

Delivering Antigenic Peptides to Immune Cells to Control Autoimmune Diseases



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Autoimmune diseases such as multiple sclerosis (MS), type-1 diabetes (T1D), and rheumatoid arthritis (RA) have a common mechanism, which involves a subpopulation of activated rogue inflammatory T cells. The rogue T cells cause damage in self-tissues. In MS patients, the activated immune cells infiltrate the central nervous systems (CNS) to damage the myelin sheath of neuronal axons by recognizing myelin proteins as antigens. We have designed bifunctional peptide inhibitor (BPI) molecules that control the activation of T cells in an antigenic-specific manner without suppressing the general immune response. BPI molecules consist of a conjugate between antigenic and cell adhesion peptides. It is proposed that BPI molecules block the immunological synapse formation at the interface of T-cell and APC to prevent T-cell activation and proliferation. Various BPI molecules have been shown to effectively suppress autoimmune diseases in the animal models of MS, T1D, and RA. The central hypothesis is that the BPI molecule simultaneously binds to major histocompatibility complex-II (MHC-II) and ICAM-1 on antigen-presenting cells (APC) and prevents the “immunological synapse” formation. The cytokine production data show that BPI molecules alter the balance of immune cells from inflammatory to regulatory/suppressor phenotypes. The animal studies suggest that BPI molecules have the potential use as therapeutic agents for autoimmune diseases.

Dr. Siahaan is the Aya & Takeru Higuchi Distinguished Professor of Pharmaceutical Chemistry at The University of Kansas; he joined the Department as an Assistant Professor in 1991. Professor Siahaan was born in Medan, Indonesia and went to US in 1982 to complete his Ph.D. degree in Organic Chemistry at the University of Arizona under the supervision of Professor Robert B. Bates. He did postdoctoral study in the laboratory of Professor Bruce H. Lipshutz at the Department of Chemistry, University of California Santa Barbara. He then worked at La Jolla Cancer Research Foundation (Burnham Institute) followed by Sterling Winthrop Pharmaceutical Company. Since 2009, he has served as Program Director of the T32 NIH Biotechnology Training Program at KU (aimed at training predoctoral students to work on the development of biologic drugs and vaccines). His research is focused on improving drug delivery to the brain for treatment of brain diseases and to immune cells to control autoimmune diseases. Dr. Siahaan has published over 200 papers, obtained 12 patents, and edited two books. He has received several honors and awards, including Self Faculty Scholar, KU; Pfizer Research Scholar Award; J. Clarence Karcher Lecturer, University of Oklahoma; 2013 Mentor of the Year, KU; and 2014 PhRMA Foundation Award for Excellence in Pharmaceuticals. He serves as the Associate Chair of the Pharmaceutical Chemistry Department, is a member of the Executive Committee of the KU School of Pharmacy, and is on the Executive Board of Directors of the Globalization Pharmaceuticals Education Network (GPEN) Organization. He is a Fellow of the American Association of Pharmaceutical Scientists (AAPS) and a member of the editorial boards of various journals, including *Journal of Pharmaceutical Sciences*, *Medicinal Research Reviews*, and *American Journal of Clinical and Experimental Immunology*. He currently serves as the Director of the Global Health Center at the School of Pharmacy, KU.