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# LEADERSHIP TEAM

## ANDREW G. PLAUT, MD

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Dr. Plaut is a staff physician (internal medicine) at Tufts Medical Center, specializing in digestive diseases. He sees patients, does basic and translational research, and works as a Portal Director of the Tufts CTSI. His research interests are in pathogenic microbiology and immunology, and he was Director of the NIH sponsored Silvio O. Conte Digestive Disease Core Research Center at Tufts from 1986 through 2007.

Dr. Plaut's translational research has been in two areas, the main one being the structure and function of IgA, the principal form of antibody in secretions and in human milk. His specific interest is in the few diseases that are caused by the deposition of IgA into human tissues, with emphasis on the disease IgA nephropathy. This is a major cause of renal failure worldwide, and the prototype of IgA deposition illnesses.

Dr. Plaut's basic research had been on the identification and characterization of a family of proteolytic enzymes known as IgA proteases. These enzymes are produced by bacteria that cause human disease, including *Haemophilus influenzae*, *Streptococcus pneumoniae*, *Neisseria meningitidis*, *Neisseria gonorrhoea*, and a number of streptococcal species that colonize and infect the oral cavity. IgA proteases are highly specific for human IgA1 as substrate, and it is IgA1 that is deposited in the kidney of patients with IgA nephropathy. These enzymes are considered to be virulence factors, as they have the potential to interrupt antibody function at mucosal surfaces.

In a series of ongoing and recently published studies of an animal model, Dr. Plaut and colleagues at Case-Western Reserve Medical School have shown that IgA proteases, injected intravenously, are capable of removing human IgA1 that has been introduced into the mouse kidney. These results have led to a series of studies having the goal of using recombinant IgA proteases as biological therapeutics, injected into patients with IgA nephropathy with the intent to remove the renal IgA, and thus restore kidney function. This work is currently in the pre-clinical phase of development.

In a second translational research effort, Dr. Plaut and colleagues at Tufts Medical Center, Tufts University School of Medicine and the University of Toronto were among the first to conceive of the use of dipeptidyl dipeptidase (DPPIV) inhibitors for the treatment of type II diabetes mellitus. This research arose indirectly from that done with IgA proteases, as mentioned above, since DPPIV and IgA proteases share the property of cleaving after proline residues in protein substrates. DPPIV inhibitory drugs are now in clinical use, and others are being developed at several pharmaceutical firms.

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