

## DIABETES

## Functional $\beta$ cells detected in long-standing T1DM—a new hope for intervention?

C-peptide, a hallmark of  $\beta$ -cell function, can be detected in the serum of patients with type 1 diabetes mellitus (T1DM) >30 years after disease onset, report researchers from Harvard Medical School.

According to the traditional model of T1DM progression, no functional  $\beta$  cells remain and no insulin is produced after the initial 'honeymoon' phase—which lasts for about 1 year after disease onset—except in very rare cases. However, when Denise Faustman and colleagues measured the levels of C-peptide in the serum of 182 white patients (55.5% men) with T1DM recruited at the Massachusetts General Hospital, C-peptide levels were seen to decrease gradually over the years. Of note, C-peptide was still detected in 10% of patients ( $n=2$ ) in the group with a 31–40 year disease duration.

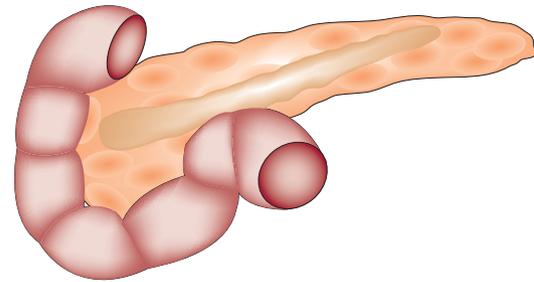
The researchers used an ultrasensitive C-peptide ELISA assay (Mercodia, Uppsala, Sweden) that detects levels of C-peptide >1.5 pmol/l, thus being 22 times more sensitive than the standard

assay. “To our astonishment the curve of pancreas decay was dramatically different than that revealed with old assays of C-peptide that are commonly used clinically,” recalls Faustman.

The median age of patients was 39 years (range 9–85 years), the median disease duration was 15 years (range 0–73 years), and the median age at onset was 13 years (range 1–56 years). The presence of GAD-65, IA-2 and ZnT8 autoantibodies was investigated in 125 patients and found in 50.4%, 36.2% and 28.3% of these individuals, respectively.

ZnT8 autoantibody levels and disease duration were associated with C-peptide levels, but age, sex and GAD-65 and IA-2 autoantibody levels were not. Of note, T1DM onset at age >40 years was associated with low C-peptide levels.

“Most clinical trials of immune interventions worldwide have only been centered on new-onset diabetes mellitus,” comments Faustman. The new data, however, indicate that developing new



therapies in the setting of long-standing disease might be a promising strategy.

Faustman also believes that the observation that T1DM has a different disease course than previously thought might change the attitudes of patients and clinicians. Patients who feel that their glucose levels are increasingly harder to control will no longer be blamed for their lifestyle habits, as this deterioration can be attributed to the slow loss of insulin over decades, not months.

Joana Osório

**Original article** Wang, L. *et al.* Persistence of prolonged C-peptide production in type 1 diabetes as measured with an ultrasensitive C-peptide assay. *Diabetes Care* 35, 465–470 (2012)