It is well established that cell-mediated immune response plays a major role in controlling HPV infections. Therefore, treatment techniques such as immunotherapy have been used to activate the immunologic response to HPV. One method of immunotherapy is the intraleisional injection of skin test antigens such as *Candida*, mumps, and/or *Trichophyton*. Studies have shown that such therapies resolve not only the treated warts but also distant, untreated warts.

To our knowledge, little work has been done to elucidate the immunologic mechanisms behind skin test antigens immunotherapy. Herein, we report immunologic response data from patients undergoing *Candida* injection immunotherapy for the treatment of warts, measured by an ex vivo interferon-γ–enzyme-linked immunospot (IFN-γ ELISPOT) assay.

Methods. The study protocol was approved by the institutional review board of the University of Arkansas for Medical Sciences (UAMS), and the clinicaltrials.gov identifier is NCT00569231. Patients were recruited during the period between February 2007 and May 2009 from the outpatient Dermatology Clinic at UAMS. Informed consent was obtained from all participants.

Eighteen patients, each with at least 2 cutaneous, nongenital, nonfacial warts and no previous *Candida* antigens treatment for warts were enrolled into the study. Each patient received an intraleisional injection of 0.3 mL of *Candida* antigen (*Candida* Allermed Laboratories, San Diego, California) into their largest wart at the baseline visit and then at each visit every 3 weeks thereafter. The clinical responses and adverse events were assessed.

The sequences of antigens used in the ex vivo IFN-γ ELISPOT assay were chosen from HPV-57 since HPV-2a, -27, and -57 were the most common HPV types detected in the warts of patients previously recruited in our clinics. The peptide sequences that contained HLA class I A2 hot spots and HLA class II DR hot spots that were similar among HPV-2a, -27, and -57 were chosen using the predictive engines of MULTIPRED®: HPV-57 E1-peptide-(231-260 and 251-286), E2-peptide-(188-208), E4-peptide-(10-30), E6-peptide-(17-55), and L1-peptide-(380-412). The IFN-γ ELISPOT assay protocol was performed as previously described, except 300,000 peripheral blood mononuclear cells were presented with 10 µM of each of the HPV-57 peptides, and the incubation period was extended to 40 hours.

**Results.** Eighteen patients were enrolled, and 11 completed the study (*Table*). Of the 11 patients who completed the study, 9 had complete resolution of their treated warts (82%), 1 had partial resolution (9%), and 1 had no response (9%). Complete resolution of the first distant untreated warts was observed in 6 of 8 patients (75%), while that of the second distant warts were observed in 6 of 6 patients (100%). The median number of injections required for complete resolution was 4. None of the 18 patients experienced vaccine-related adverse events higher than grade 2 (moderate). Typical adverse events were injection site pain and mild erythema.

The IFN-γ ELISPOT assay was performed on only 10 of the 11 patients who completed the study (*Table*).

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**Phase 1 Clinical Trial of Intraleional Injection of *Candida* Antigen for the Treatment of Warts**

Warts are benign epidermal tumors caused by human papillomaviruses (HPVs). There are more than 100 distinct HPV types that have been isolated from cutaneous and mucosal lesions, of which the closely related HPV types 2, 27, and 57 predominantly cause common warts.

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cause the sample from the 11th patient was lost to improper thawing. A positive response to HPV-57 L1-peptide-(380-412) was the response most commonly detected (6 of 10, 60%). One patient demonstrated a response to HPV-57 E4-peptide-(10-30) (10%) (data not shown). No responses were detected to the other peptides or to the Candida antigen. All samples tested positive against phytohemagglutinin-positive control. In relation to the clinical response, 6 of 9 responders had a positive response to the L1-peptide (67%), suggesting that L1-specific T cells may play a role in wart regression. The 1 nonresponder had no positive results.

Comment. In this study, serial injections of Candida antigen were shown to be a safe treatment for warts and resulted in good clinical responses. Among the 6 HPV-57 peptides examined, the immune response to HPV-57 L1-peptide-(380-412) was most commonly detected (6 of 10, 60%). One patient demonstrated a response to HPV-57 E4-peptide-(10-30) (10%) (data not shown). No responses were detected to the other peptides or to the Candida antigen. All samples tested positive against phytohemagglutinin-positive control. In relation to the clinical response, 6 of 9 responders had a positive response to the L1-peptide (67%), suggesting that L1-specific T cells may play a role in wart regression. The 1 nonresponder had no positive results.

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Multiple Myeloma–Associated Amyloidosis Presenting With Acrolocalized Acquired Cutis Laxa

Cutis laxa (CL) syndrome is an inherited or acquired disorder due to abnormal production or destruction of dermal elastic fibers. Acquired forms may be localized or generalized and frequently are related to preceding inflammatory dermatoses or monoclonal gammopathies. Acral CL is an exceptional form of acquired localized CL that may indicate an underlying multiple myeloma.1-6

Report of a Case. A 63-year-old man with no relevant medical history was seen with a 3-month history of asymptomatic skin lesions on the ventral aspect of his fingers. Physical examination revealed noticeably soft, redundant, and loose skin changes more pronounced on all the fingertips of his hands. Pressure to the fingertips resulted in a concave formation that lasted for more than 5 minutes (Figure 1). After minimal bruise, the lesions acquired an ecchymotic aspect. No other cutaneous or extracutaneous features were observed.

A biopsy specimen from his thumb showed prominent aggregates of lightly eosinophilic, amorphous material in the dermis staining positively with Congo red with green birefringence under polarized light and resistant to permanganate. Under immunohistochemical analysis, λ light chain stain stained the amyloid deposit, and findings were positive in some plasma cell aggregates (Figure 2). The amyloid deposition was also seen surrounding dermal vessels. Elastic tissue stains (Verhoeff–van Gieson stain) revealed fragmentation and diminution of elastic fibers in the dermis and clumping of the elastic fibers around dermal vessels. A biopsy specimen from the normal suprapubic skin was normal.

Findings of laboratory studies were normal except for elevated erythrocyte sedimentation rate and a prominent homogeneous band found on serum immunoelectrophoresis in the γ region reacting on immunofixation as free λ light chain. Urinary immunoelectrophoresis showed a large amount of Bence-Jones (λ) proteins. Skeletal survey findings were normal. Bone marrow aspirate contained an increased number of immature plasma cells making up 29% of the bone marrow cellularity and manifesting a pathologic immunophenotype (CD38+, CD19−, and CD56−). The plasma cells showed λ light chain restriction. The patient was diagnosed as having multiple myeloma–associated amyloidosis and acral localized acquired CL.