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INHIBITING OR ANTAGONIZING GLUCAGON: MAKING PROGRESS IN DIABETES CARE ?

Absolute or relative hyperglucagonaemia has been recognized for years in all experimental or clinical forms of diabetes. It has been suggested that excess secretion of glucagon by the islet α cells is a direct consequence of intra-islet insulin secretory defects. Recent studies have shown that knockout of the glucagon receptor or administration of a monoclonal specific glucagon receptor antibody make insulin-deficient type 1 diabetic rodents thrive without insulin. These observations suggest that glucagon plays an essential role in the pathophysiology of diabetes and that targeting the α cell and glucagon are innovative approaches in the management of diabetes. Despite active research and identification of promising compounds, no one selective glucagon antagonist is presently used in the treatment of diabetes. Interestingly, besides insulin, several drugs used today in the management of diabetes appear to exert their effects, in part, by inhibiting glucagon secretion (glucagon-like peptide-1 receptor agonists, dipeptidyl peptidase-4 inhibitors, α-glucosidase inhibitors and, possibly, sulphonylureas) or glucagon action (metformin). The potential risks associated with total glucagon suppression include α-cell hyperplasia, increased mass of the pancreas, increased susceptibility to hepatosteatosis and hepatocellular injury and increased risk of hypoglycaemia, and these should be considered in the search and development of new compounds reducing glucagon receptor signalling. More than 40 years after its initial description, hyperglucagonaemia in diabetes can no longer be ignored or minimized, and its correction represents an attractive way to improve diabetes management.

Biography

Pierre J Lefebvre received his MD Degree at the University of Liège, Belgium P. Lefebvre has published more than 25 books and 900 papers. He serves or has served on the Editorial Board of more than 20 International Journals. He has been recognised by several awards including the Masius Award (University of Liège, 1965), the University Foundation Alumni Award (Brussels, 1968), the Pfizer Award (Royal Academy of Medicine, Belgium 1979), the Claude Bernard Award (European Association for the Study of Diabetes, 1984), the Maurice Dérot Award (Paris, 1987) the Paul Langerhans Award (Deutsche Diabetes Gesellshaft, 1992), the Mizuno Award (Tokyo, 1996), the Novartis Long-Standing Achievement in Diabetes Award (2000), the Harold Rifkin Award of the American Diabetes Association (2012) etc. He has given the Alexander Marble (Boston, 1993), the Celal Oker (Istanbul, 1993) and the Banting Memorial (Diabetes UK, 2001) Lectures.

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