

Curcumin inhibits poly(dA:dT)-induced IL-18 secretion by inhibiting the ASC oligomerization in human keratinocytes

Yujin Lee¹, Junghoon Kang¹, Mihee Yun¹ & Seong-Beom Lee¹

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Abstract

Backgrounds: Interleukin (IL)-18, a member of the IL-1 family, has been implicated in the development of a variety of inflammatory skin diseases. The binding of double-stranded (ds) DNA to absent in melanoma (AIM) 2 induces the oligomerization of apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and the recruitment of pro-caspase-1, which leads to the activation of caspase-1, subsequently resulting in the secretion of IL-1 β and IL-18. Curcumin is a naturally occurring polyphenolic compound in *Curcuma longa* and is also well known to have anti-oxidant and anti-inflammatory properties. In the current study, we focused on the inhibitory effect of curcumin on ASC oligomerization in human keratinocytes.

Methods: The IL-18 level was measured by using an ELISA kit. The protein levels of AIM2 inflammasome components, such as AIM2, ASC, and pro-caspase-1, were determined by using a western blot. The level of ASC oligomerization was also determined by using a western blot.

Results: Our results show pre-treatment with curcumin attenuated poly(dA:dT)-induced secretion of IL-18 in IFN- γ -primed human keratinocytes. Pre-treatment with 10 μ M curcumin was also found to inhibit ASC oligomerization in IFN- γ -primed cells.

Conclusion: These collective results show that curcumin

inhibits the poly(dA:dT)-induced secretion of IL-18 via the suppression of ASC oligomerization in IFN- γ -primed human keratinocytes.

Keywords: Curcumin, AIM 2, Inflammasome, Keratinocytes, ASC

Introduction

Interleukin (IL)-18, a member of the IL-1 family, regulates immune responses of T lymphocytes, depending on the surrounding environment, it, along with IL-12, enhances Th1 responses, while, with IL-4, it enhances Th2 responses¹. Thus, IL-18 has been implicated in a variety of inflammatory skin diseases, including psoriasis, atopic dermatitis, urticaria, and contact dermatitis².

Absent in melanoma (AIM) 2 is a cytosolic double-stranded (ds) DNA sensor that recognizes dsDNA of microbial or host origin. The binding of dsDNA to AIM2 induces the oligomerization of apoptosis-associated speck-like protein containing a caspase recruitment domain (ASC) and recruitment of pro-caspase-1, which leads to the activation of caspase-1, subsequently resulting in the secretion of IL-1 β and IL-18^{3,4}. It has been reported that AIM2 expression is strongly induced in the epidermis of patients with various inflammatory skin diseases, such as psoriasis, atopic dermatitis, and contact dermatitis⁵, suggesting that AIM2 also plays a role in the development of skin inflammatory diseases. In addition to inflammatory cells, human keratinocytes also express AIM2 and respond to dsDNA with IL-1 β secretion⁶. Poly(dA:dT) is a repetitive synthetic dsDNA sequence of poly(dA-dT) · poly(dT-dA). Poly(dA:dT) is a well-known activator for AIM2 inflammasome. We also previously reported that transfection with poly(dA:dT) induces the secretion of IL-1 β and IL-18 in human kera-

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¹Institute of Hansen's Disease, Department of Pathology, College of Medicine, The Catholic University of Korea, 222 Banpo-daero, Seocho-gu, Seoul 06591, Republic of Korea
Correspondence and requests for materials should be addressed to S. B. Lee (✉ sblee@catholic.ac.kr)

tinocytes^{7,8}.

The activation of AIM2 inflammasomes requires priming and activation steps. During the priming step, exogenous stimuli, such as interferon (IFN)- γ and LPS, induce the expression of inflammasome components, such as pro-IL-1 β , pro-caspase-1, and a sensor, AIM2^{3,4}. In the activation step, AIM2 is activated by its corresponding ligand and the activated AIM2 then induces the oligomerization of ASC and the assembly of inflammasome complexes to induce the activation of caspase-1^{3,4}. In the activation step for AIM2 inflammasomes, potassium efflux, but not reactive oxygen species (ROS) generation, is necessary for ASC oligomerization, whereas a ROS inhibitor inhibits AIM2 inflammasomes at the priming step⁹.

Curcumin (1,7-bis(4-hydroxy-3-methoxyphenyl)-1,6-heptadiene-3,5-dione) is a naturally occurring polyphenolic compound found in *Curcuma longa* (turmeric) and is well known to have anti-oxidant and anti-inflammatory properties¹⁰. Curcumin has previously been shown to have beneficial effects on various inflammatory diseases, such as Crohn's disease, ulcerative colitis, arthritis, and psoriasis in clinical studies¹¹. In addition, curcumin also inhibits the NACHT, LRR and PYD domains-containing protein 3 (NLRP3)-induced secretion of IL-1 β by inhibiting ASC oligomerization through the inhibition of potassium efflux in LPS-primed mouse bone marrow-derived macrophages¹². However, most studies dealing with the effects of curcumin on inflammasomes have focused on its inhibitory effects on NLRP3 inflammasomes in macrophages^{12–14}.

Thus, in the current study, we investigated the inhibitory effect of curcumin on AIM2 inflammasomes in human keratinocytes. Although it is well known that curcumin has anti-oxidant properties¹⁰, our focus was not on its anti-oxidant effects, since transfection with poly(dA:dT) does not generate ROS in human keratinocytes⁸. Rather, we examined the issue of whether or how curcumin attenuates the poly(dA:dT)-induced secretion of IL-18 in human keratinocytes.

Materials & Methods

Reagents and antibodies

The reagents and antibodies used in this study are described in Supplementary Materials.

Cell cultures

Human primary epidermal keratinocytes from neonatal foreskin, HEKn (Invitrogen, Carlsbad, CA, USA) and the Human keratinocyte cell line HaCaT (CLS, Eppenheim, Germany) were grown in serum-free EpiLife medium. The method for cell culture is described in more detail in Supplementary Materials.

Cell viability assay

Cell viability was assessed using the MTT assay method. The method for cell viability assay is described in more detail in Supplementary Materials.

Inhibitor treatments

For inhibitor treatments, HEKn and HaCaT cells were plated on 6 well plates. The method for inhibitor treatments is described in more detail in Supplementary Materials.

Quantification of IL-18 and active caspase-1

The culture medium of treated cells was analyzed for human IL-18 or active caspase-1 contents using an ELISA kit as described in Supplementary Materials.

Western blot analysis

The protein levels of pro-IL-18, AIM2, ASC, pro-caspase-1, and GAPDH were determined by western blotting. The method for western blotting is described in more detail in Supplementary Materials.

AIM2 or ASC containing plasmid construction

The method for construction of plasmids containing AIM2 or ASC is described in more detail in Supplementary Materials.

Immunoprecipitation for determining the interaction between AIM2 and ASC

The immunoprecipitation method for determining the interaction between AIM2 and ASC is described in more detail in Supplementary Materials.

ASC oligomerization assay

The method for ASC oligomerization assay is described in more detail in Supplementary Materials.

Statistical analysis

All results are expressed as the mean \pm S.D. of data from at least three separate experiments. Statistical significance was determined via the student's *t* test for two points; $P < 0.001$ or $P < 0.01$ was considered to be statistically significant.

Results

Transfection with poly(dA:dT) induced the secretion of IL-18 via a caspase-1-dependent pathway in IFN- γ -primed keratinocytes

We previously reported that transfection with poly(dA:

dT) induced IL-1 β or IL-18 secretion in IFN- γ -primed HEK cells and HaCaT cells^{7,8}. We first examined the issue of whether poly(dA:dT) has an effect on IL-18 secretion in HEK cells of a new lot number and in new HaCaT cells. HEK cells and HaCaT cells were primed with or without 100 ng/mL IFN- γ for 24 h and then exposed to various concentration of poly(dA:dT). Consistent with previous reports^{7,8}, transfection with poly(dA:dT) resulted in a significant enhancement in the secretion of IL-18 in a dose-dependent manner in both cells, compared to only IFN- γ primed cells (Supplementary Figure S1A and B).

It has been reported that, similar to pro-IL-1 β , pro-IL-18 needs to be processed by caspase-1 to convert it to the active form². Consistent with previous results, when IFN- γ -primed keratinocytes were pre-treated with Ac-YVAD-cmk, an inhibitor of caspase-1, before stimulation with poly(dA:dT), the secretion of poly(dA:dT)-induced IL-18 was significantly inhibited in a dose-dependent manner (Supplementary Figure S2A and B).

Transfection with poly(dA:dT)-induced IL-18 secretion was dependent on potassium efflux in IFN- γ -primed keratinocytes

Potassium efflux has been reported to be a main trigger for the activation of NLRP3 or AIM2 inflammasomes in macrophages^{12,15,16}. Thus, we investigated the issue of whether potassium efflux is necessary for the poly(dA:dT)-induced activation of AIM2 inflammasomes in human keratinocytes. Inhibition of potassium efflux by increasing concentrations of potassium chloride in the culture media, at 20 and 50 mM, suppressed transfection with the poly(dA:dT)-induced secretion of IL-18 and the active form of caspase-1 in IFN- γ -primed HEK cells, compared to cells grown in culture media with no added potassium chloride (Supplementary Figure S3).

Pre-treatment with curcumin inhibited poly(dA:dT)-induced IL-18 secretion in IFN- γ -primed keratinocytes

We next examined whether curcumin inhibits the poly(dA:dT)-induced secretion of IL-18 in IFN- γ -primed keratinocytes. Pre-treatment with 10 and 20 μ M curcumin significantly inhibited poly(dA:dT)-induced IL-18 secretion in IFN- γ -primed HEK (Figure 1A) and HaCaT cells (Figure 1B). However, pre-treatment with 5 μ M curcumin had no effect on poly(dA:dT)-induced IL-18 secretion in HaCaT cells (Figure 1B), whereas it inhibited IL-18 secretion in HEK cells (Figure 1A).

We also examined the cytotoxicity of curcumin on HEK and HaCaT cells. Cells were treated with the indicated concentrations of curcumin for 24 h. Treatment with curcumin at concentrations of up to 20 μ M had no

effect, but at concentrations over 50 μ M, the viabilities of HEK and HaCaT cells was significantly decreased (Figure 1C and D).

Pre-treatment with curcumin at 20 μ M, but not at 10 μ M, inhibited the protein expression of AIM2 and pro-caspase-1 in IFN- γ -primed/poly(dA:dT)-treated HaCaT cells

We then investigated the issue of how curcumin inhibits poly(dA:dT)-induced IL-18 secretion. We initially examined whether curcumin inhibits the expression of AIM2 inflammasome components, such as AIM2, ASC, and pro-caspase-1. As shown in Figure 2A, priming with IFN- γ induced the expression of AIM2 and pro-caspase-1 proteins, compared with non-treated control cells. In addition, transfection with poly(dA:dT) had a synergistic effect in the expression of AIM2 and pro-caspase-1 in IFN- γ -primed HaCaT cells, compared with only IFN- γ -primed cells (Figure 2A).

Although pre-treatment with curcumin at concentrations of both 10 and 20 μ M inhibited the poly(dA:dT)-induced secretion of IL-18 in IFN- γ -primed cells (Figure 1A and B), pre-treatment with curcumin affected differently the expressions of the AIM2 inflammasome components, AIM2 and pro-caspase-1, depending on its concentration. Pre-treatment with 20 μ M curcumin significantly reduced the protein expressions of AIM2 and pro-caspase-1, whereas at a concentration of 10 μ M, it did not affect the protein expressions of AIM2 and pro-caspase-1 in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells (Figure 2A). These results indicate that pre-treatment with 20 μ M curcumin inhibits IL-18 secretion via the down-regulation of AIM2 and pro-caspase-1, but, at a concentration of 10 μ M, it inhibits IL-18 secretion through an alternate mechanism that does not involve inhibiting the expressions of AIM2 and pro-caspase-1 in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells.

On the other hand, treatment with 20 μ M curcumin did not significantly affect the viabilities of non-treated HEK and HaCaT cells (Figure 1C and D), whereas a concentration of 20 μ M caused a greater cytotoxic effect and a survivability of less than 25% in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells, compared to cells that had been pre-treated without or with curcumin at 5 and 10 μ M in HaCaT cells (Figure 2B). We thus focused on the inhibitory effect of 10 μ M curcumin on AIM2 inflammasomes in subsequent experiments.

Pre-treatment with curcumin at 10 μ M inhibits ASC oligomerization in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells

We next examined the issue of whether curcumin could

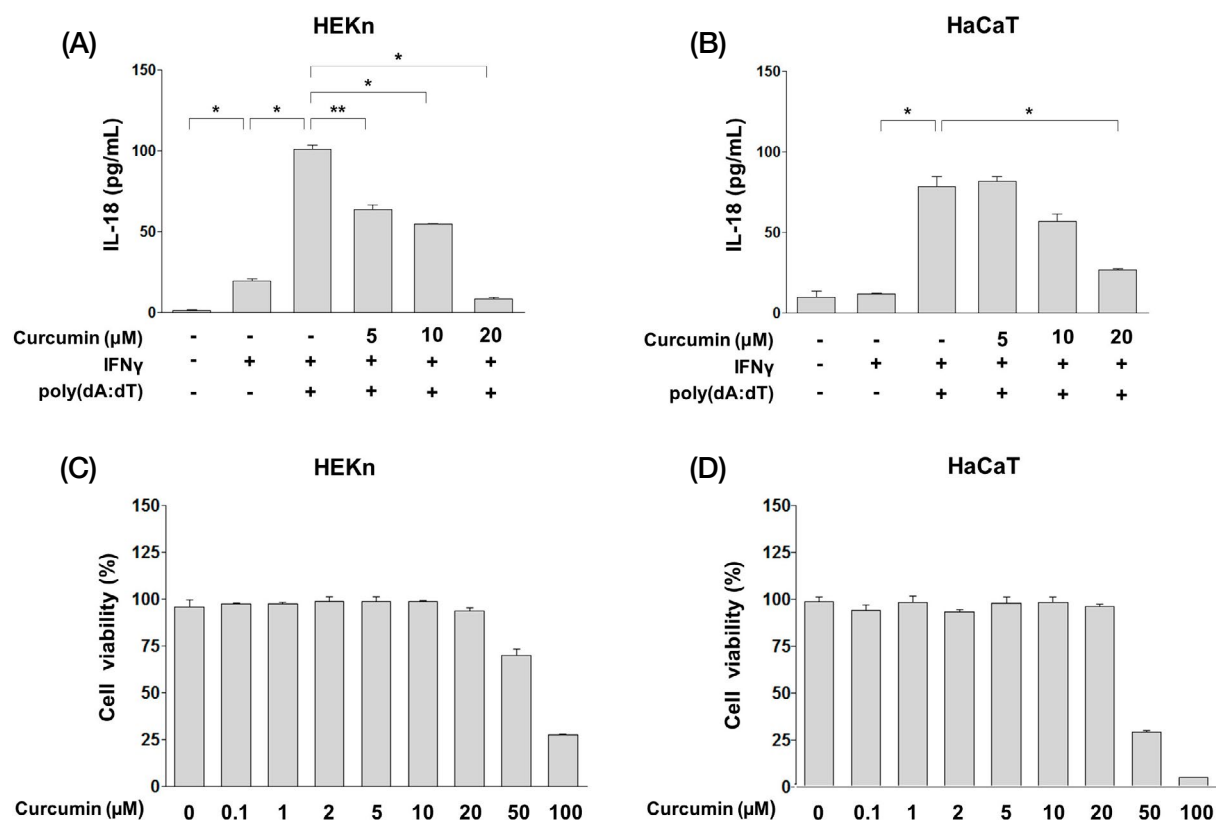


Figure 1. Treatment with curcumin inhibited poly(dA:dT)-induced IL-18 secretion in IFN- γ -primed keratinocytes. HEK293T in A and HaCaT cells in B were primed with or without 100 ng/mL IFN- γ for 24 h, treated with or without curcumin for 1 h at the designated concentrations, and then stimulated by transfection with 2 μ g/mL poly(dA:dT) for additional 24 h. (A and B) The level of IL-18 was measured by using an ELISA kit. (C and D) HEK293T in C and HaCaT cells in D were treated with curcumin at the indicated concentrations. Cell viability was determined using an MTT assay. * $P < 0.001$ and ** $P < 0.01$ between the indicated groups.

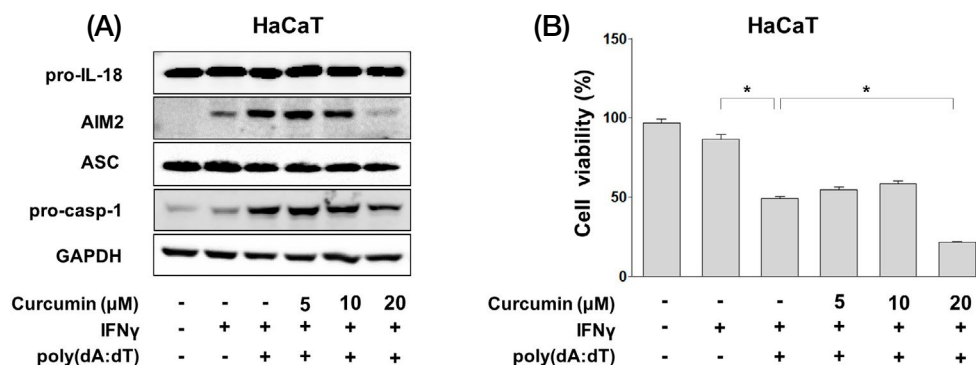


Figure 2. Pre-treatment with curcumin at 20 μ M, but not at 10 μ M, inhibited the protein expressions of AIM2 and pro-caspase-1 in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells. HaCaT cells were primed with or without 100 ng/mL IFN- γ for 24 h, treated with or without curcumin for 1 h at the designated concentrations, and stimulated by transfection with 2 μ g/mL poly(dA:dT) for additional 24 h. (A) The protein levels of pro-IL-18, AIM2, ASC, pro-caspase-1, and GAPDH were analyzed by western blotting. Pro-caspase-1: pro-caspase-1. (B) Cell viability was determined using an MTT assay. * $P < 0.001$ between the indicated groups.

inhibit AIM2-ASC interaction or ASC oligomerization. For this experiment, we transfected human embryonic kidney (HEK) 293T cells with full-length HA-AIM2 and

a non-tagged (NT)-ASC plasmid, since examining the interaction between endogenous AIM2 and ASC proteins in HaCaT cells is a nearly impossible task. When AIM2

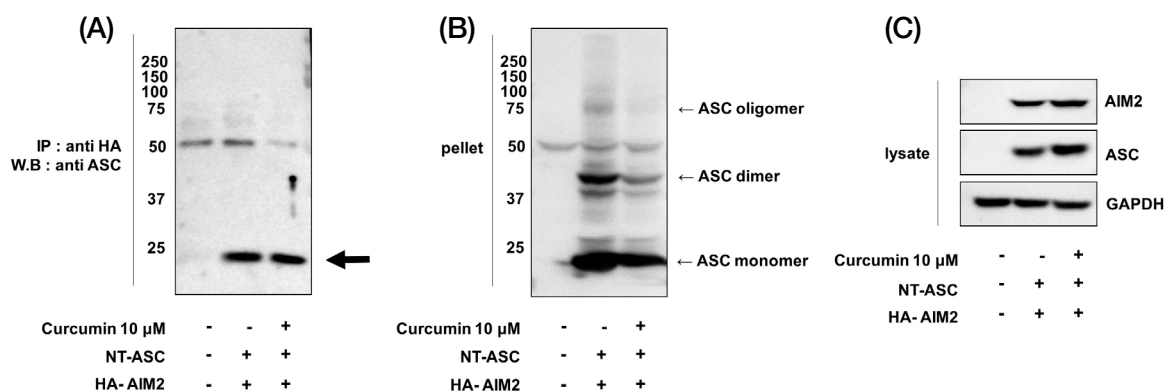


Figure 3. Pre-treatment with curcumin at 10 μ M inhibited ASC oligomerization in HEK 293T cells overexpressing AIM2 and ASC. HEK 293T cells were transfected with HA-tagged AIM2 and ASC plasmids. At 24 h after the transfection, the cells were treated with or without 10 μ M curcumin for an additional 24 h. (A) HA-tagged AIM2 was immunoprecipitated with anti-HA conjugated agarose beads and the immunocomplexes were then analyzed by western blotting with an anti-ASC antibody. Arrow: ASC monomer. Non-specific bands at 50 kDa were detected by anti-ASC antibody in the immunocomplexes of all cells. (B) For measuring the level of ASC oligomers, the insoluble pellets from total cell lysates were analyzed by western blotting using an anti-ASC antibody. (C) Total cell lysates were analyzed by western blotting using anti-ASC and anti-AIM2 antibodies.

and ASC were over-expressed in HEK 293T cells, the resulting overexpressed AIM2 spontaneously interacted with ASC (Figure 3A) and ASC formed dimers or oligomers (Figure 3B) even in the absence of poly(dA:dT) stimulation. However, pre-treatment with 10 μ M curcumin inhibited the dimerization or oligomerization of ASC (Figure 3B), but not the interaction between AIM2 and ASC (Figure 3A), compared to only AIM2 and ASC transfected HEK 293T cells. Unexpectedly, non-specific bands at 50 kDa were detected by anti-ASC antibody in the immunocomplexes of all cells (Figure 3A).

We then assessed the inhibitory effect of curcumin on the oligomerized ASC complex in HaCaT cells. Priming with IFN- γ caused a slight increase in the level of ASC oligomers and transfection with poly(dA:dT) showed an additive effect in the formation of ASC oligomers in IFN- γ -primed HaCaT cells, compared with only IFN- γ -primed cells (Figure 4). Consistent with the effect of 10 μ M curcumin on ASC oligomerization in HEK 293T cells overexpressing AIM2 and ASC (Figure 3B), pre-treatment with 10 μ M curcumin inhibited ASC oligomerization in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells, compared to only IFN- γ -primed/poly(dA:dT)-transfected cells (Figure 4). Interestingly, in our experimental system, ASC dimers were detected in non-treated control cells and the level of these components was not affected by treatment with IFN- γ and/or poly(dA:dT) (Figure 4). However, pre-treatment with 10 μ M curcumin resulted in a decrease in the level of ASC dimers in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells (Figure 4). These results suggest that pre-treatment with curcumin at a concentration of 10 μ M suppresses AIM2 inflammasome formation through

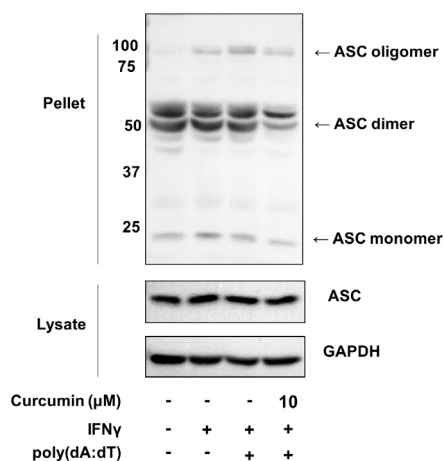


Figure 4. Pre-treatment with curcumin at 10 μ M inhibited ASC oligomerization in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells. HaCaT cells were primed with or without 100 ng/mL IFN- γ for 24 h, treated with or without 10 μ M curcumin for 1 h, and stimulated by transfection with 2 μ g/mL poly(dA:dT) for an additional 24 h. For measuring the level of ASC oligomers, the insoluble pellets from total cell lysates were analyzed by western blotting with an anti-ASC antibody.

the inhibition of ASC oligomerization in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells.

Discussion

Interestingly, the effect of curcumin on the poly(dA:dT)-induced secretion of IL-18 varied according to the concentration of curcumin in both HEK293T and HaCaT cells.

Pre-treatment with curcumin at concentrations of 10 and 20 μM significantly inhibited poly(dA:dT)-induced IL-18 secretion in IFN- γ -primed HEK293T and HaCaT cells (Figure 1A and B). However, curcumin at 5 μM inhibited the poly(dA:dT)-induced secretion of IL-18 in IFN- γ -primed HEK293T cells (Figure 1A), whereas it had no effect on IL-18 secretion in HaCaT cells (Figure 1B). In addition, pre-treatment with curcumin at a concentration of 20 μM , but not at 10 μM , showed a greater cytotoxic effect (Figure 2B) and caused a reduction in the expression of AIM2 and pro-caspase-1 proteins (Figure 2A), and subsequently inhibited poly(dA:dT)-induced IL-18 secretion in IFN- γ -primed human keratinocytes (Figure 1).

However, the objective of this study was to investigate the inhibitory effect of curcumin on the ASC oligomerization in human keratinocytes. Thus, we restricted our focus to the inhibitory effect of 10 μM curcumin, which inhibits IL-18 secretion (Figure 1), but does not affect the expression of AIM2 inflammasome components, in human keratinocytes (Figure 2). We speculated that the inhibitory effect of 20 μM curcumin on the expression of AIM2 and pro-caspase-1 was due to the inhibitory effect of curcumin on IFN- γ or poly(dA:dT)-mediated nuclear factor (NF)- κB signaling related to the expression of AIM2 and pro-caspase-1, since NF- κB signaling, a major target of curcumin, is downstream in the IFN- γ or poly(dA:dT) pathway^{17,18}. In addition, the cytotoxicity of 20 μM curcumin may contribute to the down-regulation of AIM2 and pro-caspase-1. Although the activation of AIM2 inflammasomes, by priming with IFN- γ and activating with transfection with poly(dA:dT), showed cytotoxic effects due to inflammasome-induced cell death, resulting in cell viabilities of about 50%, compared to control cells, pre-treatment with 20 μM curcumin showed an additive cytotoxic effect, with a survivability of less than 25% (Figure 2B). It is generally thought that curcumin functions to reduce oxidative stress by increasing anti-oxidant activity or by inhibiting enzymes that generate ROS. In contrast, it has also been reported that curcumin generates ROS and subsequently induces cell death, depending on the cell types or its concentration¹⁹.

Our results show that AIM2 and pro-caspase-1 protein levels are upregulated in IFN- γ -primed HaCaT cells (Figure 2A). Moreover, poly(dA:dT) showed an additive effect on their expressions (Figure 2A). In contrast to expressions of AIM2 and pro-caspase-1, our results show that treatment with IFN- γ and/or poly(dA:dT) did not affect the expression of pro-IL-18 or ASC. It has been reported that, although IL-18 is structurally similar to the IL-1 family of cytokines and the active form of both IL-1 β and IL-18 requires processing by a cysteine protease caspase-1, while pro-IL-1 β needs priming with a stimulator, such as LPS and IFN- γ , for its expression, pro-

IL-18, an inactive precursor of IL-18, is constitutively present in various cells, such as keratinocytes, dendritic cells, and macrophages². In addition, previous studies have reported that treatment with ATP or poly(dA:dT) had no effect on the expression of ASC in LPS-primed macrophages²⁰. We also previously reported that treatment with IFN- γ and/or poly(dA:dT) did not affect expression of ASC in HEK293T cells⁷ and HaCaT cells⁸.

Jin *et al.*²¹ and Wang *et al.*²² previously reported that the reconstitution of AIM2 inflammasomes in HEK293T cells by the co-transfection of AIM2, ASC, pro-caspase-1, and pro-IL-1 β , induced the secretion of IL-1 β . Our results also show that AIM2 and ASC spontaneously formed a complex (Figure 3A) and that ASC formed dimers or oligomers (Figure 3B) in HEK293T cells overexpressing AIM2 and ASC, even in the absence of poly(dA:dT) stimulation. However, when HEK293T cells were transfected with only plasmids containing pro-caspase-1 and pro-IL-18, overexpressed pro-caspase-1 was spontaneously activated and cleaved pro-IL-18 into IL-18, we thus were not able to examine the inhibitory effect of curcumin on AIM2 inflammasome-induced IL-18 secretion in HEK293T cells that had been transfected with AIM2, ASC, pro-caspase-1, and pro-IL-18 (data not shown).

In addition, treatment with 10 μM curcumin inhibited ASC oligomerization in HEK293T cells overexpressing AIM2 and ASC (Figure 3B) and in IFN- γ -primed/poly(dA:dT)-transfected HaCaT cells (Figure 4). We hypothesize that this may be due to the inhibitory effect of curcumin on potassium channels, since potassium efflux is necessary for AIM2-dependent ASC oligomerization^{16,23}. Our results also show that the inhibition of potassium efflux suppressed transfection with the poly(dA:dT)-induced secretion of IL-18 and the active form of caspase-1 in IFN- γ -primed HEK293T cells, suggesting that potassium efflux is a trigger for the activation of AIM2 inflammasomes in human keratinocytes (Supplementary Figure S3). Although, in the current study, we did not directly measure changes in intracellular potassium levels before and after the curcumin treatment, previous findings are consistent with curcumin inhibiting the flow of potassium by blocking potassium channels. Previous studies have also reported that curcumin inhibits the flow of potassium by blocking Kv1.4 channels in bovine adrenal cell²⁴, Kv2.1 channels in HEK293 cells²⁵, and Kv11.1 channels in THP-1 cells²⁶.

Interestingly, Yin *et al.*¹² reported that curcumin prevented the action of NLRP3 inflammasomes by inhibiting potassium efflux in bone marrow-derived macrophages. However, in contrast to our results, in that study, the authors reported that treatment with 40 μM curcumin did not inhibit poly(dA:dT)-induced IL-1 β secretion in LPS-primed bone marrow-derived macrophages. The

reason for such a discrepancy is not currently clear, but could be due to differences in cell types, curcumin concentrations, and the ligands used for priming.

We previously reported that treatment with Epigallocatechin-3-gallate attenuates the AIM2-induced secretion of IL-1 β at both the priming and activation steps in human keratinocytes⁷. At that reports, we showed that treatment with poly(dA:dT) increased the level of ASC dimers in IFN- γ -primed HEK293 cells⁷. However, at that time, we were able to detect only ASC dimers, but not its oligomers, in the pellets. In the current study, to detect such ASC oligomers, we changed the composition of the incubation buffer for the cell pellet and did not use disuccinimidyl suberate (DSS), a compound that causes protein cross-linking, which is usually used for detecting ASC oligomers in THP-1 cells and macrophages^{16,20,27}. Using this system, we observed that the level of ASC oligomers changed depending on the treatment with curcumin, IFN- γ and/or poly(dA:dT) (Figure 4). Interestingly, in our system, ASC dimers were detected in non-treated control cells and their level were not affected by treatment with IFN- γ and/or poly(dA:dT) in HaCaT cell (Figure 4). In contrast, Coll *et al.*²⁰ reported that ASC dimers were present in cell pellets only from poly(dA:dT)-treated immortalized bone marrow-derived macrophages, but not in non-treated control cells. Although it is difficult to directly compare our results with those of previous studies due to differences in experimental protocols, the reasons for these discrepancies would be helpful in terms of understanding the propensity of naïve ASC to form dimers, which undergo further assembly into oligomers in response to an inflammasome stimulator.

Curcumin has attracted worldwide attention due to its various health benefits, pro- or anti-oxidants and anti-inflammatory properties. Numerous clinical studies, conducted over three decades, have already indicated that curcumin has therapeutic potential against a wide range of human diseases, including cancer, inflammatory diseases, neurodegenerative diseases, and infectious diseases¹¹. In addition, methods for formulating and delivering curcumin have been extensively studied in attempts to increase its bioavailability²⁸.

Conclusion

Taken together, our results demonstrate that curcumin inhibits poly(dA:dT)-induced IL-18 secretion by inhibiting ASC oligomerization in IFN- γ -primed human keratinocytes, thus providing a new mechanism that explains the inhibitory effect of curcumin on AIM2 inflammasome activation.

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Conflict of Interest Yujin Lee, Junghoon Kang, Mihee Yun and Seong-Beom Lee declare that they have no conflict of interest.

Human and animal rights The article does not contain any studies with human and animal and this study was performed following institutional and national guidelines.

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