PLoS One. 2013 Aug 9;8(8):e70429. doi: 10.1371/journal.pone.0070429. eCollection 2013.

Identification and validation of a multigene predictor of recurrence in primary laryngeal cancer.

Fountzilas E, Kotoula V, Angouridakis N, Karasmanis I, Wirtz RM, Eleftheraki AG, Veltrup E, Markou K, Nikolaou A, Pectasides D, Fountzilas G.

Source

Department of Medical Oncology, "Papageorgiou" Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece. elenafou@gmail.com

Abstract

PURPOSE:

Local recurrence is the major manifestation of treatment failure in patients with operable laryngeal carcinoma. Established clinicopathological factors cannot sufficiently predict patients that are likely to recur after treatment. Additional tools are therefore required to accurately identify patients at high risk for recurrence. This study attempts to identify and independently validate gene expression models, prognostic of disease-free survival (DFS) in operable laryngeal cancer.

MATERIALS AND METHODS:

Using Affymetrix U133A Genechips, we profiled fresh-frozen tumor tissues from 66 patients with laryngeal cancer treated locally with surgery. We applied Cox regression proportional hazards modeling to identify multigene predictors of recurrence. Gene models were then validated in two independent cohorts of 54 and 187 patients (fresh-frozen and formalin-fixed tissue validation sets, respectively).

RESULTS:

We focused on genes univariately associated with DFS ($p<0.01$) in the training set. Among several models comprising different numbers of genes, a 30-probe set model demonstrated optimal performance in both the training (log-rank, $p<0.001$) and 1(st) validation ($p=0.010$) sets. Specifically, in the 1(st) validation set, median DFS as predicted by the 30-probe set model, was 34 and 80 months for high- and low-risk patients, respectively. Hazard ratio (HR) for recurrence in the high-risk group was 3.87 (95% CI 1.28-11.73, Wald's $p=0.017$). Testing the expression of selected genes from the above model in the 2(nd) validation set, with qPCR, revealed significant associations of single markers, such as ACE2, FLOT1 and PRKD1, with patient DFS. High PRKD1 remained an unfavorable prognostic marker upon multivariate analysis (HR=2.00, 95% CI 1.28-3.14, $p=0.002$) along with positive nodal status.

CONCLUSIONS:

We have established and validated gene models that can successfully stratify patients with laryngeal cancer, based on their risk for recurrence. It seems worthy to prospectively validate PRKD1 expression as a laryngeal cancer prognostic marker, for routine clinical applications.