be involved directly in the pathogenesis of psoriasis through autoimmune phenomena, induction of cytokines, T-cell activation and/or direct stimulation of keratinocyte hyperproliferation.10-13 However, increased prevalence of antibodies to HPV5 are also found in autoimmune bullous diseases and other conditions where epidermal repair is prominent.14

There is continuing debate as to the prevalence and relevance of specific β-PV types in psoriasis,15-18 compounded by the frequent presence of these HPV types in normal hair follicles and skin,3,4 albeit at low viral copy numbers. Differences in the methods used for HPV detection across different studies make it difficult to compare data directly. Most studies of psoriasis have used type-specific primers for HPV5 and HPV36 thus biasing detection towards these particular β-PV types, possibly at the expense of other co-existent HPVs. Furthermore, many earlier studies failed to control for potential confounders such as the use of topical corticosteroid creams, systemic immunosuppressive agents or psoralen plus ultraviolet A (PUVA) photochemotherapy and no previous studies have examined coincident HPV carriage in skin scrapes and plucked hair follicles in individuals with psoriasis.

The purpose of this study was to use a broad and unbiased method for HPV DNA detection to examine whether β-PV is indeed more prevalent in normal skin from individuals with psoriasis compared with unaffected individuals, and whether specific HPV types are over-represented. It was also an opportunity to examine concordance for carriage of HPV in multiple sites within the same individual.

Methods

Recruitment of subjects and samples taken

In total, 43 subjects were recruited: 20 were patients with untreated psoriasis and 23 were healthy controls. Plucked eyebrow hairs and skin scrapes were taken from all subjects. All subjects gave informed consent and the study had ethical approval from the East London and City Health Authority Research Ethics Committee.

The 20 patients with chronic plaque psoriasis were recruited from the dermatology outpatient clinics at Barts and the London NHS Trust and the Homerton University Hospital, Hackney. All were new patients with previously untreated psoriasis, not using topical corticosteroids nor receiving any form of systemic immunosuppressive treatment nor ever having received PUVA photochemotherapy. Ten eyebrow hairs with attached hair bulbs (five from the left side, five from the right) were plucked with sterile forceps and collected into Eppendorf tubes. A superficial skin scraping was taken from sun-exposed forearm skin,

as far as possible from any psoriatic plaque, using a sterile disposable scalpel and collected into individual mycology collection envelopes consisting of black card with sealed edges. Skin samples and plucked hairs were immediately frozen in liquid nitrogen and stored at -80 °C prior to analysis. Twenty-three normal volunteers with no history of psoriasis or skin cancer, and no clinical evidence of viral warts, were also recruited for HPV DNA detection in plucked eyebrow hairs and skin scrapes from sun-exposed forearm skin. These normal controls were recruited from hospital staff and from relatives of patients attending the dermatology department. Relatives or carers of patients with psoriasis were excluded as controls and sampling from hospital staff occurred at a time and place removed from any patient contact. Whenever two samples (either from the same individual or from two separate individuals) were collected simultaneously, care was taken to ensure that separate, sterilized forceps, scalpels, Eppendorf tubes and mycology collection bags were used for each sample to minimize the possibility of cross-contamination.

Human papillomavirus DNA detection and genotyping

DNA was extracted from all material using the QIAamp DNA Mini Kit (Qiagen, Crawley, U.K.). Skin scrapes and hair bulbs were carefully transferred into 180-μL ATL lysis buffer (Qiagen) and DNA extracted according to the manufacturer's protocol for tissue. Strict measures were taken to prevent and monitor cross-contamination during the DNA extraction process including ultraviolet (UV) irradiation of bench hoods between each extraction and rigorous pre- and post-polymerase chain reaction (PCR) separation, and use of DNA extraction and PCR controls. When paired samples were processed, DNA extraction, PCR amplification and sequencing were performed separately. The quality of extracted DNA was verified by PCR amplification of β-globin sequences in total genomic DNA samples using the primers GH20 and PC04.19 β-globin-negative samples were excluded from further analysis. HPV-PCR amplification was performed using a panel of nested and degenerate primers located within the L1 open reading frame as previously described.20 Negative PCR controls included buffer alone (extraction control), water and placental DNA. HPV plasmids (5, 36, 21) were used as positive controls. PCR amplimers were directly sequenced on an ABI 377 automated sequencer and subjected to BLAST analysis. This method detects HPV types from alpha, beta, gamma, mu and nu genuses, as well as novel types.20,21 HPV-PCR amplification was also performed using type-specific primers to HPV5, HPV36 and HPV21. HPV21 was chosen as another β-PV carried in the normal population (personal observation) yet not previously reported in association with psoriasis. In our hands, published primers to HPV5 and HPV36 were found to amplify nonspecific products as verified by sequencing.21 We therefore designed new nested PCR primers less homologous to human sequences than those previously published (as confirmed by BLAST analysis). Due to considerable sequence homology between these HPV types, consensus primers were used for the first round reactions and for the forward nested primer. Consensus primers and type-specific nested reverse primers were as follows: Outer forward, CTGTAGGCAGTGTAAGCATTTT; outer reverse, ACACCAATC ACCAAACCCT; nested forward, CTACCAGTTGACCTGTTTTGTG; five nested reverse, TACTACC TTTAGAATTAGGA; 21 nested reverse, TGCAGCCGCAA GGTGTA; 36 nested reverse, TGCAGGTCACCGGTCAGCAA. These type-specific primer sets were verified with plasmid DNA and gave clean sensitive type-specific results (data not shown).

Statistical analysis

For the majority of analyses, HPV-positivity was considered the main outcome. A sample was considered to be HPV-positive if positive for any known HPV or partially characterized novel HPV type using type-specific or degenerate PCR and confirmed by DNA sequencing. A sample was considered negative in cases where a positive band of the correct size was

identified, but the PCR product revealed human genomic sequences. Thus, there was possibly an underestimate of the number of HPV types present in this dataset.

Formal comparison of HPV positivity between hair and skin samples as well as between cases and controls was made by logistic regression. Observations from different samples from a single individual were not treated as independent, although the individuals themselves were. The lack of independence means that model-based variance estimates are inappropriate. Instead we used the robust sandwich estimate of variance.22

To estimate concordance for HPV types present in hair and skin, we considered only those individuals with results for both samples. There were 38 such individuals. In order to assess the significance of the observed concordance, we performed a simulation test by randomly re-assigning the skin samples 100 000 times. For each random assignment, the number of concordant pairs for hair and skin samples was counted. The results from the 100 000 runs were compared with the number of concordant types in the original dataset. Analysis was performed in Stata (Stata Corporation, Statistical software: Release 8.0 (2003); College Station, TX: U.S.A.).

Results

The results of HPV DNA testing in skin scrapes and plucked hairs from 20 untreated adult psoriasis patients (mean age 51·0 years, range 31-76 years) and 23 normal volunteers (mean age 36·9 years, range 24-50 years) are shown in Table 1. HPV DNA was detected using both degenerate nested PCR20,21 and type-specific primers for HPV5, HPV36 and HPV21. DNA extraction from skin scrapes was inadequate for two psoriasis patients (pso4 and pso6) and from plucked hairs for two others (pso2 and pso18). DNA extraction was inadequate from plucked hairs for one normal volunteer (con109). Therefore, HPV DNA results from 18 skin scrapes and 18 plucked hairs from 20 psoriasis patients were available for comparison with those from 23 skin scrapes and 22 plucked hairs from 23 normal volunteers (Table 1).

β-PV DNA predominates in both, but was detected more frequently in skin scrapes and plucked hairs from patients with psoriasis than in samples from healthy controls

There was no significant difference in the prevalence and spectrum of HPV types in skin scrapes compared with hair samples for either group alone or when combined [HPV-positive hairs (combined): 27/40 (67·5%); HPV-positive skin scrapes (combined): 24/41 (58·5%); $P = 0·343$ adjusted for clustering within individuals and age] (Table 1). Skin scrape and hair sample results were therefore pooled in subsequent analyses (but allowance is made for the lack of independence between the two samples from an individual). HPV DNA was detected in 30/36 (83·3%) hair and skin samples from patients with psoriasis and in 21/45 (46·7%) samples from control individuals ($P = 0·03$, adjusted for clustering and age). Despite using degenerate primers, which had been optimized for detection of non-β as well as β-papillomaviruses, β-PV was significantly more prevalent than non-β cutaneous types in both psoriasis and normal skin. β-PV was detected in 29/30 (96·7%) of HPV-positive psoriasis samples and 19/21 (90·5%) of HPV-positive control samples. In contrast, non-β-PV was detected in 2/30 (6·7%) of HPV-positive psoriasis samples and 2/21 (9·5%) of HPV-positive control samples.

A similar spectrum of diverse β-PV types was found in both psoriasis and normal skin scrape/hair samples

The spectrum of β-PV was similar in both psoriasis and normal control samples (Table 1), with the commonest HPV types being HPV5, HPV21 and HPV14 in psoriasis and HPV5,

HPV21 and HPV24 in control skin (Table 2). Seven of the most frequently identified HPV types in psoriasis (HPV5, HPV21, HPV14, HPV36, RTRX7, PSOX1 and HPV15) show considerable overlap with the six most frequently identified HPV types in controls (HPV5, HPV21, HPV24, HPV15, PSOX1 and HPV10). We found no excess of HPV5 or HPV36 in normal skin from patients with psoriasis compared with control skin. Using type-specific primers, HPV5 was detected in 7/36 (19·4%) psoriasis and 8/45 (17·8%) control samples (P = 0·869) and HPV36 was detected in 3/36 (8·3%) psoriasis and 1/45 (2·2%) control samples (P = 0·368), both P-values corrected for clustering and age. Using degenerate PCR, HPV5 was detected in 5/36 (13·9%) psoriasis and 6/45 (13·3%) control samples (P = 0·865, adjusted for clustering and age); HPV36 was detected in 2/36 (5·6%) psoriasis and none of the control samples (Fisher's exact test, P = 0·194). The presence of multiple β-PV types was more frequent in samples from psoriasis patients (13/36; 36·1%) than from controls (7/45; 15·6%), but this difference was not significant when adjusted for clustering and age (P = 0·251). This was also true when analysed per patient rather than per sample, multiple β-PV types being found in 11/20 (55·0%) psoriasis patients and 5/23 (21·7%) controls (P = 0·099 when adjusted for age).

Intra-patient concordance for β-human papillomavirus detection in eyebrow hairs and forearm skin scrapes was high with 16 matches identified in 12 individuals

Intra-patient concordance for HPV type was determined at two separate sites (eyebrow hairs and forearm skin) (Table 2). Of 43 individuals, 38 had samples for both hair and skin scrapes; 18/38 (47·4%) were positive for at least one HPV type at both sites and 8/38 (21·1%) tested negative for all HPV types at both sites. To calculate a sensitivity of hair testing for HPV we found that, of 22 samples positive for HPV in the skin sample, 18 (81·8%) were positive for hair also. A positive predictive value was also calculated; of 26 individuals with positive hair samples, 18 (69·2%) had positive skin samples. Thus, hair samples were more frequently positive than skin samples when testing for HPV carriage, but were concordant with skin in nearly 70% of cases.

When considering just β-PV types, 16/38 (42·1%) were positive for at least one type in both skin and hair samples and 9/38 (23·7%) were negative for β-PV types at both sites. Sensitivity and positive predictive value of hair testing for determining β-PV status in skin at a distant site were 80·0% and 64%, respectively.

Twelve of 38 (31·6%) individuals were concordant for the same HPV type at more than one site. Two individuals (pso10 and con113) were concordant for two types and one individual (con106) was concordant for three types (Table 1). The expected number of matches (based on results from 100 000 runs) was 2·78 giving a ratio of observed/expected of 5·75 (16/2·78); there were fewer than 16 matches on all runs (P < 0·00001).

We also considered the proportion of unique HPV types present in an individual's plucked hair sample and in their skin scrape sample as this provides an estimate of the accuracy of HPV typing of hairs for assessing HPV types present in skin. When considering the type-specific *sensitivity* of hair testing, of 37 type-person combinations found in skin, 16 (43·2%) were also found in hair. When considering the type-specific positive predictive value of hair testing, of 40 type-person combinations in hair, 16 (40%) were present in the same individual's skin scrape.

Discussion

It has been proposed that β-PVs, especially HPV5 and HPV36, play a pathogenic role in psoriasis.11 However, they are also commonly detected in hair and normal skin.1,4 In 1998, it was suggested7 that psoriasis might be the human reservoir for HPV5 based on the

observation that HPV5 DNA was detected in 91·7% of psoriatic skin scrapings in 48 patients compared with 35·5% of controls, using a nested PCR method specific for β-PV.23 Antibodies to HPV5 were also detected in a significantly higher proportion of psoriasis sera (24·5%) than control sera (2-5%). Several subsequent studies similarly demonstrated a higher prevalence of β-PV, particularly types 5 and 36, in psoriatic skin compared with normal controls.7,24

However, previous reports detecting high levels of HPV5 and HPV36 are potentially biased by the use of type-specific primers or by the inclusion of patients in whom psoriasis has been treated with topical or systemic immunosuppressive agents or phototherapy. All these treatment modalities would be expected to reduce host restriction to β-PV infection and should be controlled for, yet this has not previously been done. In order to address these limitations, we recruited newly diagnosed, previously untreated individuals with psoriasis, none of whom had received phototherapy or indeed topical or systemic immunosuppressants. In addition, both degenerate and type-specific primers were employed to establish the broadest possible profile of HPV DNA detection.

Using both methods, the prevalence of HPV DNA in both plucked eyebrow hairs and skin scrapes was significantly higher in individuals with psoriasis (83·3%) than in normal controls (46·7%) but we did not find that HPV5 or HPV36 were over-represented. In fact, the spectrum of HPV types found in both groups was similar, with over 90% represented by known or novel β-PV types. Diverse β-PV types were present in both groups with considerable overlap in the most frequently identified types. Of the four HPV types found most frequently in the controls, three were also common in individuals with psoriasis. These data were established with careful selection of untreated patients and support the premise that skin in individuals with psoriasis might be more permissive for the presence of HPV than normal skin, but not specifically for HPV5. We believe that the increased prevalence of HPV5 previously reported in psoriasis is most likely the consequence of previous treatments, particularly PUVA photochemotherapy, and there is much to support this view. For example, in one study HPV5 was detected significantly more frequently in the lesional skin from PUVA-treated compared with untreated patients.7 Wolf *et al.*25 subsequently found that hair samples from patients with psoriasis with a history of PUVA exposure were significantly more likely to be HPV DNA-positive (69-73%) than those with no history of PUVA exposure (36%). In addition, we26 and others27 have previously reported a high prevalence of HPV5 in PUVA-associated skin cancers, but not in UV-driven skin cancers,21 suggesting that it is PUVA exposure, not psoriasis *per se*, that is associated with the detection of HPV5.

Psoriasis is a T-cell-mediated inflammatory skin disease and a two-step pathogenesis has been proposed involving polyclonal T-cell activation by superantigens, trauma or other factors as an important first step. Subsequently, recognition of putative autoantigen by these pre-activated autoreactive T cells leads to release of cytokines and maintenance of a psoriasis phenotype.28 Majewski *et al.*10,11 proposed a model for the aetiology of psoriasis whereby HPV-encoded proteins contribute to epidermal hyperproliferation and serve as potential antigens recognized by autoreactive T- and B-lymphocytes. Two loci for EV appear to map close to susceptibility genes for psoriasis on chromosome 17 (*PSOR 2*) and also on chromosome 2.29,30 Thus, the genetic defect in EV that lifts the restriction on productive β-PV infection may also be present in psoriasis (at least in part) with persistence of β-PV infection driving the epidermal proliferation characteristic of this disease.31 Others have disagreed, believing that cytokine release in psoriasis facilitates replication of normally latent HPV5, rather than HPV5 infection driving the psoriasis.15 Ruhland and de Villiers concluded that HPV infection was not causal in psoriasis, but that pro-inflammatory cytokines released in psoriatic skin might differentially activate the promoter region of

specific HPV types, favouring their replication and thus detection in psoriasis compared with normal skin.32

Our study examines only the presence of viral DNA, not the physical or replicational status of the virus and consequently cannot resolve this debate. However, the commonality of the β-PV profile found in both psoriasis and controls, together with the multiplicity of HPV types found in psoriasis favours a general permissiveness towards β-PV replication rather than a specific causative role by any particular HPV type. This, together with the increase in HPV5 consequent on PUVA photochemotherapy, may be sufficient to explain the apparent association of HPV5 with psoriasis. The use of type-specific primers in previous studies has obscured the diversity of types that evidently exist in both normal and inflammatory skin, whereas in this study the use of degenerate primers also allowed identification of multiple HPV types. The multiplicity of β-PV types found within the same psoriasis sample and the frequent occurrence of novel β-PVs are very reminiscent of HPV DNA detection in immunosuppressed organ transplant recipients.21,33 It may be that the normal host restriction to β-PV infection is relaxed in psoriasis, as it is in immunosuppressed transplant recipients.

A secondary aim of this study was to examine concordance for the carriage of β-PV in plucked eyebrow hairs compared with skin scrapes from sun-exposed forearm, and here we found a high degree of intra-patient concordance. Given the diversity of β-PV found in normal skin/hairs (and seemingly in psoriasis) and the large number of known or novel β-PVs in existence, it is unlikely that the same HPV type will be found at a distant skin site by chance. A previous study reported agreement in β-PV status between HPV-positive skin cancers and eyebrow hairs taken from the same individual and went on to demonstrate in four of five pairs of positive samples that the same HPV type was present.34 Others have reported similar findings with collection of different skin lesions over months or years from the same (immunosuppressed) individual showing persistent infection with the same HPV type in biopsy specimens taken at different skin sites and at different time points.21,33 A recent study showed persistence of a given β-PV profile in eyebrow hairs in normal individuals tested over a 2-year period.4 These combined data, together with the apparently ubiquitous nature of β-PV in normal skin, suggest that an individual becomes colonized with a particular profile of β-PV, probably from early infancy,35 and that this profile tends to persist, presumably to the exclusion of carriage with alternative β-PV.

In summary, we found diverse β-PV types in normal skin scrapes and hair follicles from patients with psoriasis and those without. Although we found an increased prevalence and more frequent mixed β-PV infections in patients with psoriasis, the spectrum of β-PV types was similar to those from normal controls and no specific HPV type predominated. These data do not lend support to the hypothesis that specific HPV types are causal in the pathogenesis of psoriasis, although we cannot exclude the possibility that HPV carriage in psoriatic plaques may differ substantially from the sites tested. We conclude that in untreated psoriasis some aspect of the inflammatory process, either through release of pro-inflammatory cytokines, or the hyperproliferative state that ensues, is permissive for the presence of β-PV. Subsequent treatment of psoriasis with immunosuppressive agents is likely to augment diverse β-PV replication and indeed evidence suggests that PUVA may specifically and selectively increase the prevalence of HPV5. The contribution of this to the natural history of psoriasis and to the subsequent development of skin cancers in PUVA-treated patients is currently unclear.

The high intra-patient concordance shown in this study supports early colonization of normal human skin by a specific HPV ‘signature’ that is persistent, possibly to the exclusion of other types. To what extent this signature is a determinant of subsequent skin disease

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remains to be established. Finally, the high intra-patient concordance that exists implies that screening for β-PV carriage in eyebrow hair may provide a reasonable estimate of the β-PV status of an individual's skin, and could thus be used as a surrogate in large, population-based epidemiology studies.

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Table 1

HPV DNA detection in skin and hair follicles from psoriasis and controlsa

[a] Number depicts HPV type as confirmed by sequencing.
−, negative for HPV DNA; HPV, human papillomavirus; ND = not done; nov, novel HPV type (most closely related given in brackets); PCR, polymerase chain reaction; RTRX5, PSOX1 etc., partially characterized HPV sequence; TS, type-specific PCR.

	Degenerate nested PCR		Type-specific	
PCR method sample type	**Skin scrape**	**Plucked eyebrow hair**	**Scrape**	**Hair**
Pso1	5	-	5	5
Pso2	-	ND	-	ND
Pso3	nov(HPVX14b), nov(15), nov(gi2664389), vs20-4	uwBD119a, 80, 16, nov(15)	-	5
Pso4	ND	-	ND	-
Pso5	5, 36, 5b, 14d	-	5, 36	-
Pso6	ND	5, 14d	ND	5
Pso7	5	5, nov(20)	5	5
Pso8	14d	14d	-	-
Pso9	6	38	-	-
Pso10	21	36, 21	21, 36	36, 21
Pso11	RTRX9	nov(TN111)	-	-
Pso12	nov(RTRX9), RTRX7, nov(TN111)	RTRX7	-	-
Pso13	21	-	21	-
Pso14	clone ga1-3	17, 24	-	-
Pso15	21, VS20-4	21, RTRX1, 17	21	21
Pso16	PsoX1, nov(75)	15	-	-
Pso17	-	RTRX9	-	-
Pso18	21	ND	21	ND
Pso19	RTRX7	15	21	-
Pso20	-	37	-	-
Con102	-	-	-	-
Con103	10	10	-	-
Con104	5, 24	24	5	-
Con105	-	-	-	-
Con106	5, 21, 15	5, 21, 15	5, 21	5, 21

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	Degenerate nested PCR		Type-specific	
PCR method sample type	**Skin scrape**	**Plucked eyebrow hair**	**Scrape**	**Hair**
Con107	-	-	-	-
Con108	-	5	-	5
Con109	24	ND	-	ND
Con110	-	-	-	-
Con111	-	-	-	-
Con112	5	-	5	-
Con113	PSoX1, 24	PSoX1, 24	-	-
Con114	-	-	-	5
Con115	-	-	-	-
Con116	-	-	5	-
Con117	-	-	-	-
Con118	-	15	-	-
Con119	21	ICPX1, 21	21	21
Con120	-	17, nov(36)	36	-
Con121	-	-	-	-
Con122	-	5	-	5
Con123	-	nov(80)	-	-
Con124	-	vs-73-1	-	-

Table 2

Number of individuals (samples) positive for each human papillomavirus (HPV) type

[a] Number depicts HPV type as confirmed by sequencing.

[b] Where an HPV type was found in more than one sample from a given individual, the total sample number positive for that HPV type is given in parentheses.

Typea	Controls	Patients with psoriasis	Total
β-*HPV types*			
5	7 (8)	5 (7)b	12 (15)
14d	0	3 (4)	3 (4)
15	2 (3)	2	4 (5)
17	1	1	2
21	2 (4)	5 (21)	7 (11)
24	3 (24)	1	4 (5)
36	1	2 (3)	3 (4)
37	0	1	1
38	0	1	1
80	0	1	1
CLONEGA1_3	0	1	1
ICPX1	1	0	1
RTRX1	0	1	1
RTRX7	0	2 (3)	2 (3)
RTRX9	0	2	2
PSOX1	2 (3)	1	3 (4)
UWBD119A	0	1	1
VS_73_1	1	0	1
VS20_4	0	2	2
nov15	0	1 (2)	1 (2)
nov20	0	1	1
nov36	1	0	1
nov75	0	1	1
nov80	1	0	1
novGI1664389	0	1	1
novHPVX14B	0	1	1
novRTRX9	0	1	1
novTN111	0	2	2
Non β-*HPV types*			
6	0	1	1
10	1	0	1
16	0	1	1