Genetic Susceptibility to Periprosthetic Joint Infection: Insights from Familial Analysis

Michael Jurynec, Laura Certain[1], Brenna Blackburn[1], Jeremy Gililland[1]
[1]University of Utah

INTRODUCTION:

Prior work has indicated that susceptibility to periprosthetic joint infection (PJI) is likely to have a genetic component. However, the genetic variations that contribute to this susceptibility are unknown. In this exploratory study, we analyzed genomic data from a family with a high rate of PJI to identify candidate genes that may contribute to increased risk of PJI.

METHODS:

We performed whole-exome sequencing on four siblings, three of whom had undergone total joint arthroplasty (TJA), of whom two suffered from recurrent PJI. We identified rare coding variants present in the two siblings that had PJI and absent in the sibling who had undergone TJA without PJI. We considered variants with a REVEL (rare exome variant ensemble learner) score of >0.7 as possibly pathogenic and therefore of interest. We eliminated genes that had no REVEL score or were different only due to alignment errors. We then searched each candidate gene in the National Center for Biotechnology Information (NCBI) Gene database to see if any had a role in immune function or wound healing.

RESULTS:

Comparison of rare genetic variants found in the affected siblings (TJA + PJI) but not the unaffected sibling (TJA no PJI), yielded a list of 23 genes with a REVEL score >0.7. Searching each of these in the NCBI database yielded two with a plausible role in susceptibility to PJI: JAGN1 and SERPINA10. The former (JAGN1) is necessary for neutrophil differentiation and survival, and mutations are associated with immune deficiency. The latter (SERPINA10) affects coagulation and clotting.

DISCUSSION AND CONCLUSION:

This exploratory genetic analysis of a family with an unusually high rate of PJI identified two genetic variants that might affect wound healing and susceptibility to infection. Analysis of further families with high rates of PJI will be needed to confirm the relevance of this finding.