

Prognostic significance of the Wnt pathway in squamous cell laryngeal cancer.

[Psyrris A](#)¹, [Kotoula V](#)², [Fountzilias E](#)³, [Alexopoulou Z](#)⁴, [Bobos M](#)³, [Televantou D](#)³, [Karayannopoulou G](#)⁵, [Krikelis D](#)⁶, [Markou K](#)⁷, [Karasmanis I](#)⁸, [Angouridakis N](#)⁷, [Kalogeras KT](#)⁹, [Nikolaou A](#)⁸, [Fountzilias G](#)¹⁰.

Author information

- ¹Division of Oncology, Second Department of Internal Medicine, Attikon University Hospital, Athens, Greece. Electronic address: dpsyrris@med.uoa.gr.
- ²Department of Pathology, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece; Laboratory of Molecular Oncology, Hellenic Foundation for Cancer Research, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.
- ³Laboratory of Molecular Oncology, Hellenic Foundation for Cancer Research, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.
- ⁴Health Data Specialists Ltd., Athens, Greece.
- ⁵Department of Pathology, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.
- ⁶Department of Medical Oncology, "Papageorgiou" Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.
- ⁷First Department of Otorhinolaryngology, "AHEPA" Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.
- ⁸ENT Department, "G. Papanikolaou" General Hospital, Thessaloniki, Greece.
- ⁹Department of Medical Oncology, "Papageorgiou" Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece; Translational Research Section, Hellenic Cooperative Oncology Group, Data Office, Athens, Greece.
- ¹⁰Laboratory of Molecular Oncology, Hellenic Foundation for Cancer Research, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece; Department of Medical Oncology, "Papageorgiou" Hospital, Aristotle University of Thessaloniki School of Medicine, Thessaloniki, Greece.

Abstract

OBJECTIVES:

We sought to determine the prognostic significance of the Wnt signaling pathway in operable squamous cell carcinoma of the larynx.

MATERIALS AND METHODS:

In an annotated cohort of 289 operable laryngeal cancers we evaluated the prognostic impact of E-cadherin, P-cadherin and β -catenin protein expression with immunohistochemistry, as well as the mRNA expression of 7 key effectors of the Wnt pathway including secreted frizzled-related protein 4 (SFRP4), SNAI2 (SLUG) and WNT5A with qPCR (relative quantification [RQ]).

RESULTS:

Using median immunoreactive scores as a pre-defined cut-off, patients whose tumors overexpressed both cytoplasmic E-cadherin and β -catenin experienced longer median OS as compared to those whose tumors overexpressed β -catenin only (median OS 124 vs. 72 months, $p=0.0301$) and patients whose tumors overexpressed both cytoplasmic and membranous E-cadherin experienced longer DFS as compared to those whose tumors overexpressed cytoplasmic E-cadherin only (median 118 vs. 91 months, $p=0.0106$). Upon hierarchical clustering of SFRP4, SNAI2 and WNT5A RQ values, profiles including co-expression of all 3 genes but also profiles with under-expression of SNAI2 and WNT5A were associated with worse outcome as compared to profiles not related to the Wnt pathway. In multivariate analysis, clustering was an independent predictor for DFS ($p=0.0221$) and OS ($p=0.0077$).

CONCLUSION:

We identified gene expression profiles and IHC patterns associated with aberrant Wnt signaling conferring aggressive clinical behavior in operable squamous cell carcinoma of the larynx. Prospective validation of these results will determine whether targeting the Wnt pathway merits investigation in this disease.

Copyright © 2014 Elsevier Ltd. All rights reserved.