A serological response to Epstein-Barr virus and measles withstands a decade after infectious mononucleosis

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OBJECTIVE: TO EXAMINE WHETHER INFECTIOUS MONONUCLEOSIS (IM) IS FOLLOWED BY LONG-TERM INCREASED SPECIFIC IMMUNOREACTIVITY.

BACKGROUND: IM increases the risk of subsequent autoimmune disorders including multiple sclerosis, which is also associated with polyspecific antiviral immunoreactivity.

CONCLUSION: The EBV glycoprotein gp350 is an indicator of persistent immune stimulation after infectious mononucleosis (IM). This specific immune active post-IM state may be associated with the known risk of autoimmune IM sequele documented by epidemiological methods. A trend towards an analogous persistence of the anti-nCORE may suggest persistent post-IM polyspecificity

Serum

IM n=42 → 10 years → Post-IM n=42 (22 CSF)

Controls n=39 (15 CSF)

MS n=23 (serum +CSF)

DESIGN (**fig.1**) We assayed *EBV antibodies* Anti-EBNA1, anti-gp350 Anti-VCA IgG and IgM, and *measles antibody* nCORE in IM and after 10 years (approx.) follow-up

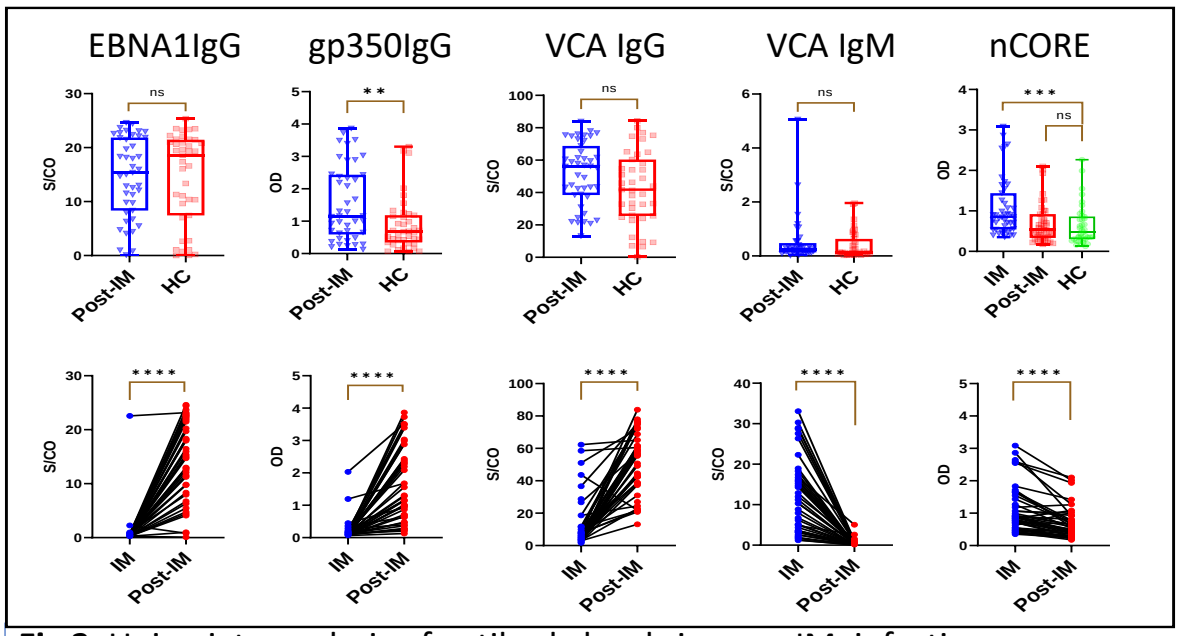

Fig 2: Univariate analysis of antibody levels in sera. IM, infectious mononucleosis; Post-IM, 10-year follow-up after IM; HC, healthy control; OD, optical density; S/CO, signal to cutoff. Top, Boxplots comparing Post-IM levels and HCs. Bottom, individual IM and post-IM samples, paired tests.

Results (fig 2) from analysis of four anti-EBV antibodies suggested that our recombinant anti-gp350 IgG reacts to a higher viral setting in IM. We proceed with extended analyses of antigp350 (fig. 3 and 4)

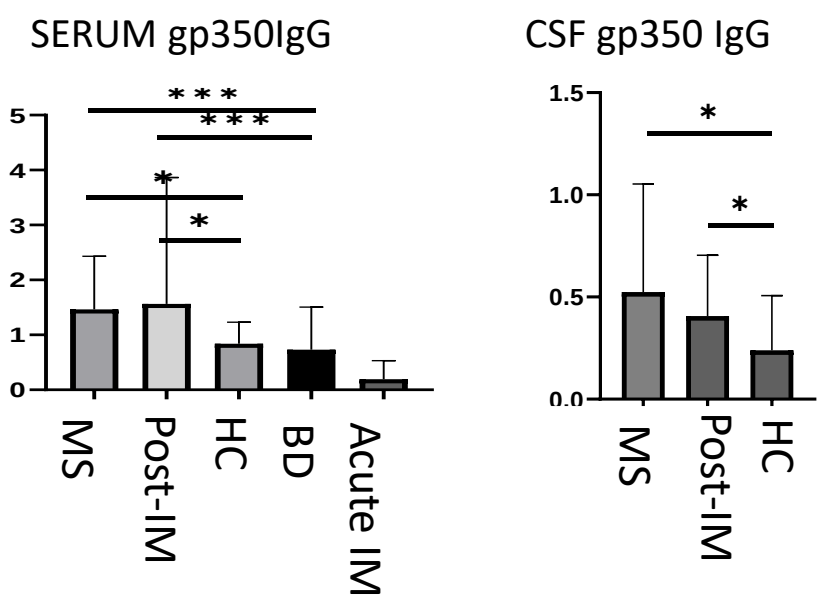

Fig. 3 Post IM persons had significantly higher reactivity against gp350 in sera and CSF than healthy individuals (HC) with a positive EBV serology (positive EBNA1 or VCA IgG) but no history of IM (HC), and healthy blood donors (BD). Post-IM persons had also increased CSF OD. Results from MS persons were used as a comparator.. Acute IM, acute infectious mononucleosis.

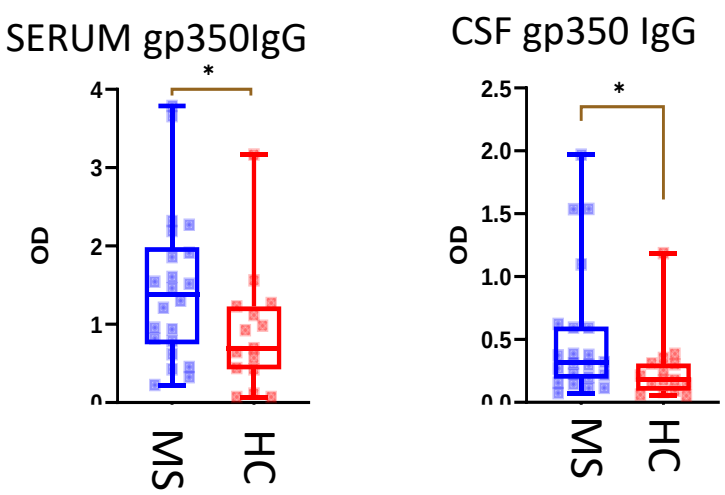

Fig 4: Expands data from Fig. 3 to highlight that serum and CSF concentrations of anti-gp350 IgG also were higher in MS patients without BBB damage than in HC with positive EBV serology. (EBNA1+ or VCA+).

RESULTS: From IM to 10 years Post-IM, anti-EBNA1 IgG, anti-VCA IgG, and anti-gp350 IgG levels increased significantly, whereas VCA IgM decreased. Anti-Gp350 IgG was higher in the Post-IM group than in HCs (p=0.007, age-adjusted 0.045), with no difference in anti-VCA or anti-EBNA IgG levels. Anti-Ncore IgG (purified anti-measles) was increased in acute IM (p<0.001) compared to HCs, and decreased at Post-IM but tended to remain higher than HCs (ns, age-adjusted p= 0.014).