Screening of a kidney cDNA library for the identification of autoimmune proteins from serum of Membranous Nephropathy patients.

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INTRODUCTION AND AIMS:
Membranous Nephropathy (MN) represents a large number of cases of Nephrotic Syndromes in the adult population and its definitive diagnosis is currently carried out through biopsy. An autoimmune condition is suspected in MN in which some glomerular structures are targeted by patient antibodies. We do not know yet the target protein (or proteins) putatively involved and responsible for the disease. The aim of this work is to identify these proteins by screening a lambda-phage library using patient serum pools.

METHODS:
We set up the following three pools of sera: (i) from MN patients, (ii) from non-MN renal patients, and (iii) from healthy individuals. A commercial cDNA phagemid library (from healthy kidney whole mRNA) was screened using the above described pooled sera, in order to detect positive signals following antigen-antibody recognition. Once we have identified a clone, it will be necessary to subclone it in an expression vector so as to obtain the pure protein and validate our result by further immunoassays.

RESULTS:
We detected one phagemid clone expressing a protein which was shown to be targeted by the antibodies of the pooled MN sera only. Control sera were both negative. The cDNA insert carried by the phagemid was subsequently sequenced. In particular, by comparing the sequence we isolated with a human DNA database, a complete matching with the synaptonemal complex protein 65 (SC65) was found.
We subsequently cloned the cDNA in an expression vector called pQE in order to perform protein production and analysis.

**CONCLUSIONS:**

Anti-SC65 autoantibodies could be involved in MN physiopathology as we observed through analysis of sera from affected patients. Considering the invasiveness and the risks associated with renal biopsies, little- or non-invasive methods such as blood sampling would be desirable. The identification of candidate patient autoantibodies targeting renal self proteins, might therefore help revealing new pathogenetic mechanisms of MN and, eventually, developing new diagnostic methods.