INTRODUCTION

Inflammation and type 2 diabetes: from basic science to treatment

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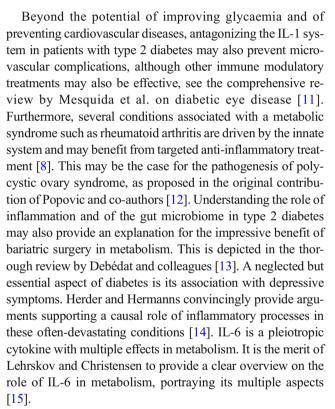
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Many discoveries in science have the following history: it starts with a controversy, then it becomes common knowledge, followed by a hype, then the first drawbacks appear, and eventually the concept is implemented by perseverant scientists. With respect to the role of the immune system in type 2 diabetes, the controversy lasted several years, which clearly delayed clinical translation. The reasons for the longduration of the controversy include the novelty of the concept and moral aspects. As type 2 diabetes is often perceived as self-inflicted and due to a lack of discipline in life-style behaviour, some specialists of the "innocent" immune type 1 diabetes were reluctant to acknowledge associations between the diseases. As will become apparent to the reader of this issue of the Seminars in Immunopathology, in the meantime, the controversy has past. Particularly convincing is the metaanalysis by Kataria and colleagues, which included 2921 patients with type 2 diabetes treated with an IL-1 antagonist [1]. They show a highly significant reduction in glycated haemoglobin. Importantly, beyond the control of glycaemia, targeting the IL-1 system may also improve complications of diabetes such as cardiovascular diseases and heart failure. Indeed, the large phase 3 CANTOS study demonstrated that a single subcutaneous injection of an anti-IL-1ß antibody every 3 months significantly lowers rate of recurrent cardiovascular events [2] and also of heart failure, especially in patients with diabetes [3]. Further, during the first 12 months of the study, IL-1 antagonism also showed a glucose-lowering effect [4]. After this period, however, anti-diabetic drugs were freely adjusted in all patients, masking the pure anti-IL-1beta effect. These results nicely confirm previous diabetes-devoted studies using IL-1 antagonists [5-10].

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Are thus all questions answered? Clearly not, the reader will enjoy the refreshing article by Böni-Schnetzler and Meier [16] on the development of islet inflammation in type 2 diabetes, highlighting the physiology of this process, which eventually becomes deleterious. This article should also increase awareness on differences in findings on islet inflammation between humans and rodents. Also, from a molecular biology point of view, an exciting topic is the transcriptional control of macrophage polarization in type 2 diabetes; an inviting overview is presented by Drareni and colleagues [17]. Finally, and importantly, Dalmas opens the door to other immune cell populations, in particular of innate lymphoid cells, which emerge as key sentinels of metabolic tissues and privileged partners of macrophages [18].



Overall, it will become apparent to the reader of this special issue that whilst the role of inflammation in the development of type 2 diabetes is now well established, several exciting aspects remain to be investigated. Basic scientists should be encouraged to further investigate the multiple facets of immune regulation of metabolism in physiology and pathology, whilst clinicians are invited to explore further indications for anti-cytokine therapies in type 2 diabetes and associated conditions. Altogether, this will pave the way to the next era of immunometabolism that is a causative treatment of type 2 diabetes and complications.

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