A robust mRNA signature obtained via Recursive Ensemble Feature Selection predicts the responsiveness of omalizumab in moderate-to-severe asthma

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Abstract

Background: Not being well controlled by therapy with inhaled corticosteroids and long-acting β2 agonist bronchodilators is a major concern for severe-asthma patients. Current treatment option for these patients is the use of biologicals such as anti-IgE treatment, omalizumab, as add-on therapy. Despite the accepted use of omalizumab, patients do not always benefit from it. Therefore, there is a need to identify reliable biomarkers as predictors of omalizumab response. **Methods**: Two novel computational algorithms, machine-learning based Recursive Ensemble Feature Selection (REFS) and rule-based algorithm Logic Explainable Networks (LEN) were used on open accessible mRNA expression data from moderate-to-severe asthma patients to identify genes as predictors of omalizumab response **Results**: With REFS, the number of features were reduced from 28,402 genes to 5 genes while obtaining a cross-validated accuracy of 0.975. The 5 responsiveness predictive genes encode for the following proteins: Coiled-coil domain- containing protein 113 (CCDC113), Solute Carrier Family 26 Member 8 (SLC26A), Protein Phosphatase 1 Regulatory Subunit 3D (PPP1R3D), C-Type lectin Domain Family 4 member C (CLEC4C) and LOC100131780 (not annotated). The LEN algorithm found 4 identical genes with REFS: CCDC113 ,SLC26A8 PPP1R3D and LOC100131780. Literature research showed that the 4 identified responsiveness predicting genes are associated with: mucosal immunity, cell metabolism, and airway remodeling. **Conclusion and clinical relevance**: Both computational methods show 4 identical genes as predictors of omalizumab response in moderate-to-severe asthma patients. The obtained high accuracy indicates that our approach has potential for clinical settings. Future studies in relevant cohort data should validate our computational approach.

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