Title: Gender Prediction based on Platelet Pairwise Agonist Scanning (PAS) Synergy Scores

Authors: M.Y. Lee, S. Diamond

During clotting, platelets must respond to multiple stimuli. Pairwise Agonist Scanning (PAS) deploys single and pairwise combinations of agonists at low, medium and high doses to explore signaling crosstalk. 1 The measured calcium mobilization following pairwise activation of platelet GPVI, PAR1, PAR4, P2Y1/P2Y12, TP, and IP receptors allowed measurement of a 135-parameter PAS synergy vector populated with normalized pairwise synergy scores (ranging from +1 to -1). 1 A phenotype database was then constructed using 40 PAS vectors from 20 donors (10 male, 10 female) each measured in duplicate. A hierarchal cluster tree was built based on the Euclidean distance between the 40 PAS vectors. Many replicate experiments of donors self-clustered (10 out of 20 donor pair vectors) at the lowest level, while the PAS vectors also strongly clustered according to sex at a higher level, indicating that platelet function is unique to the individual and that male and female platelets are functionally different. A support vector machine (SVM) algorithm was trained on this database to predict the sex of the donor based on the donor's PAS vector. The average SVM error rate was 5.975% when the dataset was randomly split into training and testing datasets in 1000 separate tests. To explore which pathway most impacted SVM accuracy, data for a given agonist was dropped from the training set and the resulting SVM error rates compared. When dropping convulxin agonist data, the error doubled. Thus, GPVI signaling and crosstalk accounted most strongly for the functional differences between the male and female platelets.

References:

1. Chatterjee, M. S., Purvis, J. E., Brass, L. F., & Diamond, S. L. (2010). Pairwise agonist scanning predicts cellular signaling responses to combinatorial stimuli. (Nature Biotechnology)."