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Is glucokinase the beta-cell glucoreceptor?

Dear Sir,

Having read the two recently published letters from Matschinsky [1] and Randle [2] I cannot resist making a comment. The authors of these letters each claim that they were the first to propose that glucokinase acts as a glucoreceptor in the process of glucose-induced insulin secretion. I am not sure that a decision on this issue is crucial, and consider that the progress of knowledge, rather than consideration on priority, is the scientific relevant matter. Incidentally, even in terms of priority, it could be argued that the first published report on the phosphorylation of D-glucose by islet homogenates [3] stems from Indianapolis rather than St Louis or Bristol. In this first report, the experimental data indicated the participation of a high- K_m phosphorylating enzyme and were indeed compatible with the presence of glucokinase [4]. More importantly, however, I believe that the claim made by Matschinsky and Randle that glucokinase is the glucoreceptor represents a misleading concept, as has been indicated on several occasions [5, 6]. It ignores a number of regulatory steps in D-glucose metabolism proximal and distal to the site of glucose phosphorylation. Even on the latter process, it neglects the fact that the rate of D-glucose phosphorylation in intact beta-cells is not dictated solely by the concentration of the hexose and intrinsic properties of glucokinase but also by a number of other factors including ATP availability, interference of

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a glucokinase regulatory protein and binding of glucokinase to mitochondrial porin [7].

The relevance of glucokinase activity to the process of glucose-induced insulin release cannot be ignored. It is equally unwise to ignore other essential regulatory mechanisms participating in the beta-cell glucose-sensing device, whoever first documented the presence of the high- K_m enzyme in islet homogenates.

Yours sincerely,
W.J. Malaisse

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Corresponding author: Professor W.J. Malaisse, Laboratory of Experimental Medicine, Brussels Free University, 808 Route de Lennik, B-1070 Brussels, Belgium