**In silico analysis of autoimmune diseases and genetic relationships to vaccination against infectious diseases**

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**ABSTRACT**

Vaccines are profoundly important to global health in preventing infectious diseases. Reported adverse events following vaccination are diverse, rare and require thorough investigation and evaluation [1]. Autoimmune diseases (AD) have been reported after some vaccinations. Because autoimmune diseases are rare and have variable and prolonged onset times, it makes it difficult to fully assess the association between the autoimmune diseases and vaccination. One of the components of pharmacovigilance and vaccine safety evaluation is consideration of biologic plausibility. Knowledge of biologic plausibility may be enhanced by an understanding of molecular immune mechanisms responsible for the adverse events, natural infections and the pathogenesis of the associated, reported AD. The situation is complicated by the complex matrix of innate and adaptive immune responses to vaccine antigens, adjuvants, preservatives and stabilizers. A bioinformatics, systems biology approach was used to collect data from the literature and curated databases to understand post-vaccination Guillain-Barré Syndrome (GBS), Rheumatoid Arthritis (RA), Systemic Lupus Erythematosus (SLE), and Idiopathic (or Immune) Thrombocytopenic Purpura (ITP).

By mining multiple curated databases and using automated text mining of PubMed literature, followed by manual review to remove errors, 667 genes associated with RA, 448 with SLE, 49 with ITP and 73 with GBS were collected. While all data sources provided valuable and unique gene associations, text mining using natural language processing (NLP) algorithms provide the most by far but required additional curation to remove incorrect associations. Sixty-four direct interactions between six vaccine ingredients and forty-six genes were also collected. Though only six genes were associated with all four ADs, thirty-seven genes were associated with three ADs. Pathway analysis found thirty-three pathways in common between the four ADs. Classification of genes into twelve immune system related categories identified more “Chemokine plus Receptors” genes were associated with RA than SLE. RA also had more genes associated with the “Th17 T-cell” subtype than other ADs. Gene networks were created, visualized and analyzed by cluster analysis of interconnected modules.

Analysis showed several clusters uniquely associated with RA including one with ten C-X-C motif chemokines, which are powerful neutrophil chemotactic factors. Other clusters contained genes common to other ADs. Figure 1 shows a sub-network of ten genes associated with GBS, Influenza A infection and genes activated in response to influenza vaccination [2]. The nodes highlighted in green and shaded in the data panel represent genes associated with GBS only and not the other three ADs. Red triangles are vaccine ingredients that interact with genes in the network. Additional pathway analysis suggests a key role for the MAPK signaling pathway in GBS.

**Figure 1. Sub-network of genes associated with GBS, Influenza A infection and response to influenza vaccination.**

Systems and methods to collect, organize and integrate large data sets are essential to enable researchers and public health agencies to utilize published data and develop hypotheses related to vaccine safety and efficacy.

**Categories and Subject Descriptors**

H.4 [Information Systems Applications]: Decision support

H.2.8 [Database Applications]: Scientific databases

**General Terms**

Experimentation

**Keywords**

ACM proceedings, Gene Networks, Immunology, Vaccines

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