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A machine learning based approach identifies a powerful 3-gene prognosticator in an acute myeloid leukemia multi-cohort study

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Acute myeloid leukemia (AML) is a heterogeneous hematological malignancy with variable response to treatment. Recurring cytogenetic abnormalities and gene mutations are important prognosticators. However, 50-70% of AML cases harbor either normal or risk-indeterminate karyotypes. The identification of better biomarkers of clinical outcome is therefore necessary to inform tailored therapeutic decisions. We applied an artificial neural network (ANN) based machine learning approach to a discovery cohort of 641 adults with newly diagnosed AML. ANN analysis identified a parsimonious 3-gene expression signature predictive of survival, which comprised CALCRL, CD109 and LSP1. We computed a prognostic index (PI) from these markers using normalized gene expression levels and β-values from subsequently created Cox proportional hazards models with coupled with clinically established prognosticators. Our 3-gene PI separated the adult patients in each ELN cytogenetic risk category into subgroups with different survival probabilities and identified patients with very high-risk features, such as those with a high PI and either FLT3-ITD or non-mutated NPM1. The ability of the 3-gene PI to stratify survival was validated in two independent adult cohorts (n=221 subjects). Our ANN derived 3-gene signature applied to cox proportional hazards models by way of validation refined the accuracy of patient stratification and improved outcome prediction.

Biography

Graham Ball is a Professor of Bioinformatics at Nottingham Trent University and CSO of CompanDX UK and CompanDX China Ltd. He is an Associate Director of the John Van Geest Cancer Research Centre and Biostatistics Lead on three clinical projects. He has been involved in the development and validation of bioinformatics algorithms using artificial neural networks for the last 18 years. He has 230 journal papers and five patents in this area. His current research is focused on characterization of biological systems, including diagnostic and classification modelling of cancer molecular pathology, host response to disease and identification of molecular targets for therapy.

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