dependent manner. Moreover, simvastatin decreased phosphorylation of signal transducer and activator of transcription (STAT) 3, which is another critical player linked to AA (Fig 1, *E* and *F*). Simvastatin also significantly inhibited poly(I:C)- and IFN-γ–induced reactive oxygen species (ROS) production in a dose-dependent manner (Fig 1, *G*).

Finally, we determined whether simvastatin regulates Wnt/β-catenin signaling and hair growth. Simvastatin increased cell viability and TOPflash activity, indicating transcriptional activation of β-catenin (Fig 2, *A* and *B*). However, simvastatin did not affect other hair growth–related genes (Fig 2, *C*).

Statins exert pleiotropic anti-inflammatory properties in vitro and in vivo. Previously, statins have been reported to modulate cytokine secretion and T-cell responses and to inhibit the secretion of proinflammatory cytokines.[4] In this experiment, we showed that simvastatin directly attenuates inflammatory reactions in hair follicle cells, especially in ORS cells. However, simvastatin did not produce a significant effect on the expression of CXCL 9-11 and MHC class I. This indicates that simvastatin may not regulate IFN-γ–induced gene expression but that it can inhibit TNF-α–induced nuclear factor κB transcriptional activity in ORS cells, resulting in inflammatory response reduction in AA progression. One of the therapeutic mechanisms of simvastatin in AA is considered to be inhibition of the Janus kinase (JAK)/STAT signaling pathway. We additionally showed the effect of simvastatin on inhibition of the nuclear factor κB pathway, STAT3 pathway, and ROS production, which are closely related to the pathophysiology of AA.

There are in vitro studies showing that statins modulate Wnt/β-catenin signaling in various cells.[5] Our results indicate that simvastatin could induce hair regrowth by activating Wnt/β-catenin signaling and exerting its anti-inflammatory effect simultaneously in patients with AA.

In summary, we suggest that simvastatin improves AA through pleiotropic anti-inflammatory properties; inhibition of NF-κB, the JAK/STAT pathway, and ROS production; and activation of the Wnt/β-catenin signaling pathway.

Jung-Min Shin, PhD,[a] Kyung-Eun Jung, MD,[a] Su-Hyuk Yim, MD,[a] Babar Rao, MD,[b,c] Dong-kyun Hong, MD,[a] Young-Joon Seo, MD,[a] Chang-Deok Kim, PhD,[a] and Young Lee, MD[a,b]

From the Department of Dermatology, School of Medicine, Chungnam National University, Daejeon, Korea[a]; Department of Dermatology, Rutgers Robert Wood Johnson Medical School, Somerset, New Jersey[b]; and Department of Dermatology, Weill Cornell Medical Center, New York, New York.[c]

Drs Shin and Jung contributed equally to this article.

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Correspondence to: Young Lee, MD, 266 Munhwa-ro, Jung-Gu, Daejeon, Korea

E-mail: resina20@cnu.ac.kr

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Long-term sequelae from Stevens-Johnson syndrome/toxic epidermal necrolysis in a large retrospective cohort

To the Editor: Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN) is a rare, severe drug reaction associated with significant mortality.[1] Although the reaction itself is self-limited, associated morbidity may last well beyond the initial hospitalization. However, little is known about the frequency and risk factors associated with long-term SJS/TEN-related sequelae.[2,3]

Table I. Frequency of long-term sequelae among survivors of SJS/TEN

Characteristics	Data available (N = 150)	Any sequelae (n = 68, 45.3%)	No sequelae (n = 82, 54.7%)	*P* value	Severe sequelae* (n = 23, 15.3%)	Mild sequelae† (n = 45, 30.0%)	No sequelae (n = 82, 54.7%)	*P* value
Age, years, median (IQR)	42.5 (26.0-56.9)	39.6 (26.7-57.1)	43.6 (25.4-56.6)	.64	38.56 (22.6-46.6)	43.26 (28.3-57.40)	43.6 (25.4-56.6)	.28
Female sex, n/total (%)	82/150 (54.7)	42/68 (61.8)	40/82 (48.7)	.11	14/23 (60.9)	28/45 (62.2)	40/82 (48.7)	.28
White, n/total (%)	71/150 (47.3)	28/68 (41.1)	43/82 (52.4)	.17	7/23 (30.4)	21/45 (46.7)	43/82 (52.4)	.17
Black, n/total (%)	46/150 (30.7)	23/68 (33.8)	23/82 (28.0)	.45	11/23 (47.8)	12/45 (26.7)	23/82 (28.0)	.80
Asian, n/total (%)	21/150 (14.0)	10/68 (14.7)	11/82 (13.4)	.82	3/23 (13.0)	7/45 (15.6)	11/82 (13.4)	.94
Hispanic, n/total (%)	6/150 (4.0)	2/68 (2.94)	4/82 (4.87)	.55	0/23 (0.0)	2/25 (8.0)	4/82 (4.89)	.41
Median % BSA, admission (IQR)	10 (5-30)	20 (10-30)	9 (5-20)	<.01	30 (13-30)	20 (10, 30)	9 (5-20)	<.01
Median % BSA, maximum (IQR)	19 (7.5-30)	30 (15-60)	9.5 (5-25)	<.01	50 (30-75)	20 (10-40)	9.5 (5-25)	<.01
Median SCORTEN (IQR)	1 (1-2)	2 (1-3)	1 (1-2)	.04	2 (1-2)	2 (1-3)	1 (1-2)	.09
Severe ocular involvement, n/total (%)‡	19/150 (12.7)	17/68 (25.0)	2/82 (2.44)	<.01	12/23 (52.2)	5/45 (11.1)	2/82 (2.44)	<.01
Severe oral involvement, n/total (%)§	51/150 (34.0)	32/68 (47.1)	19/82 (23.2)	<.01	18/23 (78.3)	14/45 (31.1)	19/82 (23.2)	<.01
Severe genitourinary involvement, n/total (%)‖	19/150 (12.7)	11/68 (16.2)	8/82 (9.76)	.24	7/23 (30.4)	4/45 (8.89)	8/82 (9.76)	.02
Drug cause, n/total (%)	136/150 (90.7)	63/68 (92.6)	73/82 (89.0)	.45	23/23 (100.0)	40/45 (91.1)	73/82 (89.0)	.25
Infection cause, n/total (%)	14/150 (9.33)	4/68 (5.88)	10/82 (12.2)	.19	0/23 (0.0)	4/45 (8.89)	10/82 (12.2)	.20
Days from symptom onset to admission, mean (95% CI)	3.8 (2.7-4.9)	3.7 (2.9-4.5)	3.9 (2.1-5.8)	.96	2.3 (1.7-3.0)	4.4 (3.2-5.6)	3.9 (2.1-5.8)	.03
Days from symptom onset to dermatology consult, mean (95% CI)	4.8 (3.9-5.7)	4.4 (3.5-5.2)	5.2 (3.6-6.7)	.50	3.0 (2.2-3.9)	5.0 (3.8-6.2)	5.2 (3.6-6.7)	.04
Days from symptom onset to diagnosis, mean (95% CI)	4.7 (4.0-5.3)	4.5 (3.6,-5.3)	4.8 (3.8-5.9)	.65	3.0 (2.2-3.9)	5.2 (4.1-6.4)	4.8 (3.8-5.9)	<.01
Days from symptom onset to drug d/c, mean (95% CI)	0.8 (07-0.8)	0.8 (0.7-0.9)	0.8 (0.7-0.9)	.35	0.9 (0.7-1.0)	0.8 (0.6-0.9)	0.8 (0.7-0.9)	.63

BSA, Body surface area; *CI*, confidence interval; *d/c*, discontinuation; *IQR*, interquartile range; *SCORTEN*, Score of Toxic Epidermal Necrosis; *SJS/TEN*, Stevens-Johnson syndrome/toxic epidermal necrolysis.

*Severe sequelae: presence of severe sequelae involving any individual body surface/organ system. Severe ocular sequelae: symblepharon, scarring, blindness; Severe oral sequelae: gingival inflammation, oral pain. Severe genital sequelae: dyspareunia, adhesions, stenosis. Severe cutaneous sequelae: severe dyspigmentation or scarring. Severe renal sequelae: end-stage renal disease, ongoing dialysis. Severe gastrointestinal sequelae: esophageal strictures.

†Mild sequelae: presence of sequelae other than severe.

‡Severe ocular involvement: presence of adhesions, synechiae, need for active ophthalmologic management such as lysis of synechiae, placement of amniotic membranes.

§Severe oral involvement: presence of severe oral erosions, need for nasogastric tube, intubation for airway management.

‖Severe genitourinary involvement: presence of severe erosions, adhesions, need for active genitourinary management such as lysis of adhesions, vaginal dilator, catheter placement.

We analyzed a large, multicenter, retrospective cohort of 368 adult patients with SJS/TEN from the United States.[4] Of 314 patients known to survive to hospital discharge, 150 (47.8%) had information available regarding postdischarge follow-up. Of these, there was no mention of SJS/TEN-related sequelae in 54.7% (82/150), and long-term sequelae were noted in the remaining 45.3% (68/150), characterized as ocular, cutaneous, gastrointestinal, genital, renal, pulmonary, or other. Sequelae were reported to be severe in 15.3% (23/150) of patients (Table I). Ocular sequelae were most common (20.6%, 31/150), followed by cutaneous (19.3%, 29/150), genital (5.3%, 8/150), oral (4.0%, 6/150), renal (2.0%, 3/150), and gastrointestinal (0.67%, 1/150). Other sequelae not fitting into these categories included depression, anxiety, chronic pain, tinnitus, and limb amputations.

At the time of initial hospitalization, 12.7% (19/150) of patients had severe ocular SJS/TEN, and 34.0% (51/150) had severe oral SJS/TEN. Such patients, as well as those with higher median body surface area involvement, were at increased risk of long-term sequelae, including sequelae characterized as severe (all $P < .01$). Patients with severe genitourinary SJS/TEN (12.7%, 19/150) were also at risk of severe long-term sequelae ($P = .02$) (Table I).

There was no association between age, sex, or race and the risk of long-term sequelae in this cohort. SJS/TEN cause/trigger and days from symptom onset to hospital admission, dermatology consultation, diagnosis, and drug discontinuation also were not associated with development of SJS/TEN-related sequelae.

These data suggest that long-term SJS/TEN-related sequelae are relatively common and frequently severe, corroborating rates of previously reported sequelae in SJS/TEN. Higher acuity of SJS/TEN at the time of initial presentation—specifically, the presence of severe mucosal disease and higher total body surface area involvement—predicts the development of long-term SJS/TEN-related sequelae.

This study is limited by its retrospective nature, which obscures a detailed accounting of the specific features of patient sequelae and almost certainly underestimates their prevalence, because information on sequelae was determined via retrospective chart review rather than prospective systematic evaluation and was not available for all patients. Because all patients were managed by dermatology hospitalists at academic referral centers, results may not be fully generalizable. Future studies should prospectively evaluate the long-term sequelae of patients with SJS/TEN as an important marker of disease outcome and treatment efficacy. Clinicians should be aware of the potential for long-term complications among SJS/TEN survivors.

Leo L. Wang, MD, PhD,[a] *Megan H. Noe, MD, MPH, MSCE,*[b] *and Robert G. Micheletti, MD*[c]

From the University of Pennsylvania Perelman School of Medicine, Philadelphia[a]*; Department of Dermatology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts*[b]*; and Departments of Dermatology and Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia.*[c]

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Correspondence to: Robert G. Micheletti, MD, 3400 Civic Center Blvd, Perelman Center for Advanced Medicine, Room 724, Philadelphia, PA 19104

E-mail: *Robert.micheletti@pennmedicine.upenn.edu*

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The relationship of diagnosed acne and weight status in adolescent girls

To the Editor: The incidence of adolescent acne and obesity has increased in recent decades; however, a strong association between weight and acne has not been established. Pediatric studies have found higher levels of acne in individuals with increased insulin resistance or greater milk consumption,