

SIGNIFICANCE STATEMENT

Membranous nephropathy (MN) is an autoimmune disease in which autoantibodies against the podocyte surface proteins THSD7A or PLA2R1 are found. The autoantibody binding domains of THSD7A are unknown. This paper identifies autoantibodies against multiple epitopes in patients with THSD7A-associated MN and characterizes the most N-terminal part of THSD7A as an immunologic hotspot region. The preferential antibody generation against this region could be reproduced in immunization experiments in mice and rabbits. This study presents novel data regarding the pathogenesis of MN and may pave the way for innovative epitope-specific therapeutic approaches.