
Thinking Matters Symposium

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Importance of Understanding Genetic Predisposition

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Importance of Understanding Genetic Predisposition

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Abstract

Hypersensitivity reactions can be sudden and are often fatal. Many of these reactions occur as a result of allergies to prescribed medication. Adverse drug reactions or (ADR's) were show in a recent study to affect over 6% of hospitalized patients and resulted in over 100,000 deaths a year in the US alone. This poster will review the importance of understanding genetic predisposition, through articles about possible genetic causes of allergies to penicillin and other beta-lactams. Changes in a specific HLA gene located on chromosome 6 showed a correlation to penicillin reactions in over 600,000 participants. Another study found a conclusive relationship between 42 scientific articles that focus on the role the human genome plays ADR's out of the more than 3000 they scanned. The intent is to see what common biological pathways come up as factors in these articles that focus on hypersensitivity reactions and to compare them to one another. In doing this they concluded that there in a strong correlation with the HLA region producing IR against penicillin.

Introduction

- **Genetic predisposition** refers to an organism's genetic makeup, and how that will be expressed in its phenotype through the likelihood of reactions.
- Understanding why a reaction occurs in some more often than others has always been a question that has been pondered in the scientific community.
- The importance of fully understanding the role of an organism's genetic makeup can be used to determine the likelihood of future issues.
- By looking at research into hypersensitivity reactions to penicillin and other beta lactams, researchers have determined a common correlation in the human genome (Figure 1) , that is a tell if that individual will have a reaction.

Methods

- The data used in this study was collected from over 619,300 participants, The researchers then ran a genome-wide association study (GWAS), to determine a correlation in genetic markers in the individual's genome.
- They meta-analyzed almost 20 million genetic markers of their control and case study groups.

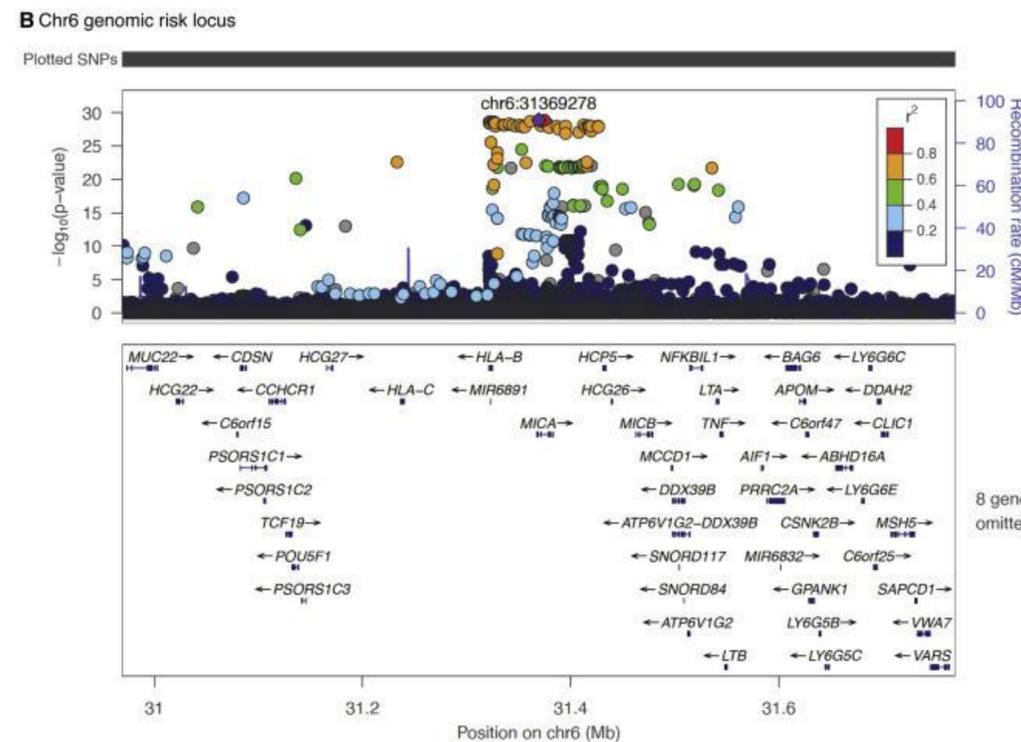
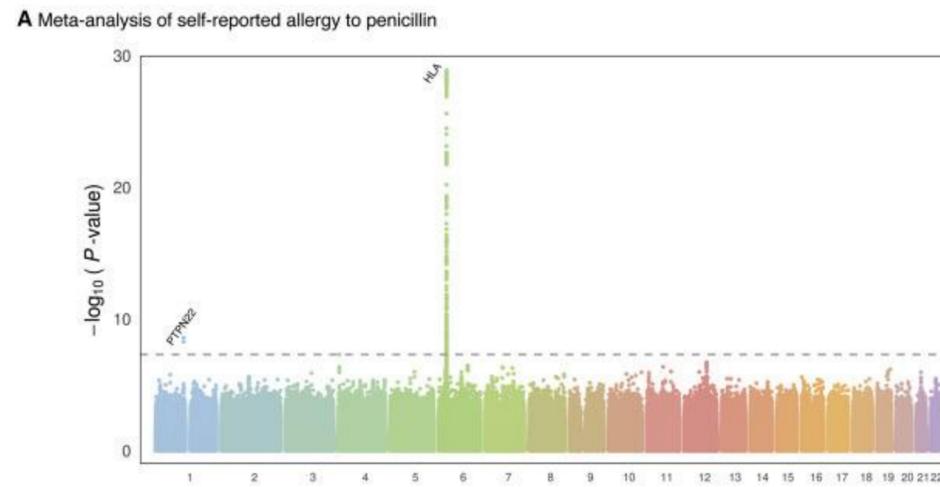


Figure 1: (A) Manhattan plot, each dot represents a SNP, with the dotted line showing the genome wide significance amongst analysis of individuals with self reported penicillin allergy (x-axis indicates chromosomal position) . (B) Colored SNPs according to their respective linkage disequilibrium. (The Lead SNP (rs114892859) marked with a diamond). From "Genome-wide Study Identifies Association between HLA-B*55:01 and Self-Reported Penicillin Allergy." *American journal of human genetics* vol. 107,4 (2020) by Krebs, Kristi et al

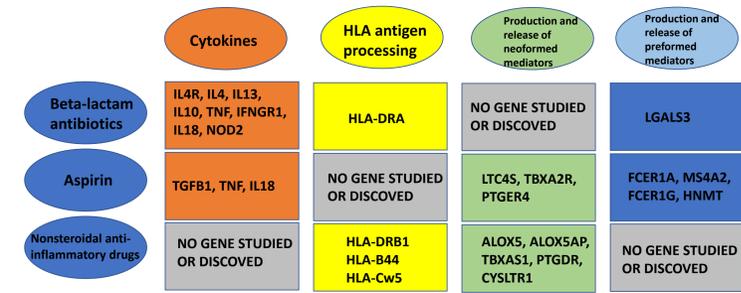


Figure 3: Visual of the pathogenic pathways that were surveyed from 42 articles that are potentially involved in beta-lactam allergy, along with that of Aspirin and NSAIDs. Notice the overlapping of pathways between the Beta-lactams, Aspirin, and Nonsteroidal anti-inflammatory drugs. From "Genetic variants associated with drugs-induced immediate hypersensitivity reactions: a PRISMA-compliant systematic review. *Allergy* 2016" by Oussalah A, Mayorga C

Conclusion

- It is important to be able to predict adverse drug reactions and understand why they happen.
- Fully understanding the role that genetic predisposition plays on the human genome can greatly impact health care.
- These discovered correlations amongst those individuals with self reported penicillin allergy, shows that the HLA region of the genome plays some role of the adverse reactions to penicillin and other beta-lactams.
- Although much is unknown about the specifics that genetic make up has on an individual, it shows that there is importance and value in attempting to understand the greater role that the genome plays in our lives.
- Further research into genetic predisposition is important and will lead to discoveries that will greatly impact our species and science itself.

References

- Krebs, Kristi et al. "Genome-wide Study Identifies Association between HLA-B*55:01 and Self-Reported Penicillin Allergy." *American journal of human genetics* vol. 107,4 (2020): 612-621.
- Oussalah A, Mayorga C, Blanca M, Barbaud A, Nakonechna A, Cernadas J, Gotua M, Brockow K, Caubet J-C, Bircher A, Atanaskovic M, Demoly P, Kase-Tanno L, Terreehorst I, Laguna JJ, Romano A, Gueant J-L on behalf of the Task force 'Genetic predictors of drug hypersensitivity' of the European Network on Drug Allergy (ENDA) of EAACI. Genetic variants associated with drugs-induced immediate hypersensitivity reactions: a PRISMA-compliant systematic review. *Allergy* 2016; 71: 443-462.

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Results

- After the results, to further confirm association with penicillin allergy, they looked at case studies with a self reported penicillin allergy. They found a correlation with the HLA-B*55:01 allele after meta-analysis. (Figure 2)
- This data showed a 33% higher odds of penicillin allergy amongst carriers of this allele.
- An unrelated research group meta-analyzed over 3000 studies and found 42 that included research into genetic predisposition for the reactions and found that there is a strong association in penicillin allergies between the HLA region and production of the immune-response genes (IR) which regulate the ability to produce an immune response (Figure 3).

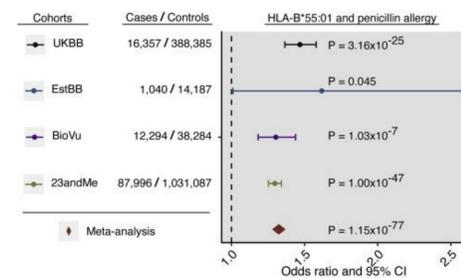


Figure 2: The Allele Association of HLA-B*55:01 with Self-Reported Penicillin Allergy. From "Genome-wide Study Identifies Association between HLA-B*55:01 and Self-Reported Penicillin Allergy." *American journal of human genetics* vol. 107,4 (2020) by Krebs, Kristi et al