Pleiotropic Effects in Thrombotic-Related Traits Using Bivariate Variance Components Models

Alfonso Buil[1,2], Angel Martinez[2] Juan Carlos Souto[2], Jordi Fontcuberta[2] and Jose Manuel Soria[1,2]

[1] Unitat de Bioinformatica de Malalties Complexes, Institut de Recerca del Hospital de la Santa Creu i Sant Pau de Barcelona, Spain
[2] Unitat d'Hemostasia i Trombosi, Hospital de la Santa Creu i Sant Pau de Barcelona, Spain

Introduction The major pathways in hemostasis (coagulation and fibrinolysis) are complex enzymatic systems composed of multiple inter-related proteins. Variation in several of these proteins has been associated with risk of thrombosis. On the other hand, the variation of the levels of these proteins has a significant genetic component. In our study we looked for evidence of shared genetic effects (pleiotropic effects) among several of these proteins.

Methods We used the sample from the Genetic Analysis of Idiopathic Thrombophilia (GAIT) Project, that included 399 individuals (68 of them affected with venous thrombosis) grouped in 21 families. In each individual we measured 50 quantitative traits related with the hemostatic systems.
We analyzed the data using bivariate variance component models as described in [1] and implemented in the software SOLAR [2]. Bivariate variance components models applied to family data allow the partition of the correlation between two traits into genetic and environmental components. The estimated genetic component of this correlation is a measure of the shared genetic effects between the traits, that is, a measure of pleiotropy.

Results First, we estimated the genetic correlation between each of the 50 quantitative traits and thrombosis. Fifteen of the traits gave a significant genetic correlation with thrombosis at a nominal level of 0.05. Then, we estimated the genetic correlations among all of the possible pairs of the 15 selected traits. From this matrix of genetic correlations we extracted two clusters of traits that were genetically correlated among them.

Conclusion Using Bivariate Variance Components Models with a sample of individuals in families, we detected two clusters of quantitative traits that share pleiotropic effects among them and with thrombosis.

References

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