Development of a Novel Gene Expression-Based Prognostic Score in Malignant Pleural Mesothelioma

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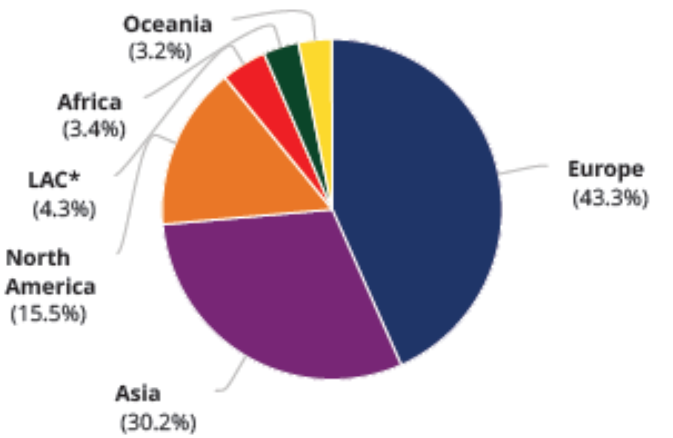
Introduction: Malignant pleural mesothelioma (MPM) is a rare cancer type with an increasing incidence worldwide. There are no curative therapies for advanced MPM. Most of the MPM cases are associated with previous occupational exposure to asbestos. From a genomic standpoint, MPM is characterized by a high level of tumor suppressor genes alterations. Different genomic alterations however can converge on a limited number of dysregulated gene expression profiles. That makes a prognostic gene expression based scores an appealing approach to develop novel biomarkers in rare cancers such as MPM.

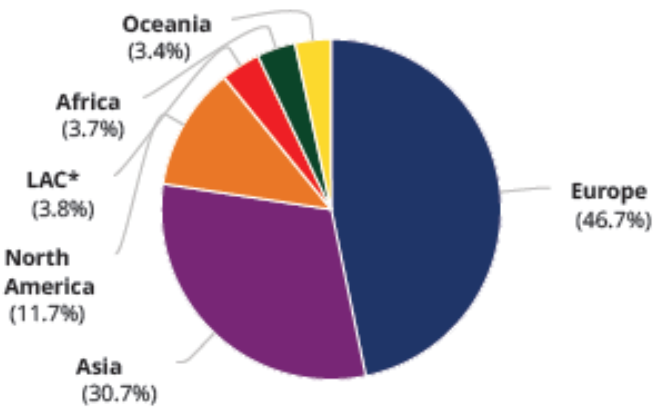
Aim: We aimed to develop a rational gene expression based prognostic score in MPM using publicly available datasets

Incidence, both sexes



Population	Number
Europe	13 197
Asia	9 209
North America	4 728
*Latin America and the Caribbean	1 310
Africa	1 027
Oceania	972
Total	30 443

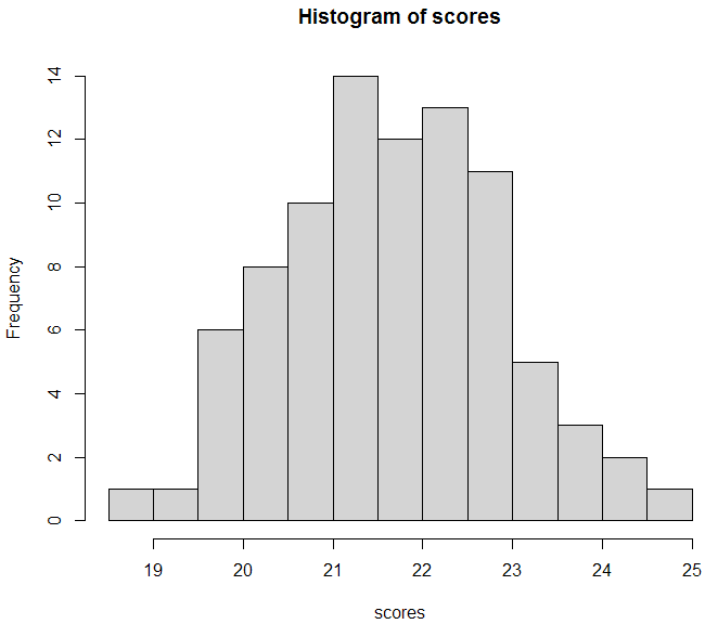
Mortality, both sexes

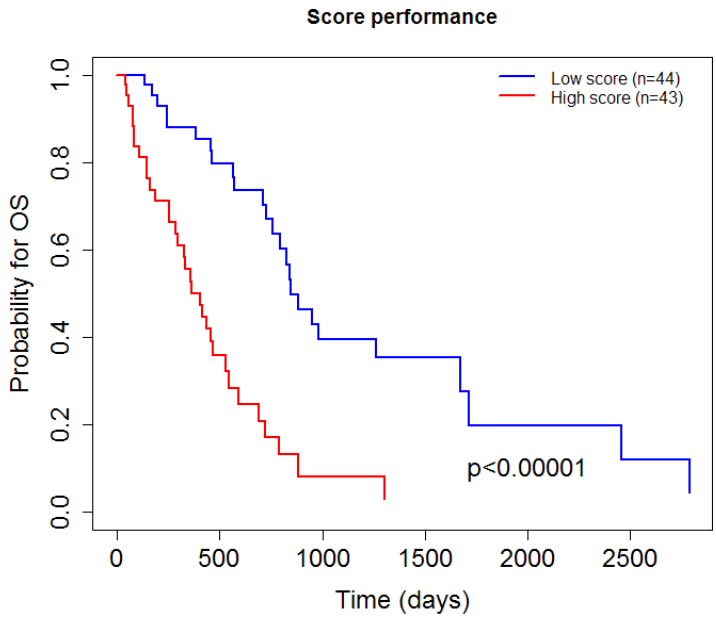


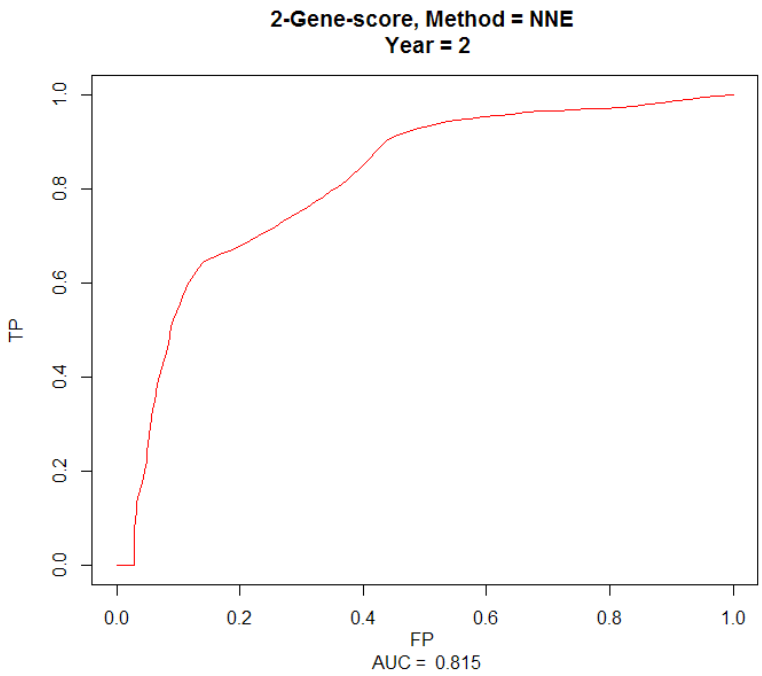
Population	Number
Europe	11 953
Asia	7 846
North America	3 001
*Latin America and the Caribbean	963
Africa	937
Oceania	876
Total	25 576

Materials and methods: We developed the prognostic score using processed RNASeq data for 87 newly diagnosed MPM patients analyzed through the Cancer Genomes Atlas (TCGA-MESO dataset) project. The prognostic model was built using the Robust Likelihood-Based Survival Modeling with Microarray Data method, which was implemented through the *rbsurv* package for R.

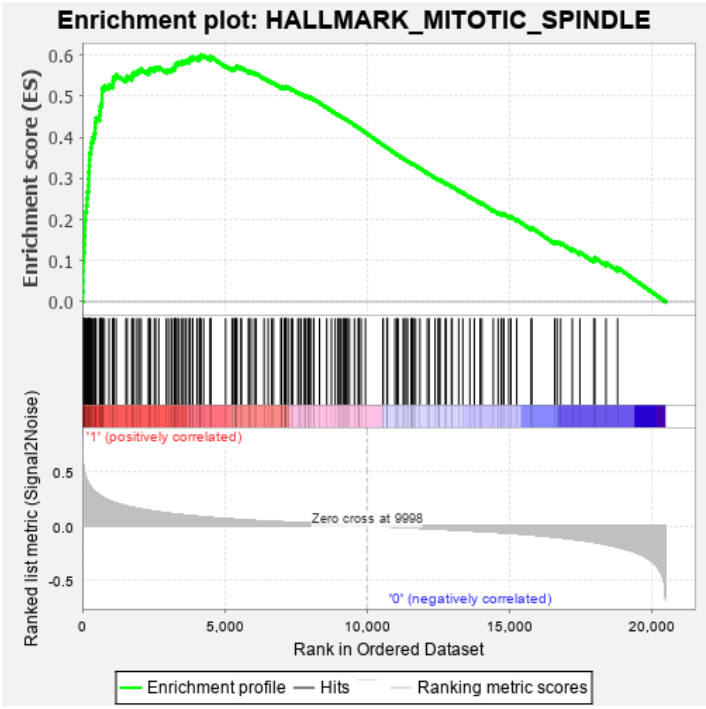
Results: We narrowed down the model building to analysis to 179 genes, which have been shown previously to be of importance to MPM development. Our statistical approach showed that a model including two genes was the best predictor for overall survival (OS) ($p<0.0001$). Receiver operating characteristics (ROC) curve analysis also showed that the score was a very good predictor of 2-year survival (Area under the curve (AUC) = 0.815). The discrete score based on the median of the continuous score stratified the patients into low and high score groups. The discrete score also correlated with OS ($p<0.0001$).

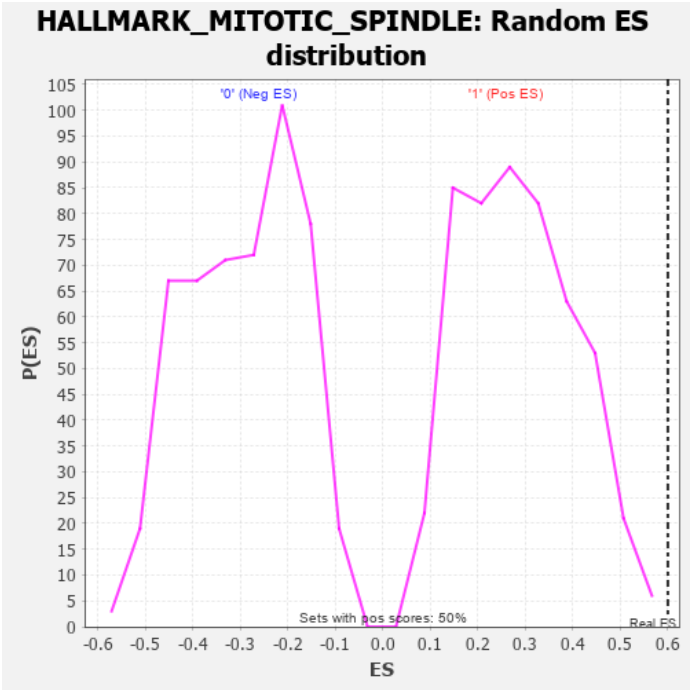


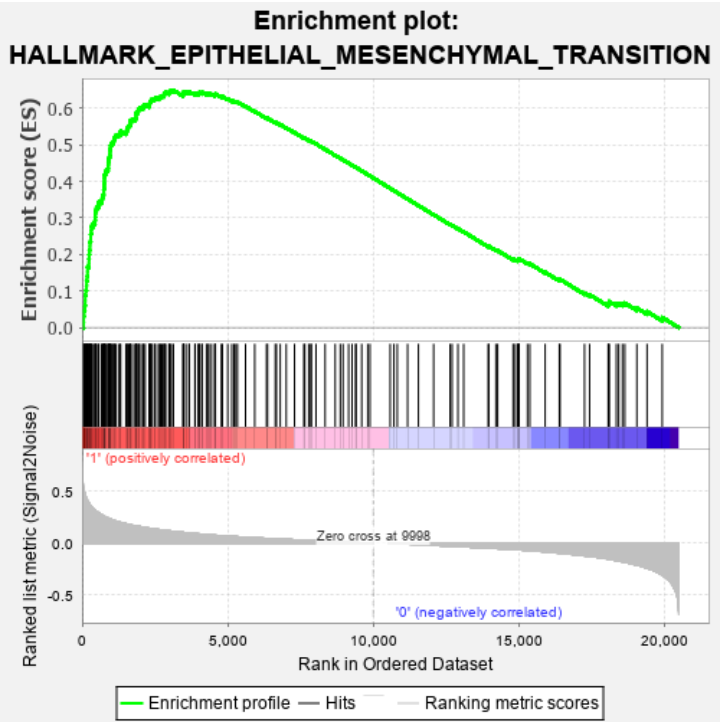


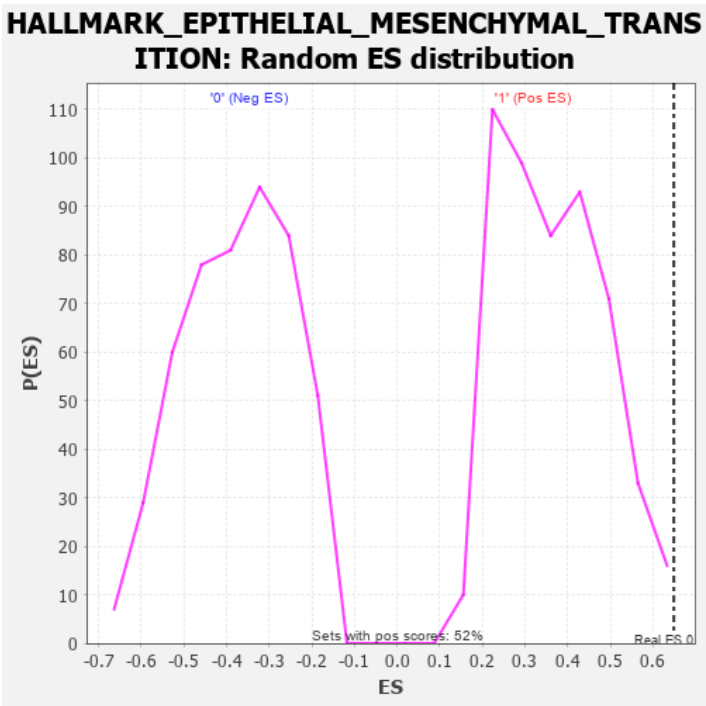


Furthermore, we were able to demonstrate that low and high score groups of patients had differential gene expression profiles as well as differential mircoRNA expression profiles.









Conclusion: This is the first study to demonstrate a very good performance of only 2-genes expression model in MPM. We are currently extending our work to validate the score on a number of gene expression datasets from different analytical platforms.