develop models to predict response to TNFi therapy before the initiation of treatment. Failure to validate and reproduce the performance of these predictive biomarkers in new patient populations and clinical trials was a typical outcome. Differing characteristics between patient populations, laboratory methods and procedures in generating molecular data and other biases inherent to single-cohort retrospective blood studies have hindered precision medicine progress not only in rheumatology but in other medical specialties as well.

[0004a] In some aspects, provided herein is a use of an anti-TNF therapy in the manufacture of a medicament for treating an autoimmune disorder in a subject, wherein the anti-TNF therapy is to be administered to the subject, wherein the subject has been determined to be responsive via a classifier established to distinguish between responsive and non-responsive prior subjects in a cohort that have received the anti-TNF therapy, wherein the classifier is developed by assessing: one or more genes whose expression levels significantly correlate to clinical responsiveness or non-responsiveness; and at least one of: presence of one or more single nucleotide polymorphisms (SNPs) in an expressed sequence of the one or more genes; or at least one clinical characteristic of the responsive and non-responsive prior subjects, wherein the classifier is validated by an independent cohort different than the cohort who have received the anti-TNF therapy, and wherein the one or more genes comprise: ALPL, ATRAID, BCL6, CDK11A, CFLAR, COMMD5, GOLGA1, IL1B, IMPDH2, JAK3, KLHDC3, LIMK2, NOD2, NOTCH1, SPINT2, SPON2, STOML2, TRIM25, or ZFP36.

[0004b] In some aspects, provided herein is a non-transitory computer-readable storage media encoded with a computer program including instructions executable by at least one processor to create an improved sample classification application comprising: at least a classifier stored on the media, wherein the classifier is capable of distinguishing between a responsive and a non-responsive subject for anti-TNF therapy, wherein the classifier is developed by assessing: one or more genes whose expression levels significantly correlate to clinical responsiveness or non-responsiveness to anti-TNF therapy; and at least one of: presence of one or more single nucleotide polymorphisms (SNPs) in an expressed sequence of the one or more genes; or at least one clinical characteristic of the responsive and non-responsive prior subjects, wherein the classifier is validated by an independent cohort than the cohort who have received the anti-TNF therapy, and wherein the one or more genes comprise: ALPL, ATRAID, BCL6, CDK11A, CFLAR, COMMD5, GOLGA1, IL1B, IMPDH2, JAK3, KLHDC3, LIMK2, NOD2, NOTCH1, SPINT2, SPON2, STOML2, TRIM25, or ZFP36.

[0004c] In some aspects, provided herein is a kit comprising the non-transitory computer-readable storage media as described herein.

[0005] In some aspects, the methods and compositions described herein permit care providers to distinguish between or among categories of subjects – e.g., subjects likely to benefit from a particular therapy (e.g., anti-TNF therapy) from those who are not, those who are more likely to achieve or suffer a particular outcome or side effect, etc. In some embodiments, such provided technologies thus reduce risks to patients, increase timing and quality of care for non-responder patient populations, increase efficiency of drug development, or avoid costs associated with administering ineffective therapy to non-responder patients or with treating side effects such patients experience upon receiving the relevant therapy (e.g., anti-TNF therapy).

[0006] In some aspects, the present disclosure provides methods of treating subjects with particular therapy (e.g., anti-TNF therapy), in some embodiments, a method comprising: administering a therapy to subjects who have been determined to be responsive via a classifier established to distinguish between subjects expected to be responsive vs non-responsive to the therapy. In some embodiments, a classifier identifies 60% or greater of non-responders within a treatment-naive cohort. In some embodiments, a classifier identifies 60% or greater of non-responders within a treatment-naive cohort of at least 350 subjects.

[0007] A classifier can be a molecular signature response classifier derived from differences in gene expression between known responders and non-responders within a cohort. In some embodiments, one or more genes having statistically significant differences in expression between responders and non-responders are included as part of a molecular signature response classifier. In some embodiments, proteins associated with genes having statistically significant differences in expression between responders and non-responders are mapped onto a human interactome to validate relationship between selected genes and disease biology.

[0008] Provided classifiers further incorporate additional elements, e.g., clinical characteristics or single nucleotide polymorphisms useful for classifying response or non-response in a given patient.

[0009] In some embodiments, the present disclosure provides methods of treating subjects suffering from an autoimmune disorder, in some embodiments, a method comprising: administering an anti-TNF therapy to subjects who have been determined to be responsive via a classifier established to distinguish between responsive and non-responsive prior subjects in a cohort who have received the anti-TNF therapy; wherein a classifier is developed by assessing: