Association between circulating HLA-antibodies and cytokines and chemokine ligands in uremic patients awaiting kidney transplantation

As HLA-antibodies predict inferior graft and patient survival, potentially related to enhanced inflammation, this study aims to define patterns of increased circulating inflammatory cytokines (IL) and chemokine ligands (CCL) in sensitized patients awaiting kidney transplantation. Serum from 219 patients and 56 healthy controls was evaluated for HLA-Abs, 20 ILs, and 30 CCLs. Patients were distributed as: G1 (Non-sensitized) n=114, 52.1%; G2 (HLA-I-Abs) n=50, 22.8%; G3 (HLA-II-Abs) n=16, 7.3%; G4 (HLA-I/II-Abs) n=39, 17.8%. Within these groups, marker levels, marker clustering, and differences in levels within clusters were evaluated. Levels exceeding the 5th or 95th percentile values of controls in at least 60% of subjects within a profile were considered meaningfully altered. Correlation network analysis was used to recognize clusters; markers with intra-cluster correlations ≥ 0.80 were considered core. Among groups 1-4, six, four, four and six clusters were recognized respectively, and five among controls. Profile differences in cluster configuration were noted, with G3 clustering appearing strongest. Of note, IL-4 was the only marker core to sensitized patient’s clusters. There were no quantitative differences among all patients’ groups, albeit many markers were significantly different from the control values. Thus, profile changes between sensitized and non-sensitized patients appear related to qualitative differences in marker relationships, rather than quantitative changes in which IL-4 may play a role.

Biography

Ahmed Shoker was trained in Internal Medicine at the University of British Columbia in Vancouver and moved to Toronto to complete his training in Nephrology and Transplantation Immunology. He moved to the University of Saskatchewan in 1991. Currently, he is a Professor of Medicine in Nephrology and Transplantation at the University of Saskatchewan. He is the Medical Director of the Saskatchewan Transplant Program. He has interest in both basic and clinical investigation. He participated in over 35 national and international clinical studies in Transplantation and Nephrology. He has authored and co-authored over 130 peer reviewed manuscripts. His current interest is in the area of cardiovascular disease in renal patients. Recent publications included measurement of inflammatory mediators in patients with decreased renal transplant function. Because of the significant impact of diabetes on the renal patient, he has focused his current interest in management of diabetes mellitus in the kidney transplant patient and patients with chronic renal insufficiency.

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