COMMENTS AND RESPONSES

Response to Comment on: Lin et al. Long-Term Changes in Adiposity and Glycemic Control Are Associated With Past Adenovirus Infection. Diabetes Care 2013;36:701–707

We would like to thank Yamada et al. (1) for their comments about our article (2) and for their interest in our work. They state that the association of Ad36 infection with better glycemic control that we reported does not correspond with their previous meta-analysis (3). Although there may be a number of possibilities to explain the difference, it should be noted that the meta-analysis by Yamada et al. (3) included 2,870 subjects for BMI analyses but only 1,083 subjects for determining the association of Ad36 with glucose levels. However, data are now available for additional 3,037 subjects that show an association of various components of glycemic control with Ad36 seropositivity in humans. These additional data are from our study (2) and four additional studies (Rogers et al. 2008, Krishnapuram et al. 2011 and 2012, Dubuisson et al. 2011, rev. in 4), which were published before the meta-analysis by Yamada et al. (3) but were not included in their analyses.

Yamada et al. assert that it is important to conduct prospective studies to obtain more definitive evidence about the role of Ad36 in human metabolism. We agree. In fact, our study (2) is a 10-year prospective study. We are unclear about the specific objections Yamada et al. have to this design. Concerning the lack of statistical significance in some subgroups in our study—please note that this is a new and interesting finding. When analyzed collectively, subjects show an association of Ad36 with adiposity and glycemic control. However, when analyzed separately by sex and BMI groups, differences between subgroups emerge for statistical associations. In fact, this is a strength of the study because it informs about the specific groups that may contribute to the overall association.

Finally, Yamada et al. have expressed a concern about the biological mechanism and clinical relevance. Clearly, humans are not a suitable model to determine the mechanism of action of Ad36. However, numerous studies have used various cell culture and animal models to understand the underlying mechanism as summarized elsewhere (4–6). In vitro, the cell signaling modulated by Ad36 to influence cellular lipid and glucose metabolism has been determined and a viral gene necessary and sufficient for the effects of Ad36 has been identified (4). The in vivo studies collectively show that experimental infection of animals with Ad36 increases adiposity, improves glycemic control, and attenuates liver fat accumulation. Importantly, these findings are mirrored in human associations (4,6). Although research in this area is ongoing in many laboratories worldwide, because of the congruence of the majority of cellular, animal, and human data, it is not at all premature to consider the potential clinical relevance and implications of these findings.

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