**Supplemental digital content 2**

**Additional methods**

*Interleukin-22 binding protein genotyping*

From peripheral blood mononuclear cells, genomic DNA was isolated using QIAamp DNA Mini Kit (Qiagen, Venlo, The Netherlands) according to the manufacturer's instructions. The DNA was stored in EB buffer (Qiagen) at -20 °C and single nucleotide polymorphisms (SNP) in the *IL22BP* gene (*rs6570136* and *rs2064501*) were detected by the Competitive Allele Specific PCR (KASP) system (LGC Genomics, Teddington, UK). The frequency distribution in our cohort was in accordance with the data available in the 1000genome browser1.

*Plasma cytokines*

Quantification of IL-6 and tumor necrosis factor-alpha (TNF-α) was carried out by multiplex (MSD, V-PLEX Custom Human Cytokine, Meso Scale Diagnostics Rockville, MD, USA)

*Western Blot*

Western blot was performed on patient serum, which was diluted x4 and x8 in laemmli sample buffer (Bio-Rad, Hercules, CA, USA), heated to 95°C for 15 minutes and run on midi format stain-free SDS gels (12% Bis–Tris SDS gel, Criterion TGX, Bio-Rad). Protein ladder and r-lipocalin-2 (1757-LC, R&D systems) were included. Proteins were transferred to a PVDF membrane (Trans-Blot Turbo, Bio-Rad) using the Trans-Blot Turbo Transfer System (Bio-Rad). After blocking with 1% bovine serum albumin, the blots were probed with biotinylated lipocalin-2 antibody (BAF1757, R&D Systems) followed by incubation with streptavidin-HRP (890803, R&D systems) and developed using chemiluminescence, Clarity Western ECL substrate (Bio-Rad). Images were analyzed using the ChemiDoc system from Bio-Rad with Lab 4.0.1 software. Verification that the dimeric lipocalin-2 bands could be reduced to monomeric bands was performed with addition of 20% beta-mecaptoethanol to the laemmli buffer.

1. Genomes Project C, Auton A, Brooks LD, et al. A global reference for human genetic variation. *Nature.* 2015;526(7571):68-74.