ANTI-M-TYPE PHOSPHOLIPASE A2 RECEPTOR (PLA2R) ANTIBODIES: DIAGNOSTIC PERFORMANCE AND CLINICAL SIGNIFICANCE IN IDIOPATHIC MEMBRANOUS NEPHROPATHY (IMN)

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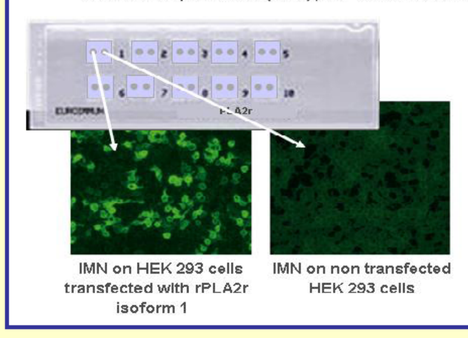
OBJECTIVES

Background: IMN, the leading cause of nephrotic syndrome in caucasian adults, shows an heterogeneous and not predictable disease course with progression to end stage kidney disease in up to 40% of cases. Diagnostic and prognostic biomarkes were not available since lately, when an important role for auto-antibodies recognizing podocyte antigens has emerged. Among them, PLA_2r was found to be the main auto-antigenic target, since a specific immune response was documented in 52-82% of IMN pts.

Aims:1) to evaluate the diagnostic performance of anti-PLA2r antibody assay in a large cohort of IMN and disease controls. 2) to correlate the presence and titres of anti-PLA_2r antibodies with the traditional serological disease activity/risk stratification markers.

PATIENTS AND METHODS

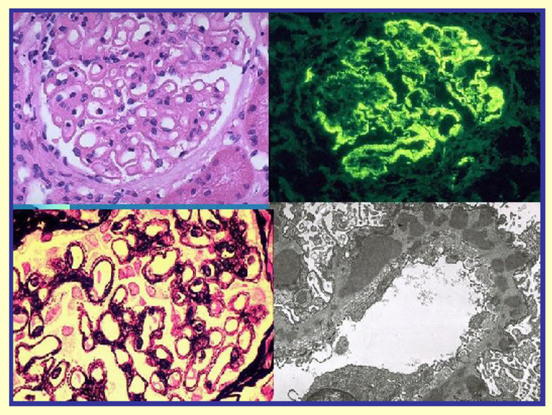
IIFT on biochips coated with HEK293 cells expressing the relevant protein (left), or nontransfected cells (right)



samples diluted 1:10/100/1000 were incubated over a slide containing the two biochips (in the same well). IIF test performed as usually.

137 IMN at diagnosis/relapse (120/17), 89 non-membranous primary GN and secondary MN, 43 healthy controls.

Anti-PLA2r were detected by indirect immunofluorescence assay (IIFT) employing HEK-293 cells transfected with the PLA2r cDNA (Euroimmun).



RESULTS

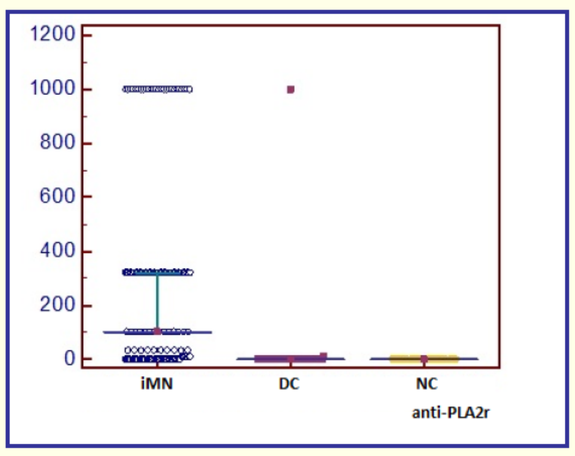


Fig 1

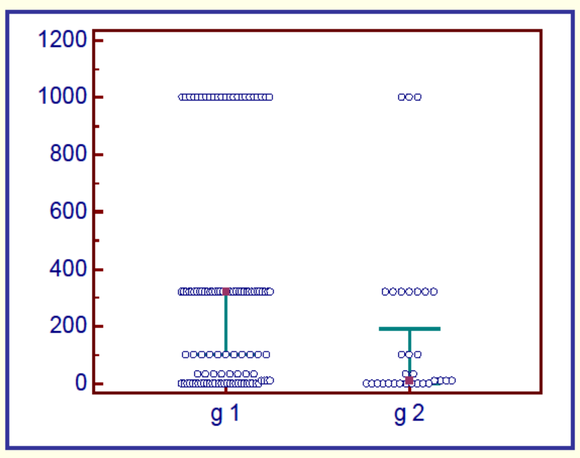


Fig 2

- Anti-PLA2r were present in 106/137 IMN patients but in only 2/89 glomerular disease controls (sensitivity 71.5%, specificity 97.7%, Fig.1).
- Anti-PLA2r did not correlate with basal sCreat, sProt and sAlb. We found, on the contrary, a statistical significant correlation with uProt (r: 0.23, $p<0.001$).
- Moreover, anti-PLA2r titre was significantly higher ($p= 0.025$) in patients with nephrotic range proteinuria (> 3.5 g/day, g1) in comparison with patients with non-nephrotic proteinuria (≤ 3.5 g/day, g2; Fig.2).

CONCLUSIONS

Anti-PLA2r antibodies represent the first diagnostic biomarker in idiopathic glomerulonephritis with a very good diagnostic performance.

Anti-PLA2r antibodies are valuable in supporting IMN diagnosis.

We also confirm the high accuracy of the IIFT assay in a large cohort of patients and controls.

Anti-PLA2r titre correlates with the amount of proteinuria and, therefore, it could be useful to monitor disease activity.

REFERENCES:

1. *Beck LH et al. "M-type phospholipase A2 receptor as target antigen in idiopathic membranous nephropathy". N Engl J Med 2009;361(1):11-21.*
2. *Hoxha E. et al. "An immunofluorescence test for phospholipase-A2-receptor antibodies and its clinical usefulness in patients with membranous glomerulonephritis". Nephrol Dial Transplant 2011;26(8):2526-32.*
3. *Hofstra JM. et al. "Antiphospholipase A2 receptor antibodies correlate with clinical status in idiopathic membranous nephropathy". Clin J Am Soc Nephrol 2011;6(6):1286-91.*

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