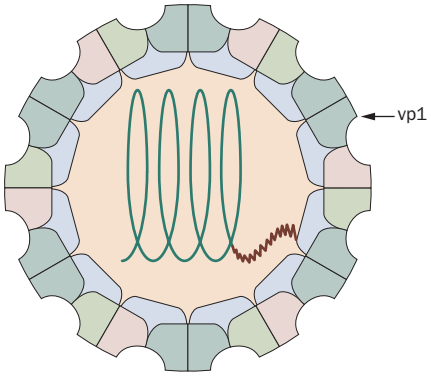
PANCREAS

Enteroviral capsid protein detected in pancreatic islets



Detection of an enteroviral capsid protein in the pancreatic β cells of children with type 1 diabetes mellitus (T1DM) provides further evidence of a link between enteroviral infection and development of this disease.

Circumstantial evidence indicates that enteroviral infection might be involved in the molecular changes that culminate in the autoimmunity characteristic of T1DM. Nevertheless, direct evidence of viral infection of the pancreatic β cells has proved difficult to obtain. "Very few pancreas samples are available which were removed from patients soon after diagnosis of T1DM," explains lead researcher Noel Morgan (Peninsula Medical School, Exeter, UK). Morgan and his colleagues chose, therefore, to study a unique collection of formalin-fixed, paraffin-embedded pancreas samples established over a 25-year period by Alan Foulis (Glasgow Royal Infirmary, UK).

Pancreas samples were taken at autopsy from 72 children, most of whom had died within 6 months of being diagnosed with T1DM. Foulis had previously detected interferon α in the islet β cells of many of these samples—a finding highly suggestive of viral infection. The team was further encouraged to proceed by a report that described the presence of Coxsackie B4 enterovirus in the pancreatic β cells of a small number of patients with T1DM.

The researchers decided to analyze expression of a viral capsid protein, vp1, which is expressed by many different enteroviruses and can be detected by immunohistochemistry with use of commercial antisera. A wide range of controls were used to account for differences in tissue fixation and the possibility of nonspecific crossreactivity of the antisera. Such stringent control allowed Morgan's team to establish conditions under which vp1 could be detected in the pancreatic β cells.

Over 60% of the children with T1DM had clear evidence of vp1 immunostaining in some islet cells, whereas this protein was detected in only three islets of the 39 pancreas samples from nondiabetic children. Vp1 immunostaining was restricted to insulin-producing β cells and correlated with expression of a marker of enteroviral infection. Of particular interest, vp1 immunostaining was also detected in 40% of adults with T2DM.

The data obtained by Morgan and coworkers suggest that persistent low-level infection of the pancreatic β cells precedes an immune response. Enteroviral infection could, therefore, act as the trigger that sets in motion a train of molecular events that ultimately leads to autoimmune β-cell destruction. As development of T1DM has a strong genetic component, an individual's response to enteroviral infection might be modulated by their genetic background. Furthermore, enteroviral infection could contribute to the development of T2DM in adults with compromised metabolic function by reducing the capacity of their β cells to produce insulin.

Morgan acknowledges that further work is required to verify his team's findings. In particular, the serotype(s) of the enteroviruses involved must be determined. "If one or more enteroviruses can be firmly implicated in the initiation of autoimmunity in T1DM, then the possibility of a vaccine that should reduce the likelihood of an individual developing T1DM is raised," he speculates.

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Original article Richardson, S. J. *et al.* The prevalence of enteroviral capsid protein vp1 immunostaining in pancreatic islets in human type 1 diabetes. *Diabetologia* **52**, 1143–1151 (2009).