Autoimmune diseases affect 5-8% of the population and are usually associated with the presence of autoantibodies, i.e. antibodies that recognize fragments of own body. Intriguingly, such autoantibodies are also present in healthy people with no family history of autoimmune diseases. It is not clear why the autoimmunity develops only in certain carriers of autoantibodies and most probably a pivotal factor that drives the pathology is still unknown. We hypothesize that the disease manifestation can be dependent on genetic defects in components belonging to the complement system, a proteolytic cascade of proteins that eventually lead to the destruction of target cells. One of the activation routes named the classical complement pathway is initiated by antibody binding to the cell surface. Our body can counteract the misguided complement attack to a certain extent thanks to the existence of complement inhibitors present either on the cell surface or in serum as soluble molecules. Perhaps this is why some people with autoantibodies do not develop any disease. Mutations of the classical pathway components that render them insensitive to inhibitors may disable such natural protection and lead to disease manifestation. Recently our group identified such previously unknown mutations in patients suffering from rare kidney diseases and now we plan to verify whether they exist in a wider group of patients suffering from different and more frequent autoimmune diseases. Positive results may impose new therapeutic approaches. e.g. introduction of agents targeting mutated proteins instead of expensive broad-range inhibitors of the immune system.