Integration of Known DNA, RNA and Protein Biomarkers Provides Prediction of Anti-TNF Response in Rheumatoid Arthritis: results from the COMBINE study

OBJECTIVE: In rheumatoid arthritis (RA) several recent efforts have sought to discover means of predicting which patients would benefit from treatment. However, results have been discrepant with few successful replications. Our objective was to build a biobank with DNA, RNA and protein measurements to test the claim that the current state-of-the-art precision medicine will benefit RA patients. METHODS: We collected 451 blood samples from 61 healthy individuals and 185 RA patients initiating treatment, before treatment initiation and at a 3 month follow-up time. All samples were subjected to high-throughput RNA sequencing, DNA genotyping, extensive proteomics and flow cytometry measurements, as well as comprehensive clinical phenotyping. Literature review identified 2 proteins, 52 single-nucleotide polymorphisms (SNPs) and 72 gene-expression biomarkers that had previously been proposed as predictors of TNF inhibitor response (ΔDAS28-CRP). RESULTS: From these published TNFi biomarkers we found that 2 protein, 2 SNP and 8 mRNA biomarkers could be replicated in the 59 TNF initiating patients. Combining these replicated biomarkers into a single signature we found that we could explain 51% of the variation in ΔDAS28-CRP. This corresponds to a sensitivity of 0.73 and specificity of 0.78 for the prediction of three month ΔDAS28-CRP better than -1.2. CONCLUSIONS: The COMBINE biobank is currently the largest collection of multi-omics data from RA patients with high potential for discovery and replication. Taking advantage of this we surveyed the current state-of-the-art of drug-response stratification in RA, and identified a small set of previously published biomarkers available in peripheral blood which predicts clinical response to TNF blockade in this independent cohort.

General information
Publication status: Published
Organisations: Department of Systems Biology, Center for Biological Sequence Analysis, Integrative Systems Biology, Karolinska Institutet, Uppsala University, AbbVie
Number of pages: 7
Pages: 322-328
Publication date: 2016
Peer-reviewed: Yes

Publication information
Journal: Molecular Medicine
Volume: 22
ISSN (Print): 1076-1551
Ratings:
BFI (2016): BFI-level 1
Scopus rating (2016): CiteScore 2.9 SJR 1.449 SNIP 0.896
Web of Science (2016): Impact factor 3.457
Web of Science (2016): Indexed yes
Original language: English
Keywords: TNF-alpha, Biobank, Drug response, Pharmacogenetics, Rheumatoid arthritis
Electronic versions:
Integration_of_known_DNA_RNA_and_protein.pdf
DOIs:
10.2119/molmed.2016.00078
Source: PublicationPreSubmission
Source ID: 125508700
Research output: Contribution to journal › Journal article – Annual report year: 2016 › Research › peer-review