

Immunologic Cascade Eyed for Type 1 Prevention

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Multiple lines of research are aimed at halting the immunologic cascade that leads to the development of type 1 diabetes.

In a press briefing with the 9th International Congress of the Immunology of Diabetes Society and American Diabetes Association Research Symposium, four speakers discussed ongoing research around the world involving the identification of individuals, primarily children, at risk for type 1 diabetes and efforts to halt the advance of autoimmune β -cell destruction.

The briefing was sponsored by Type 1 Diabetes TrialNet, a group of studies looking at the development, prevention, and early treatment of type 1 diabetes, and jointly funded by the National Institutes of Health, the Juvenile Diabetes Research Foundation, and the American Diabetes Association.

TrialNet chairman Dr. Jay S. Skyler gave an overview of efforts to block type 1 diabetes.

Studies targeting individuals found to be at increased genetic risk for type 1 diabetes include the Trial to Reduce Insulin-Dependent Diabetes in the Genetically at Risk (TRIGR), comparing the role of hydrolyzed infant formula versus cow's milk-based formula in the development of the disease; the Nutritional Intervention to Prevent Diabetes (NIP) study, which looks at the role of omega-3 fatty acids; and the BABYDIET study investigating whether the delay of gluten introduction into the diet might prevent type 1 diabetes in high-risk infants.

At the stage of multiple antibody positivity, studies are looking at the potential impact of intervention with oral insulin, aerosolized intranasal insulin, and of a glutamic acid decarboxylase-aluminum vaccine. And at the time of new-onset diabetes, administration of mycophenolate mofetil, anti-CD20, thymoglobulin, and interleukin-2 plus sirolimus are among the compounds being looked at, said Dr. Skyler, professor of medicine, pediatrics, and psychology in the University of Miami's division of endocrinology, diabetes, and metabolism.

Dr. Olli Simell, a TrialNet principal investigator, described his work in Finland, where 1 in every 120 children develops type 1 diabetes, compared with 1 in 300 in the United States. Since 1994, the Diabetes Prediction and Prevention (DIPP) project has screened more than 100,000 newborns for type 1 diabetes susceptibility genes and identified more than 10,000 at-risk children. As of October 2007, 328 have been found to have at least two types of autoantibodies in at least two consecutive samples, and 181 of them have developed diabetes.

Thus far, DIPP has shown that although the age of diagnosis of diabetes is fairly evenly distributed throughout childhood, autoantibodies emerge before age 3 years in more than 90% of children who develop the disease. The study has also identified new serum markers that differentiate future progressors from nonprogressors by 1 year of age, said Dr. Simell, professor and chairman of pediatrics at the University of Turku (Finland), and chief physician in the department of pediatrics at Turku University Hospital.

Dr. Massimo Trucco, also a TrialNet prin-

cipal investigator, outlined an ongoing randomized phase I study evaluating the safety of a diabetes-suppressive cell vaccine consisting of autologous monocyte-derived dendritic cells treated ex vivo with antisense phosphorothioate-modified oligonucleotides targeting the primary transcripts of the CD40, CD80, and CD86 costimulatory molecules. Seven volunteers with type 1 diabetes are receiving autologous control dendritic cells; eight receive the immuno-regulatory dendritic cells. If all goes well in the

safety trial, efficacy trials in new-onset type 1 patients could begin in the spring of 2008, said Dr. Trucco, director of the division of Immunogenetics at Children's Hospital of Pittsburgh and the Hillman Professor of Pediatric Immunology and professor of pediatrics at the University of Pittsburgh.

A third TrialNet principal investigator, Dr. Michael Haller, spoke of autologous stem cell transfusion as a possible means of reversing type 1 diabetes by restoring immune tolerance. In a pilot study of 21 chil-

dren with type 1 diabetes (mean age 4.5 years), 8 who received cord blood had significantly lower insulin requirements (0.45 vs. 0.69 units/kg a day) and hemoglobin A_{1c} values (7.0% vs. 8.04%) than did 13 controls, with little or no decline in insulin production over 6 months. An increase in the number of regulatory T cells in the blood samples of subjects 6 months after the infusion may explain some of the benefits, said Dr. Haller, of the department of pediatrics at the University of Florida, Gainesville. ■

GENITAL WARTS THE UNSPOKEN BURDEN

- ▶ ~1 million new cases every year*¹
- ▶ Increased prevalence in 15- to 24-year-old females^{†,2}
- ▶ Can develop in as little as 3 months after infection³
- ▶ Can be distressing and embarrassing⁴

HPV[‡] Types 6 and 11 cause ~90% of genital warts cases⁵

*Estimate includes men and women.

[†]Peak prevalence occurs in females 20 to 24 years of age.²

[‡]HPV=human papillomavirus.

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