PamIndex: biomarker discovery for PamChip® assays

Rik de Wijn, Alexandre Maurel and Faris Naji; Bioinformatics Group, PamGene International B.V., 's-Hertogenbosch, The Netherlands.

Study Design

The main data analysis approach in biomarker studies is learning by example: supervised class prediction uses example samples with known status to train a model that can be used to predict the status of new samples (Fig1). The standard tool for creating class prediction models in Bionavigator uses a method called PLS-DA.

In order to test if a useful biomarker has indeed been found, the model may be applied to a independent testing set of example samples. Alternatively, the original example samples may be used for testing by applying cross-validation (Fig 2).

Key Findings

Application of a PLS_DA class prediction model to new samples, for instance when using a testing set or during cross validation, results in a prediction score: the PamIndex. When the PamIndex > 0 the samples are assigned to one group (here the non-responders) or to the other when PamIndex < 0. When a sample has a PamIndex that is further away from the decision boundary at PamIndex = 0, it is less likely to really belong to the opposite group.
In Figure 3 the Pamindex resulting from a leave one out cross validation is visualized in a waterfall plot.

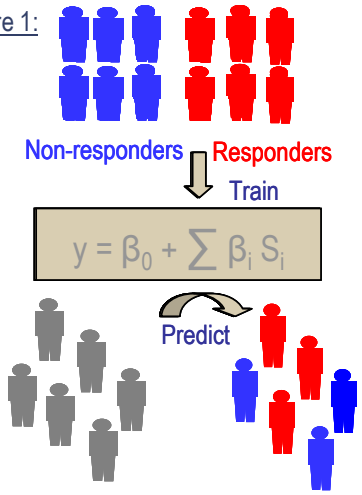
"Author Quote"

"PamIndex plots have become a standard way to present PamChip® based biomarker results".

Background

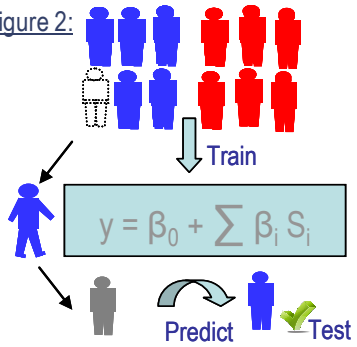
PamChip® based kinase and nuclear hormone receptor assays are frequently applied in biomarker discovery studies, seeking to predict e.g. drug response in cancer patients. These studies include measurement of phosphorylation profiles and compound effect profiles (inhibition profiles) on cell lines, xenografts and clinical sample material[1-3]. PamGenes data analysis package Bionavigator[4] contains an easy to use component for finding and evaluating such biomarkers.

Figure 1:



From PamChip® measurements on samples with known status (e.g. examples of responders and non-responders) a class prediction model is trained. This model can subsequently be used to predict the status of new samples.

Figure 2:



With Leave-one-out-cross-validation the application of the model on new samples is simulated. A model is created based on the set of example samples with one sample left out to take up the role of a new sample. Prediction on this sample can be verified. This is repeated for all samples.

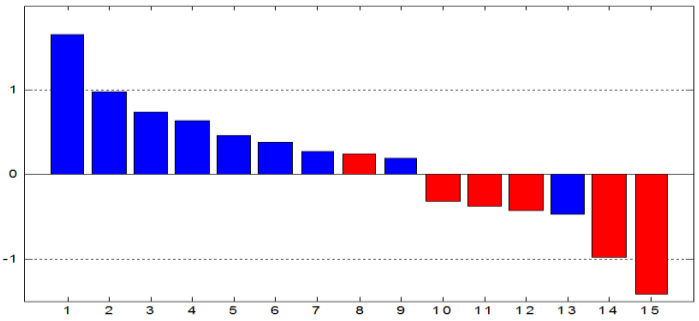


Figure 3: PamIndex (y-axis) resulting from leave one out cross validation with responder (blue) and non-responder (red) samples. The predicted group is non-responder when PamIndex > 0 and responder when PamIndex < 0. You can see that the prediction is correct for 13 out of 15 samples.

References:

1. Versele et al. Mol. Cancer Ther. 8 (2009) p1846;
2. Folkvord et al. Int. J. Radiat. Oncol. Biol. Phys. 78 (2010) p555;
3. Hilhorst et al. J. Clin. Oncol 29 (2011) Suppl. Abstract 10521.
4. Bionavigator Application Note #201017 (www.pamgene.com).

Conclusion

Class prediction analysis is central in biomarker discovery. Bionavigator implements PLS-DA, a class prediction method that works well with the various types of PamChip® data.

Application note: #201110 (10-2011)

Contact us:
Wolvenhoek 10, 5211 HH Den Bosch, the Netherlands
☎+31 73 615 80 80, ✉ info@pamgene.com