

LETTERS TO THE EDITOR

Prevalence of Infection With Adenovirus-36 in Belgium and Holland and Association With Obesity

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TO THE EDITOR: The article titled "Lack of Evidence for the Role of Human Adenovirus-36 in Obesity in a European Cohort" by Goossens *et al.* (1) reports a very low prevalence of human adenovirus-36 (Ad-36) and no evidence of association with obesity in 540 Dutch and Belgian individuals. There are several concerns with this article. First, the findings are in contrast to other papers in the literature from the United States, Italy, and Korea (2–8). We reported that 30% of obese and 11% of nonobese US adults had Ad-36 antibodies and a strong association with obesity ($P < 0.001$) (2). We found a 30% prevalence of Ad-36 antibodies in obese children in Korea and a strong association with obesity ($P < 0.01$) (3). Na *et al.* (4) found Ad-36 antibodies in 29% of obese and 14% of nonobese children in Korea. Trovato *et al.* (5,6) in two studies from Italy noted a prevalence of Ad-36 antibodies of >40% and an association with obesity. Broderick *et al.* (7) did not find an association of Ad-36 with obesity in military personnel in San Diego, California, but the prevalence of antibodies was 37%. Gabbert *et al.* (8) presented a study at the Annual Meeting of The Obesity Society in October 2009, showing a prevalence of 22% in obese children and 7% in lean children in San Diego with a strong association with BMI.

A personal communication attributed to me that 8% of Belgians were Ad-36 positive was described in the Goossens *et al.*'s article, but this needs to be clarified as it was not intended for publication.

The almost 15-year-old study was that of another investigator for whom we measured the Ad-36 antibodies in a relatively small number of patients, and I cannot recall the

specific percentage. Unfortunately, the original data are not available to me now.

Of more concern, one of the authors of this article sent 25 samples of serum to my laboratory in 2007 because their assay found a very low prevalence of Ad-36 antibodies in their population. We found that 9 of the 25 (36%) were positive by serum neutralization assay. These findings are in contrast to the results reported in the Goossens *et al.*'s article from subjects presumably from the same area. Goossens *et al.* also reported that they were unable to find Ad-36 DNA by PCR assay in 31 adipose tissue samples. We found Ad-36 DNA in 25% of adipose tissue samples from obese and severely obese people in the United States (9).

A potential explanation of the differences between the Goossens *et al.*'s article and previous publications may be problems with the assays. We have concerns about human serum samples being repeatedly frozen and thawed as we have observed that the antibody titers in such samples seem to decrease. The authors stated that the rabbit serum positive control that I had sent to one of the authors in 2007 did not demonstrate any loss of titer upon repeated freezing. However, this antibody was produced by injecting an Ad-36 vaccine into a rabbit and we postulate that it may not be an appropriate control for human serum. As for the PCR assay for Ad-36, we have found it to be very difficult to perform and sensitive to the method of collection, method of DNA extraction, and type of primers and probe used. Ad-36 DNA is present in low concentration in adipose tissue. The authors used only 10 mg of adipose tissue, which is considerably less than what we and Dhurandhar's group use (10). Adipose tissue has many fewer cells for weight due to the large amounts of stored triglycerides so larger amounts of tissue are needed. Also, the authors did not use the same PCR method that has been reported by us and other authors (9–11).

Finally, the conclusions of this article may overreach the data. The authors propose that "Ad-36 does not play a role as a direct cause of BMI increase and obesity in humans in Western Europe." However, if correct,

their data apply only to Belgium and The Netherlands. Italy is in Western Europe and the Italian publications show ~43% of total subjects were positive and that there was a strong correlation of Ad-36 with obesity (5,6).

DISCLOSURE

Obtech provided assays for detection of Ad-36 and has several patents regarding Ad-36 assays.

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