Lerman et al., 2017). Thus, the findings by Bissonnette et al. (2017) do not corroborate the results of these studies, which investigate changes in the anatomical consequences of atherosclerosis in contrast to the cellular metabolic disturbances. These somewhat conflicting results underscore that much remains unknown about the exact mechanisms of premature cardiovascular disease in psoriasis and the role of systemic anti-psoriatic agents in cardiovascular risk reduction.

In the study by Bissonnette et al. (2017), the primary endpoint was changes in mean target-to-background ratio of the ascending aorta. Additionally, activity in the carotid arteries was assessed. However, choosing the ascending aorta as the representative aortic segment may not always be the best approach. For example, Besson et al. (2014) investigated the performance of different semiquantitative measures to distinguish control subjects from patients with large vessel vasculitis and found that target-to-background ratio performed well in all segments of the vessel except in the ascending aorta (Besson et al., 2014). In line with this, we also recently found increased aortic wall inflammation in psoriasis patients compared with control subjects without inflammatory diseases in all segments of the vessel except the ascending part (Hjuler et al., 2017). Specifically analyzing fluorodeoxyglucose (FDG) uptake in the ascending aorta may be sensible when imaging aneurysms of the ascending aorta and certain aortopathies. However, it is well known that atherosclerotic plaques may be found throughout the entire aorta and, in contrast to such aortopathies, are less common in the ascending aorta (Khoury et al., 1997; Liang et al., 2009). Even though there is no consensus in this field, it has been suggested that whole-vessel aortic target-to-background ratio based on maximal standardized uptake values is well-suited to the assessment of global arterial inflammation as a marker of cardiovascular risk for the assessment of global arterial inflammation (Bucerius et al., 2016).

In addition to these methodological considerations, we are well-advised to adopt a cautious approach when considering both positive and negative results of trials with FDG positron emission tomography outcomes, because it is unknown to what extent increased FDG uptake translates into higher cardiovascular risk and whether changes in FDG uptake reflect a beneficial treatment effect.

Whether a different approach to the image analysis would have changed the outcome of the study by Bissonnette et al. (2017) is unknown, but these results call for awareness when choosing the endpoint in cardiovascular imaging studies in psoriasis. We suggest evaluating not only the ascending aorta, but the entire aorta and all aortic segments to obtain a high sensitivity of changes in aortic inflammation and consistency across various studies.

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CONFLICT OF INTEREST
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Response to Hjuler et al.

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We want to thank Hjuler et al. (2017) for their comments on our article (Bissonnette et al., 2017). We agree that many unknowns remain on the mechanisms of atherosclerosis in patients with psoriasis. Our hypothesis was that adalimumab reduced vascular inflammation in patients with moderate-to-severe psoriasis. Measurement of vascular inflammation in the aorta and the carotids did not confirm this hypothesis. The target-to-background ratio was measured in an area that was

R Bissonnette et al.
Response to Hjuler et al.

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localized between the beginning of the ascending aorta and the left subclavian artery, which includes the ascending aorta and the aortic arch. Another study, recently presented at the 2017 meeting of the American Academy of Dermatology, which compared the effects of adalimumab, placebo, and UVB phototherapy on vascular inflammation, also showed no difference between adalimumab and placebo (American Academy of Dermatology Association, 2017). As alluded to by Hjuler et al., studies on vascular inflammation are complex. How changes measured in vascular inflammation translate into risks of occlusive cardiovascular events has not been well studied. Numerous variations in techniques measuring vascular inflammation have been used and published including the analyses of different arteries, study of the most disease segment (highest fluoro-2-deoxy-D-glucose update), study of larger segments with average uptake, and use of arterial/venous ratios or absolute standardize uptake values, SUV). Additional research is needed comparing the sensitivity and specificity of these various approaches. The publication by Hjuler et al. suggesting that there was an increase in vascular inflammation in all segments of the vessel except the ascending aorta in patients with psoriasis as compared with controls is interesting. This suggests that the optimal strategy to measure vascular inflammation may vary according to the pathology under study.

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Characterization of Autoantigen Presentation by HLA-C*06:02 in Psoriasis

TO THE EDITOR
Psoriasis is a stubborn skin problem that is considered to be a T-cell-mediated chronic inflammatory skin disease and affects 2–3% of individuals worldwide (Harden et al., 2015). Studies have suggested that human leukocyte antigen C (HLA-C) is a strong susceptibility gene in psoriasis presenting autoantigens (Okada et al., 2014; Zhou et al., 2016).

Recently, Arakawa and colleagues (2015) identified a nonapeptide, “VRSRRCLRL,” as an autoantigenic peptide (pVR) for psoriasis from one HLA-C*06:02 positive patient. They further confirmed this autoantigen in 20 of 42 patients. We have also measured responses to pVR in six patients with psoriasis progressing. Fresh peripheral blood mononuclear cells were isolated and stimulated with the peptide. Patients 1 and 4 showed markedly increased frequencies of CD8+ T cells expressing IL-17A and IFN-γ and were further typed to be HLA-C*06:02 positive (Supplementary Figure S1 and Table S1 online). Among the nonresponsive patients, three were typed to be HLA-C*06:02 and one was typed to be other alleles suggesting other possible autoantigens involved (Besgen et al., 2010; Johnston et al., 2004; Lande et al., 2014). From another recent report, pVR was also likely to be the autoantigen in one of their patients for

Abbreviation: HLA-C, human leukocyte antigen C

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