# WHAT SHOULD BE THE CUT-OFF FOR VGKC COMPLEX ANTIBODIES ?

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## BACKGROUND

Voltage-gated Potassium Channel (VGKC) complex was initially described with acquired neuromyotonia and subsequently with limbic encephalitis, neuromyotonia, insomnia, and autonomic dysfunction (Morvan syndrome). VGKC complex autoantibodies is detected by radioimmunoprecipitation assays and do not bind to VGKC channel proteins per se but bind synaptic and axonal neuronal proteins that coprecipitate with detergent-solubilized VGKCs. The autoantigens are the leucine-rich glioma-inativated protein 1 (LGI1) in the central nervous system and contactin-associated protein like2 (CASPR2) in both the peripheral and central nervous system. CASPR2 IgG was reported to associate with peripheral presentations, poor diagnosis, and risk for tumors, and LGI1 IgG with limbic encephalitis and better diagnosis.

## OBJECTIVE

The aim of this study was to determine a cut-off for VGKC complexe antibodies to continue investigations and test LGI1 and CASPR2.

## METHODS

From February 1, 2011 to June 18, 2013, 693 samples were tested for VGKC complex antibodies in radioimmunoassay (RSR, Cardiff). Among them, 117 were found to be VGKC complex IgG positive. Althought the cut-off recommended by the customer is 85 pmol/l, we tested the sera in LGI1 and CASPR2 on transfected cells (Euroimmun, Lübeck) when the VGKC level were upper of 30 pmol/l. Under this value, results are negative. From 30 to 85 pmol/l, results are weakly positive and upper 85 pmol/l, results are positive.

## RESULTS

From February 1, 2011 to June 18, 2013, we tested 693 serums for anti-VGKC macromolecular complex antibodies. We analysed these samples with a radioimmunoassay. Although the cut-off recommended by the customer is 85 pmol/L, we tested samples for LGI1 and CASPR2 with transfected cells when anti-VGKC antibodies were upper of 30 pmol/L. Under this value, results are negative and, from 30 to 85 pmol/L, resultats are weakly positive and upper 85 pmol/L, resultats are positive. Among the 693 patients tested, 117 were positive for VGKC macromolecular complex. 31 were positive for LGI1, 12 for CASPR2, and 2 for both.

Of these 117 patients, 50% had low (30-85 pmol/L) (n = 58), 24% had medium (85-200 pmol/L) (n = 28), and 26% had high (> 200 pmol/L) (n = 31) VGKC complex IgG values. Among the low values, 5.2% LGI1 (n = 3) and 3.5% CASR2 (n = 2) IgG positive were found, among the medium value, 14.3% LGI1 (n = 4) and 13.6% CASR2 (n = 1) and with the high values, 80 % LGI1 (n = 24) and 30 % CASR2 (n = 9) were detected.

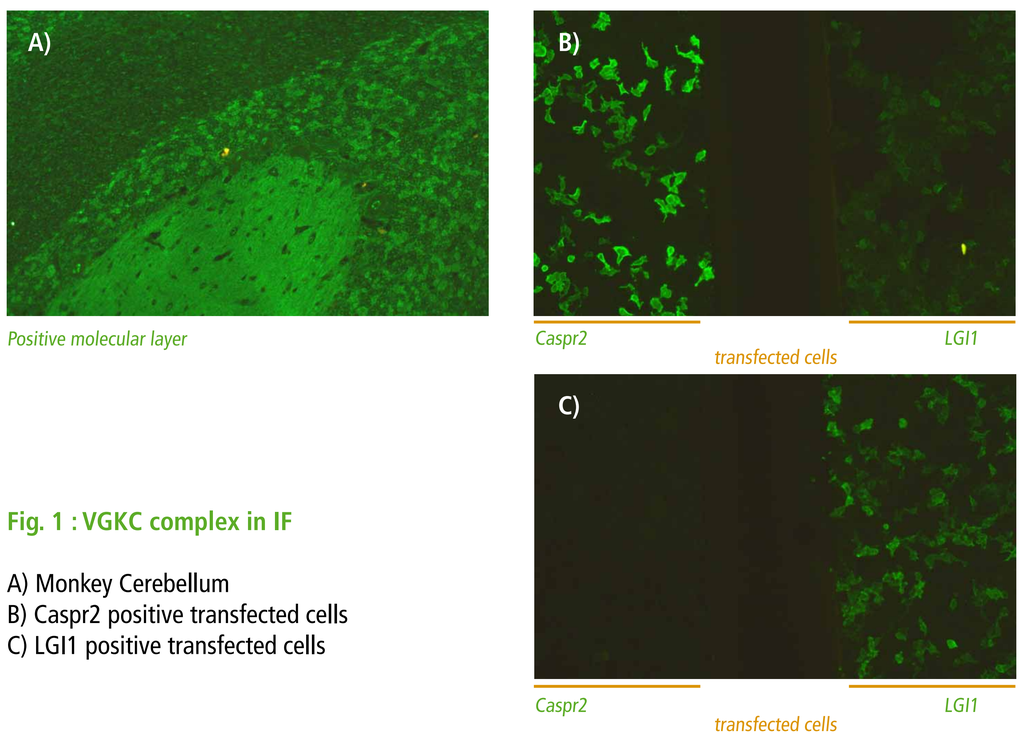


**Fig. 1 : VGKC complex in IF**

A) Monkey Cerebellum
B) Caspr2 positive transfected cells
C) LGI1 positive transfected cells

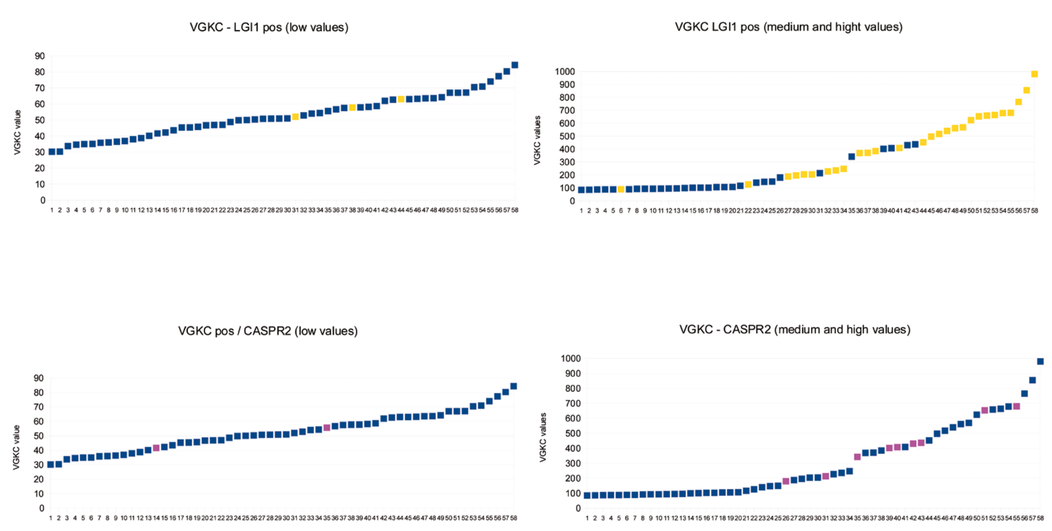


**Fig. 2 : Distribution of LGI1 and CAPR2 antibodies according to the value of autoantibodies VGKC**

## CONCLUSIONS

This study demonstrates the correlation between high level of VGKC complex IgG value and the presence of LGI1 and CASPR2 antibodies. The higher the VGKC value, the more positive are especially LGI1 but also CASPR2 IgG antibodies. Upper 200 pmol/L, 80% are LGI1 positive. Additional antigenic components of VGKC macromolecular complex remain to be defined. Cerebrocortical manifestations were recorded in patients with either LGI1 or CAPR2 antibodies, and, as LGI1 and CASPR2 antibodies were also detected in low value of VGKC, we propose to keep a cut-off at 30 to avoid the false negatif.

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