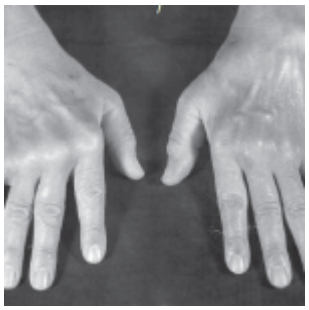
A new genetic approach for diagnosing Common Variable Immunodeficiency



Common variable immunodeficiency (CVID) is the most common symptomatic group of primary immunodeficiency (PID) syndromes. The hallmark of CVID diagnosis is decreased IgG and either low IgA or IgM, absent or deficient specific antibody responses to infection or vaccination, and importantly the exclusion of other causes of hypogammaglobulinemia.

CVID often manifests most commonly as sinopulmonary infections. However, more than half of people with CVID experience autoimmunity, interstitial lung disease, lymphoid hyperplasia, inflammatory bowel disease, nodular regenerative hyperplasia of the liver, granulomatous infiltrations, or malignancy.

In the June 13 2016 edition of Frontiers in Immunology, an article describes the use of whole exome sequencing (WES) for diagnosing CVID. WES is where all the genes expressed in the human genome are sequenced and possible mutations can be identified. This has been used before to uncover genetic defects of patients suffering from specific primary immunodeficiencies (PIDs). These authors now apply this to identify the causative genetic defects in patients suffering from CVID. To do so, the authors performed WES on 50 subjects with CVID with at least one of "early onset, autoimmune/inflammatory manifestations, low B lymphocytes, and/or familial history of hypogammaglobulinemia." From 433 variations found in genes associated with PID, they identified 17 "probable disease-causing mutations" in 15 patients. Variations included mutations in genes associated with intracellular signalling of immune cells, such as NFKB1, STAT3, CTLA4, PIK3CD, IKZF1, LRBA, and STXBP2.

The authors conclude by saying that "This approach may be of considerable value in CVID subjects with more severe phenotypes, such as those examined here." Although the genetic causes of CVID are multiple, this study contributes to a more cost-effective method of understanding, and possibly treating, the cause of the most severe cases.

Maffucci, P. et al, 2016. Genetic Diagnosis Using Whole Exome Sequencing in Common Variable Immunodeficiency. *Frontiers in Immunology*.