In their correspondence, they state that one potential explanation for the apparent discrepancy in the data is that they used primary BECs and we used a BEC cell line. While we did use the A549 cell line for some studies, we show in Fig 2D (RSV infection) and supplemental Fig 1, *E* (SeV infection), that siRNA-mediated knockdown of RIG-I in normal human bronchial epithelial (NHBE) cells inhibited approximately 90% of the TSLP gene induction. Also, we showed that NF-κB could be ChIP'd from 2 sites in the TSLP gene promoter following viral infection of these same cells (supplemental Fig 2). We had previously defined these NF-κB sites as important for the induction of TSLP gene expression by IL-1β or TNF-α treatment of NHBE cells.[4] Thus, we have shown that RIG-I–induced activation of NF-κB is critical for TSLP gene induction in BECs. We have also used siRNA knockdown of TLR3 and TLR4 in NHBEs and have found that the knockdown of each individually leads to an approximately 40% to 50% reduction in RSV-mediated TSLP gene induction (Lee and Ziegler, unpublished results). The TLR3 result is consistent with the finding that RIG-I activation induces TLR3 gene expression. By using both constitutively active IRF3 or IRF 7 (Fig 3) or dominant negative IRF3 or IFR7 (data not shown), we could find no role for these factors in respiratory virus induction of TSLP in BECs.

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Absence of homogenization might explain the benefits of raw cow's milk

To the Editor:

van Neerven et al[1] discuss the factors in raw cow's milk that might contribute to protection against allergies. However, it is possible that it is not the presence of factors in raw milk, but rather the absence of a factor in processed milk—specifically homogenization—that is responsible for the "protection."

The fat globules in raw milk are 3.3 μm in average diameter and are composed of triglycerides surrounded by a milk fat globule membrane made of phospholipids and protein. In raw milk, these fat globules, which are more buoyant than water, rise to the surface and form cream. Homogenization of treated cow's milk prevents this separation by forcing the milk under pressure through very narrow tubes, resulting not only in a decrease in the average fat globule diameter from 3.3 μm to 0.4 μm but also a 600-fold increase in the total number of fat globules and an approximately 10-fold increase in their total surface area.[2] The tremendous increase in total surface area results in the attraction of proteins to the surface of the new smaller fat globules.[2] This close association of proteins with lipids has implications for the intralymphatic absorption and immunologic presentation of those proteins.[3]

In murine studies, homogenized cow's milk is more likely than raw milk to both induce sensitization and provoke allergy symptoms on challenge.[4,5] Because smaller lipid-protein conjugates have better transdermal absorption than do larger particles,[6] the decrease in the size of homogenized cow's milk fat globules may also have implications for the transdermal sensitization hypothesis of Lack.[7] And because IgE promotes facilitated antigen presentation leading to the production of IgE to different epitopes,[8] early IgE production to such a major food source could act as an initiator allergen, promoting allergy in general.

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Reply

To the Editor:

Miller[1] stated in his correspondence in response to our Rostrum article that it is possible that it is not the presence of factors in raw milk, but rather the absence of homogenization, that might explain the protective effect of farm milk consumption.

We agree that homogenization and/or heating of milk may indeed have a biological effect on cow's milk allergy. This is indicated by the animal studies referenced, but to our knowledge, there is no human data to support this. In our article, we have discussed the possible factors in raw milk that may be involved in the prevention of asthma.[2] In the farm milk studies that were discussed, inverse associations between farm milk consumption and inhalation allergies were demonstrated. Importantly, Loss et al[3]