

Comment on: Korpos et al. The Peri-islet Basement Membrane, a Barrier to Infiltrating Leukocytes in Type 1 Diabetes in Mouse and Human. *Diabetes* 2013;62:531–542

Charmaine J. Simeonovic and Christopher R. Parish

Korpos et al. (1) claim that “limited information exists on the nature of the ECM [extracellular matrix] of the pancreas and, in particular, on the composition of peri-islet capsule,” and that they provide the “the first comprehensive analysis of the [ECM] composition of peri-islet capsules.”

We dispute the strength of these claims. In mice we originally reported in 2008 that a basement membrane (BM) exists around islets, and eight unique components were identified (type IV collagens $\alpha 1$, $\alpha 2$, laminin $\alpha 2$, $\beta 1$, $\gamma 1$, nidogen 1, nidogen 2, perlecan) as well as two composite components (laminin Engelbreth-Holm-Swarm, collagen IV) (2). It was also shown that type IV collagens $\alpha 3$, $\alpha 4$, $\alpha 5$, $\alpha 6$ were not present (2). Korpos et al. (1) were able to find a further three unique components (laminin $\alpha 4$, $\beta 2$, agrin) and one composite component (laminin 322).

In 2008 in humans (3,4), at least four unique components (laminin $\alpha 1$, $\alpha 5$, $\beta 1$, $\gamma 1$) were identified and in their Supplementary Figure 1 staining of collagen IV $\alpha 1/\alpha 2$ and nidogen 1 in the peri-islet BM was evident (3). Korpos et al. (1) identified laminin $\alpha 5$ and perlecan and stated that “most ECM proteins analyzed showed the same localization pattern as observed in NOD pancreata.”

We also dispute the claims that Korpos et al. (1) are the first to show the connection between loss of the peri-islet BM and the progression of type 1 diabetes and that our study in 2008 was “without correlation to disease progression in mice” (2). In 2008, we showed in NOD mice “that destructive insulinitis is selectively associated with

complete destruction of the peri-islet BM but not that of other adjacent BMs of acini, capillaries or intact islets without MNC infiltration” (2).

Korpos et al. (1) also say, “leukocyte penetration of the peri-islet BM in association with a macrophage subpopulation in NOD mice and human type 1 diabetic samples and, hence, potentially a novel therapeutic target specifically acting at the islet penetration stage.” We were the first to suggest this and, significantly, to provide evidence that protecting the peri-islet BM against leukocyte infiltration protects against type 1 diabetes (5).

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From the ¹Department of Immunology, The John Curtin School of Medical Research, The Australian National University, Canberra, Australia.

Corresponding author: Charmaine J. Simeonovic, charmaine.simeonovic@anu.edu.au

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