Supplementary Materials

Serology

Serum obtained was frozen at -70°C and shipped on dry ice to Cedars-Sinai Medical Center, Los Angeles, CA. All sera were analyzed by the laboratory in a blinded fashion, without knowledge of patient diagnosis or other clinical information. The presence of anti-saccharomyces cerevisiae antibody (ASCA), antibodies to outer membrane porin C (OmpC), antibodies to bacterial flagellin (Cbir1), and anti-neutrophil-specific nuclear antibody (ANCA) was determined by enzyme-linked immunosorbent assay (ELISA) and evaluated as ELISA unit (EU) values (Supplemental Table 1). The cutoff for positivity was determined on the basis of results in well-defined patients with CD and was set at 20 EU/mL for ASCA, 16.5 EU/mL for OmpC, 21 EU/mL for Cbir1, and 12 Eu/mL for ANCA.

Exploratory Pharmacogenetic Analysis

Genetic influences that might differentially affect patient response to therapy were investigated at Cedars-Sinai Medical Center, Los Angeles, CA with whole genome SNP profiling of DNA samples from 86 consenting patients using the ImmunoChip, which supports denser genotyping in the vicinity of inflammation-associated and immunologically-related genes. Because the sample size was underpowered for Genome Wide Association Studies, we tested two focused genetic hypotheses for association with disease worsening. We tested whether absence of the minor allele of TNFSF15/tumor necrosis factor-like ligand 1A (TL1A) was associated with disease worsening (defined as an adverse event report of “Crohn’s disease,” “anal abscess,” “anal fistula,” or “disease progression” or patient withdrawal from study due to “disease progression”) or lack of response in this study, based on prior evidence of an association with disease worsening in response to secukinumab treatment. We also tested for association of
treatment outcome with a set of 32 SNPs in the IL-17 ligand and receptor gene regions
(Supplemental Figure 1).

Supplementary References

1. Trynka, G. et al. Dense genotyping identifies and localizes multiple common and rare variant
association signals in celiac disease. Nature genetics 43, 1193-1201, doi:10.1038/ng.998
(2011).

2. Hueber, W. et al. Secukinumab, a human anti-IL-17A monoclonal antibody, for moderate to
severe Crohn's disease: unexpected results of a randomised, double-blind placebo-
Supplemental Table 1. Serology markers by CD worsening versus non-worsening. There did not appear to be any difference between patients with worsening CD and those who did not worsen in the presence of antibodies, including ASCA, OmpC, Cbir1, or ANCA, which are commonly used for diagnosis and differentiation of CD and which are thought to be associated with disease worsening. However, the levels of ANCA antibodies were numerically higher in patients with worsening CD than those who did not worsen; limited patient numbers prevented formal statistical testing.

<table>
<thead>
<tr>
<th></th>
<th>Total (N = 112)</th>
<th>Worsening (N = 26)</th>
<th>Non-worsening (N = 86)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCA positive, n (%)</td>
<td>43 (38.4)</td>
<td>9 (34.6)</td>
<td>34 (39.5)</td>
</tr>
<tr>
<td>OmpC positive, n (%)</td>
<td>20 (17.9)</td>
<td>4 (15.4)</td>
<td>16 (18.6)</td>
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<tr>
<td>Cbir1 positive, n (%)</td>
<td>52 (46.4)</td>
<td>13 (50.0)</td>
<td>39 (45.3)</td>
</tr>
<tr>
<td>ANCA positive, n (%)</td>
<td>46 (41.1)</td>
<td>10 (38.5)</td>
<td>36 (41.9)</td>
</tr>
<tr>
<td>ANCA EU for positive patients, mean (SD)</td>
<td>59.0 (25.4)</td>
<td>78.7 (34.9)</td>
<td>53.7 (23.2)</td>
</tr>
</tbody>
</table>

ASCA, anti-saccharomyces cerevisiae antibody; OmpC, Escherichia coli outer membrane porin; Cbir1, bacterial flagellin; ANCA, antineutrophil cytoplasmic antibody; EU, ELISA units per milliliter
Supplementary Figure 1. Relationship between TL1A polymorphism and calprotectin changes. Exploratory pharmacogenetic analyses were performed to identify potential genetic polymorphisms predictive of disease worsening. There was no association of calprotectin changes, nor clinically defined disease worsening, with the rs6478109 intronic polymorphism of the tumor necrosis factor (ligand) superfamily, member 15 (TNFSF15)/tumor necrosis factor-like ligand 1A (TL1A).