Simultaneous detection of circulating autoreactive CD8+ T-cells specific for different islet cell-associated epitopes using combinatorial MHC multimers

OBJECTIVE - Type 1 diabetes results from selective T-cell-mediated destruction of the insulin-producing β-cells in the pancreas. In this process, islet epitope-specific CD8+ T-cells play a pivotal role. Thus, monitoring of multiple islet-specific CD8+ T-cells may prove to be valuable for measuring disease activity, progression, and intervention. Yet, conventional detection techniques (ELISPOT and HLA tetramers) require many cells and are relatively insensitive. RESEARCH DESIGN AND METHODS - Here, we used a combinatorial quantum dot major histocompatibility complex multimer technique to simultaneously monitor the presence of HLA-A2 restricted insulin B10-18, prepro-insulin (PPI)15-24, islet antigen (IA)-2797-805, GAD65114-123, islet-specific glucose-6-phosphatase catalytic subunit-related protein (IGRP) 265-273, and pre-pro islet amyloid polypeptide (ppIAPP) 5-13-specific CD8+ T-cells in recent-onset diabetic patients, their siblings, healthy control subjects, and islet cell transplantation recipients. RESULTS - Using this kit, islet autoreactive CD8+ T-cells recognizing insulin B10-18, IA-2 797-805, and IGRP265-273 were shown to be frequently detectable in recent-onset diabetic patients but rarely in healthy control subjects; PPI15-24 proved to be the most sensitive epitope. Applying the "Diab-Q-kit" to samples of islet cell transplantation recipients allowed detection of changes of autoreactive T-cell frequencies against multiple islet cell-derived epitopes that were associated with disease activity and correlated with clinical outcome. CONCLUSIONS - A kit was developed that allows simultaneous detection of CD8+ T-cells reactive to multiple HLA-A2-restricted β-cell epitopes requiring limited amounts of blood, without a need for in vitro culture, that is applicable on stored blood samples. © 2010 by the American Diabetes Association.

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