Copy number of FCGR3B, which is associated with systemic lupus erythematosus, correlates with protein expression and immune complex uptake


Copy number variation (CNV)

- Amplifications and deletions in the genome
  - 1kb-1mb variants covering ~12% genome
  - <20% overlap with identified SNPs

- Causes
  - Nonallelic homologous recombination

- Disease association
  - PMP22 duplication → Charcot Marie Tooth
    (Cell. 1991;66(2):219-32)
Systemic Lupus Erythematosus

• Immune destruction of healthy tissue, mediated by presence of autoantibodies and resulting inflammation
• Formation and delayed clearance of immune complexes
• CNV in C4 (Chr 6) and FCGR3B (Chr1) previously associated with SLE
FCGR3B

• Low affinity IgG receptor
  – Binds immune complexed IgG specifically

• Largely restricted to neutrophil expression
  – Linked to plasma membrane via glycosylphosphatidylinositol anchor
  – Also released into serum

• May bind complexes to the surface of neutrophils

• Secreted form may mediate phagocytosis
This paper shows...

- FCGR3B low copy number (CN) is associated with SLE in Caucasian patients (confirmatory)
- FCGR3B CN correlates with
  - cell surface expression and soluble levels of the protein
  - Neutrophil adherence to, and uptake of, immune complexes
- FCGR3B high CN is associated with antineutrophil cytoplasmic antibody-associated systemic vasculitis (AASV)
Association of low FCGR3B CN with UK, but not Hong Kong, SLE. qPCR was used to determine FCGR3B/CD36 ratios in normal controls and patients with SLE.

Willcocks et al. Journal of Experimental Medicine
2008:205:1573-1582
Correlation between FCGR3B CN and protein expression in a family

Correlation between FCGR3B CN and neutrophil function in a family

Willcocks et al. Journal of Experimental Medicine
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FCGR3B CN is proportional to gene expression and function in the normal population
Association of high FCGR3B CN with AASV. qPCR was used to determine FCGR3B/CD36 ratios in normal controls and cohorts of patients with AASV (cohorts described in Supplemental materials and methods).

This paper shows...

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