abnormality in DCS. Although the function of the CLE is still unclear, a role as a necessary scaffold for the lamellar bilayer organization is likely (Uchida and Holleran, 2008). Thus, CLE deficiency, coupled with disorganization of extracellular lamellar bilayers, likely merge to provoke the barrier abnormality in NLSDI (see Supplementary Figure S2 online). Finally, to overcome this metabolic disadvantage in forming the epidermal permeability barrier, epidermal proliferation likely increases, which in turn results in hyperkeratosis, phenotypic features common to virtually all of the ichthyoses (Demerjian *et al.*, 2006; Akiyama *et al.*, 2008), that is, 'A compromised permeability barrier 'drives' the hyperproliferative epidermis in NLSDI and other ichthyoses' (Elias *et al.*, 2008).

CONFLICT OF INTEREST

The authors state no conflict of interest.

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SUPPLEMENTARY MATERIAL

Supplementary material is linked to the online version of the paper at http://www.nature.com/jid

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Detection of Human Papillomavirus DNA in Plucked Eyebrow Hair from HIV-Infected Patients

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TO THE EDITOR

The risk of developing human papillomavirus (HPV)-related benign and malignant cutaneous lesions is markedly increased in immunosuppressed people such as organ-transplant recipients (Harwood *et al.*, 2000) and HIV-infected patients (Grulich *et al.*, 2007; Stier and Baranoski, 2008). Although HPV DNA in plucked eyebrow hair has been well investigated (Boxman *et al.*, 1997) in renal transplant recipients and immunocompetent patients (ICPs) and correlated with both benign and malignant cutaneous lesions (Struijk *et al.*, 2003; Plasmeijer *et al.*, 2009), very little is known about HPV prevalence in eyebrow hair from HIV patients.

The study design was approved by the research ethics committee and all

Abbreviations: HPV, human papillomavirus; ICP, immunocompetent patient

patients provided written informed consent before enrollment. The study adhered to the Declaration of Helsinki Principles. A total of 63 HIV patients (7 women and 56 men) along with 50 ICPs recruited from the staff of the medical school and matched by age and sex were included. Clinical (medical history, CDC (Centers for Disease Control and Prevention) staging, and treatment), immunological (CD4 cell count), and virological (HIV viral load) characteristics were collected. Approximately 10 eyebrow hair with follicles were plucked using a sterile pair of tweezers and gloves for each individual.

HPV detection was performed using two highly sensitive and specific assays combining a specific multiplex PCR with DNA microarray primer extension as described previously (Gheit *et al.*, 2007). In brief, for each sample, three multiplex PCR reactions were performed for the amplification of α-HPV, β-HPV, and γ-HPV types, respectively. The assays were combined in one single chip to detect 19 mucosal high-risk and potential high-risk HPV types from genus α, 18 low-risk α-HPV types, 25 cutaneous HPV types from genus β, and 6 cutaneous HPV types from genus γ (Ruer *et al.*, 2009).

For statistical tests, two-sided hypotheses were used and the statistical significance was fixed at 5%. The link between qualitative variables was assessed using χ^2 test or Fisher's exact test according to the distribution of the data, and results were presented in the form of odds ratios with their 95% confidence intervals.

In all, 63 HIV patients were enrolled at different CDC stages. The mean CD4 cell count was 568 ± 265 per mm^3 with 46% (29/63) of subjects with <500 CD4 cell mm^{-3}. The mean viral load was $702 \pm 1{,}996$ copies ml^{-1}. In all, 87% (55/63) of HIV patients were treated by antiretroviral therapies. The medical history associated with HPV infection included genital warts (27%, 17/63), cutaneous warts (1.6%, 1/63), and cervical dysplasia (3.2%, 2/63). No HIV patient was affected by skin cancer. Two ICPs had a history of melanoma, and 4 presented with cutaneous warts.

We detected HPV DNA in eyebrow hair of 92 individuals (81%), i.e., 54 HIV patients (86%) and 38 ICPs (76%; Table 1). The mean number of different HPV types was significantly higher in HIV patients ($n=4.5$) than in ICPs ($n=3$, $P<0.05$). We did not observe any age trend in the number of HPV types per individual in the two study groups. As expected, β-HPVs were predominant in both HIV patients and ICPs (84 and 76%, respectively). Among α-HPVs, we did not observe any difference between the different species. Only β1-HPV36 and β2-HPV17 types were significantly more prevalent in HIV patients (27 and 25%, respectively) than in ICPs (5 and 6%, respectively). Although β-HPV types were rarely detected, they seemed to be more prevalent in HIV patients (14 vs. 4%; odds ratio 4, 95% confidence interval 0.75–28.3), and only mucosal α-HPV types were detected in these patients.

We could not establish any significant relation between the presence of HPV DNA in eyebrow hair from HIV patients and medical history of HPV infection (cutaneous and/or genital warts and cervical dysplasia), history of skin cancer, CDC stages, HIV load (inferior or superior to 40 copies ml^{-1}), levels of CD4 cells (inferior or superior to 500 CD4 cells mm^{-3}), and highly active antiretroviral therapy (data not shown).

Although little is known about the interaction between HPV and HIV (Kojic and Cu-Uvin, 2007; van der Burg and Palefsky, 2009), HIV-infected patients are known to have an increased incidence of HPV infection, HPV-associated cervical or anal dysplasia, and cancer (Grulich *et al.*, 2007; Stier and Baranoski, 2008). However, the prevalence of HPV DNA in HIV patients in eyebrow hair has not been assessed so far.

This study confirms the high overall prevalence (76%) of HPV DNA in eyebrow hair follicles from ICPs and HIV patients (86%). Furthermore, the chance of harboring HPV in eyebrow hair was almost two times increased in HIV patients compared with ICPs (odds ratio 1.89, 95% confidence interval 0.66–5.49). These data thus confirm that HPV DNA is widely distributed among the population whatever its immune status (Boxman *et al.*, 1997; Harwood *et al.*, 2000; de Koning *et al.*, 2007, 2009; Hazard *et al.*, 2007).

As expected, HIV patients showed clinical history of mucosal HPV infection, and mucosal α-HPV DNA seemed to be more prevalent in eyebrow hair. There are no data on the cutaneous prevalence of α-HPV in HIV patients, but the high prevalence of α-HPV DNA has been already shown in anogenital mucosae (Drobacheff *et al.*, 2003) and in urine samples from HIV patients without any correlation with the CD4+ cell count or the HIV viral load (Jong *et al.*, 2009).

The prevalence and the distribution of β-HPV types in the general population without any skin lesion are largely unknown. Recently, de Koning *et al.* (2009) found a similar prevalence of β-HPV infection in eyebrow hair from both ICP and immunosuppressed patients with HPV23 also as the most prevalent type similar to this study. In this study, as expected, β-HPVs were predominant in both ICP and HIV patients and the different species showed a similar prevalence.

Despite similar prevalences, the number of different HPV types was significantly higher in HIV patients than in ICPs. This was the result of a higher prevalence of HPV 5, 8, 14, 15, 17, 22, 36, 38, and 47 in HIV patients (there was at least a 10% difference in the prevalence of these types compared with the controls). Some of these HPV types have been associated with skin cancer in earlier studies (Struijk *et al.*, 2003; Feltkamp *et al.*, 2008). Furthermore, this study confirms that immunosuppressed individuals are infected with a greater number of HPV types than ICPs of the same age group (Harwood *et al.*, 2000; de Koning *et al.*, 2009).

We did not observe any correlation between the presence of HPV DNA and immune status of HIV patients. In previous studies, Hazard *et al.* (2007) and de Koning *et al.* (2009) found that the overall cutaneous HPV DNA prevalence was not significantly associated with immunosuppressive treatment. However, the duration of immunosuppression might be associated with multiple β-HPV infection (de Koning *et al.*, 2009).

This study is however limited by the fact that despite the detection of a

Table 1. Rates of HPV DNA detection in eyebrow hairs

HPV DNA positivity[1]	ICP (*n*=50)	HIV-P (*n*=63)	ORs with 95% CIs
All genuses	76% (38)	86% (54)	1.89 (0.66–5.49)
Number of HPV types			
1	22% (11)	13% (8)	0.52 (0.17–1.55)
2	22% (4)	14% (9)	1.92 (0.49–7.99)
>2	46% (23)	59% (37)	1.67 (0.74–3.79)
Mean number ± SD*	3 ± 3.04 (*n*=50)	4.5 ± 3.96 (*n*=63)	*P*=0.03
α-HPV	4% (2)	14% (9)	4 (0.75–28.30)
β-HPV	76% (38)	84% (53)	1.67 (0.60–4.72)
β1-HPV	58% (29)	68% (43)	1.56 (0.67–3.63)
HPV5	24% (12)	34% (21)	1.58 (0.64–3.97)
HPV8	14% (7)	24% (15)	1.92 (0.65–5.79)
HPV12	14% (7)	19% (12)	1.45 (0.47–4.50)
HPV14	12% (6)	22% (14)	2.10 (0.67–6.75)
HPV19	4% (2)	13% (8)	–[2]
HPV20	18% (9)	21% (13)	1.18 (0.42–3.38)
HPV21	8% (4)	5% (3)	–[2]
HPV24	34% (17)	22% (14)	0.55 (0.22–1.38)
HPV25	0	3% (2)	–[2]
*HPV36**	10% (5)	27% (17)	3.33 (1.03–11.35)
HPV47	6% (3)	17.5 (11)	3.33 (0.79–16.04)
HPV93	6% (3)	6.4% (4)	–[2]
β2-HPV	58% (29)	57% (36)	0.97 (0.43–2.19)
HPV9	8% (4)	14% (9)	1.92 (0.49–7.99)
HPV15	18% (9)	28% (18)	1.82 (0.68–4.98)
*HPV17**	6% (3)	25% (16)	5.33 (1.33–24.78)
HPV22	6% (3)	16% (10)	2.96 (0.69–14.49)
HPV23	38% (19)	38% (24)	1 (0.44–2.32)
HPV37	6% (3)	1.6% (1)	–[2]
HPV38	25% (14)	36.5% (23)	1.48 (0.62–3.57)
HPV80	4% (2)	11% (7)	–[2]
β3-HPV	6% (3)	14% (9)	2.61 (0.60–13.01)
HPV49	2% (1)	0	–[2]
HPV75	2% (1)	9.5% (10)	–[2]
HPV76	2% (1)	6.4% (4)	–[2]
β4-HPV92	0	1.6% (1)	–[2]
β5-HPV96	6% (3)	6.4% (4)	–[2]
γ-HPV	18% (9)	17% (11)	0.96 (0.33–2.83)
HPV4	6% (3)	5% (3)	–[2]
HPV48	4% (2)	1.6% (1)	–[2]
HPV50	8% (4)	13% (8)	1.67 (0.42–7.12)
HPV65	2% (1)	1.6% (1)	–[2]
HPV95	0	1.6% (1)	–[2]

Abbreviations: CI, confidence interval; HPV, human papillomavirus; ICP, immunocompetent patient; OR, odds ratio.
[1]Number of samples positive for HPV DNA.
[2]The number of cases was not large enough for statistical analysis.*Statistically significant at 5%.
Our assay (Gheit *et al.*, 2007; Ruer *et al.*, 2009) was designed to detect 19 mucosal high-risk and potential high-risk HPV types from genus α (16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 53, 56, 58, 59, 66, 68, 70, 73, and 82), 18 low-risk α-HPV types (6, 11, 28, 34, 40, 42, 43, 44, 54, 55, 57, 61, 67, 71, 72, 74, 81, 83, and 84), 25 cutaneous HPV types from genus β (5, 8, 9, 12, 14, 15, 17, 19, 20, 21, 22, 23, 24, 25, 36, 37, 38, 47, 49, 75, 76, 80, 92, 93, and 96), and 6 cutaneous HPV types from genus γ (4, 48, 50, 60, 65, and 95).

broad spectrum of HPV DNA, we did not evaluate its persistence, or the transcriptional activity or the viral load. In addition, we cannot exclude that specific HPV types may be involved in a subgroup of HIV patients, as the power of this study may have been too low to reach statistical significance.

In conclusion, this is the first study on HPV DNA prevalence in healthy skin of HIV patients. The high prevalence of HPV infection in humans, together with the lack of specific HPV types and any relation with the immune status of HIV patients, raises the question of how HPV could affect the development of skin cancer in these patients (Feltkamp *et al.*, 2008).

CONFLICT OF INTEREST

The authors state no conflict of interest.

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Identification of Staphylococcal Protein A in Infected Atopic Dermatitis Lesions

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TO THE EDITOR

Staphylococcus aureus infection is a known trigger for skin inflammation and can modulate immune responses. Atopic dermatitis (AD), a chronic inflammatory pruritic skin disease, affects 10–20% of children and 1–3% of adults (De Benedetto *et al.*, 2009). Owing to the loss of skin integrity by scratching, as well as decreased levels of antimicrobial peptides in comparison with normal skin or other inflammatory diseases such as psoriasis (Ong *et al.*, 2002; Leung, 2003), patients with AD are particularly susceptible to staphylococcal skin infections, which can further worsen their skin disease (Bieber, 2008). Studies have suggested several underlying mechanisms for staphylococcus-mediated inflammation, which include production of inflammatory cytokines following either direct infection of keratinocytes or immune cells by the bacteria, or indirectly by

Abbreviations: AD, atopic dermatitis; LTA, lipoteichoic acid; SPA, staphylococcal protein A