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Postprandial macrophage-derived IL-1β stimulates insulin, and both synergistically promote glucose disposal and inflammation

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The deleterious effect of chronic activation of the IL-1β system on type 2 diabetes and other metabolic diseases is well documented. However, a possible physiological role for IL-1β in glucose metabolism has remained unexplored. Here we found that feeding induced a physiological increase in the number of peritoneal macrophages that secreted IL-1β, in a glucose-dependent manner. Subsequently, IL-1β contributed to the postprandial stimulation of insulin secretion. Accordingly, lack of endogenous IL-1β signaling in mice during refeeding and obesity diminished the concentration of insulin in plasma. IL-1β and insulin increased the uptake of glucose into macrophages, and insulin reinforced a pro-inflammatory pattern via the insulin receptor, glucose metabolism, production of reactive oxygen species, and secretion of IL-1β mediated by the NLRP3 inflammasome. Postprandial inflammation might be limited by normalization of glycemia, since it was prevented by inhibition of the sodium–glucose cotransporter SGLT2. Our findings identify a physiological role for IL-1β and insulin in the regulation of both metabolism and immunity.