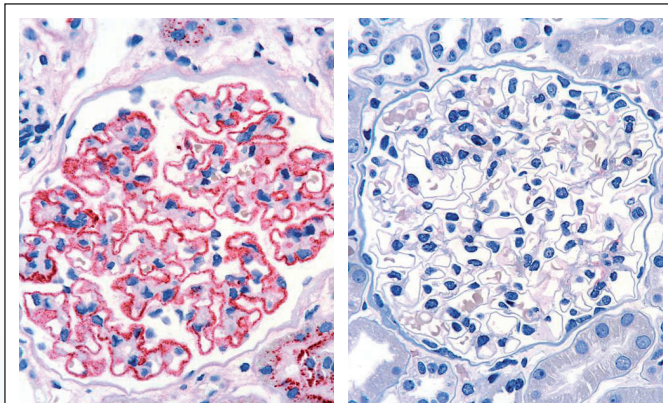




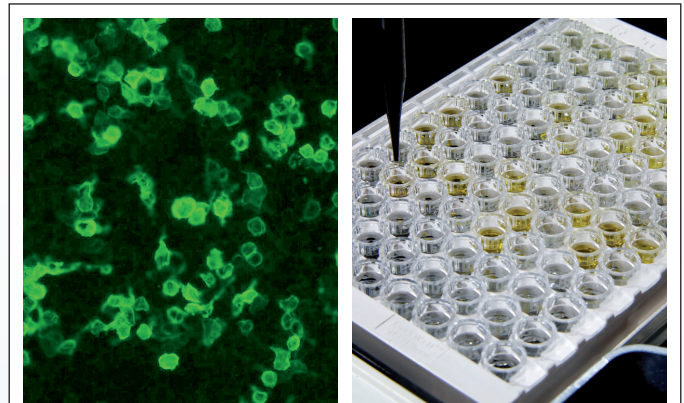
Autoantibodies against phospholipase A₂ receptors

The serological marker for primary membranous glomerulonephritis



Immunohistochemistry (IgG1 staining) of renal tissue samples

Left: inflamed renal glomeruli of a patient with pMGN; antibodies in the region of the glomerular basement membrane (red)
Right: healthy renal tissue; no antibody detection



Serological detection of autoantibodies against PLA₂R

Indirect immunofluorescence (PLA₂R-transfected cells, anti-PLA₂R positive) and microtiter ELISA

Diagnostic relevance of antibodies against PLA₂R

Primary membranous glomerulonephritis (pMGN) is associated with autoantibodies against phospholipase A₂ receptors. These are expressed in human glomeruli on the surface of podocytes. It is presumed that in vivo the antibodies trigger an inflammatory reaction after binding to their target antigen. This causes damage to the podocytes and lesions in the basement membrane. The barrier function is so strongly impaired that protein enters the urine (proteinuria).

Due to their high sensitivity and specificity for pMGN, circulating autoantibodies (IgG) against PLA₂R are an ideal diagnostic marker. They occur in 70-80% of patients with pMGN, but not in patients with other glomerulonephritides such as lupus nephritis or IgA nephritis. The anti-PLA₂R titer has a high predictive value with respect to:

- **Disease activity and course**

Anti-PLA₂R are highly specific for active MGN. High antibody titers are associated with a severe disease course.

- **Therapy monitoring**

Following immunosuppressive therapy, a decrease in the anti-PLA₂R titer is observed before an improvement in the proteinuria. An increase in the antibody titer precedes a relapse.

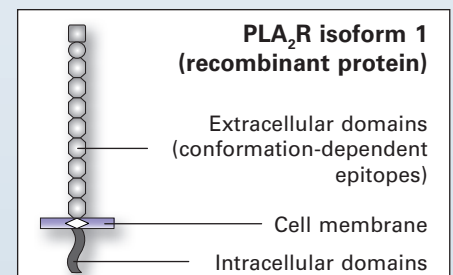
- **Risk assessment**

The anti-PLA₂R titer can be used to assess the requirement for immunosuppressive therapy. Further, the risk of relapse is particularly high when high antibody titers occur after kidney transplantation.

The serological detection of autoantibodies against PLA₂R is not only easier than conventional histological investigation of renal tissue, it is less stressful for patients. Instead of kidney puncture, only a blood sample needs to be withdrawn.

How are anti-PLA₂R detected in patient blood?

Scientists at EUROIMMUN have developed state-of-the-art test systems based on **recombinant PLA₂ receptors** for the detection of autoantibodies against PLA₂R. The recombinant proteins are based on human cDNA and are produced in a human cell line. The **Anti-PLA₂R IIFT** utilises transfected fixed cells expressing PLA₂R on the cell surface as the standard substrate. For the **Anti-PLA₂R ELISA** the recombinant receptor is biochemically purified from the transfected cells and used as the ELISA antigen.





Anti-Phospholipase A₂ Receptor IIFT (IgG)

Order no. FA 1254-1005-50 G

The Anti-Phospholipase A₂ Receptor IIFT is an established test for serodiagnostic screening, providing qualitative and semi-quantitative analysis of human autoantibodies (IgG) against PLA₂ receptors.

In a retrospective study with 100 sera from patients with biopsy-proven primary MGN, 17 sera from patients with secondary MGN and 90 sera from patients with non-membranous glomerulonephritis, a prevalence of 52% was determined with the EUROIMMUN Anti-Phospholipase A₂ Receptor IIFT (IgG). In a control panel the specificity was 100%.

Panel (n=360)	n	Anti-PLA ₂ R positive
Biopsy proven primary MGN	100	52
Secondary MGN	17	0
Non-membranous GN	90	0
Healthy blood donors	153	0

Hoxha E et al., Nephrol Dial Transplant 26(8):2526-32 (2011)

Most of the studies on anti-PLA₂R performed up until now are retrospective. They include patients who might not have exhibited antibodies any more due to spontaneous remission or immunosuppressive therapy. In some of these patients the kidney biopsy and the serum sample were taken at different time points. In these cases it is possible that the serum antibodies were no longer detectable or not yet detectable again following treatment. Further, it is conceivable that patients with biopsy-proven MGN and a negative result for anti-PLA₂R did not have primary MGN. In paraneoplastic syndromes, for example, the trigger of disease, mostly a tumour, is often only detected up to two years after appearance of the kidney disorder. Such cases would be classified as secondary MGN.

Anti-PLA₂R ELISA (IgG)

Order no. EA 1254-9601 G

The Anti-PLA₂R ELISA provides reliable determination and also quantification of autoantibodies (IgG) against PLA₂R, allowing the disease status and therapy responses of patients to be monitored.

In a study with 198 sera from patients with pMGN, 545 sera from a control panel of patients with other diseases (e.g. lupus type V, ANCA-associated vasculitis, systemic lupus erythematosus, systemic sclerosis, Sjögren's syndrome) and 291 sera from healthy blood donors, the EUROIMMUN Anti-PLA₂R ELISA (IgG) yielded a sensitivity of 96% with respect to the IIFT. The specificity amounted to 99.9% with borderline sera included.

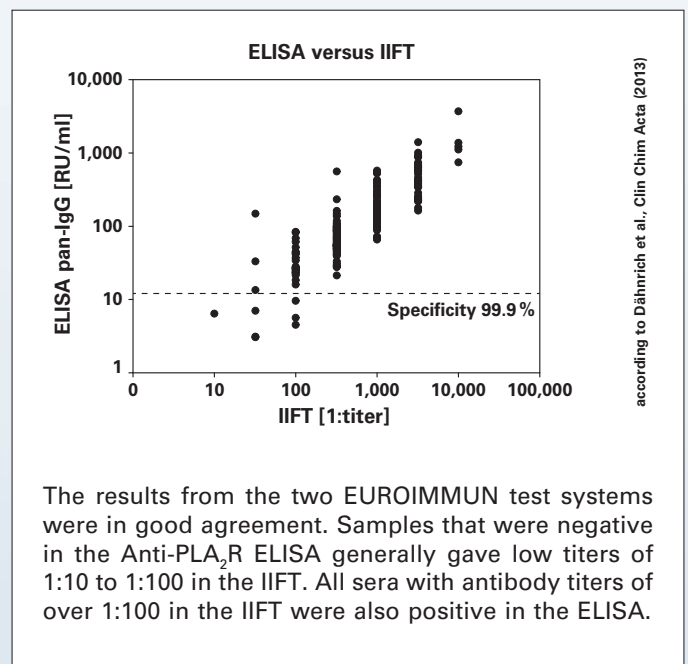
Panel (n=1061)	n	Anti-PLA ₂ R positive/borderline
Primary MGN ^{1,2,3}	198	190
Sensitivity	198	96.0 %
Other glomerulonephritides ^{1,2}	230	0
Other autoimmune diseases	315	0
Healthy blood donors	291	1
Specificity	836	99.9 %
Secondary MGN ^{1,2,3}	27	0

¹Sera from pMGN patients with positive IIFT result for anti-PLA₂R antibodies

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