Genetic biomarkers in Head and neck squamous cell carcinoma

Michal M. Masternak1, Xu Zhi1, Katarzyna Lamperska2, Paweł Golusinski3, Lukasz Luczewski3, Nicholas J. Schork4, Wojciech Golusinski3
1 College of Medicine, Burnett School of Biomedical Sciences, University of Central Florida, Orlando, USA, 2 Department of Cancer Genetics, Greater Poland Cancer Centre, Poznan, Poland, 3 Department of Head and Neck Surgery, Greater Poland Cancer Centre, Poznan University of Medical Sciences, Poznan, Poland, 4 Department of Molecular and Experimental Medicine and the Scripps Translational Science Institute, The Scripps Research Institute La Jolla, USA

Abstract

Outcome Objectives:
Head and neck squamous cell carcinoma (HNSCC) is known as one of the six most common human cancers mainly caused by consumption of tobacco and alcohol. There is also a genetic factor; however, the genetic markers are not yet established. Our objectives were to:
• Validate the genetic signature of molecular targets expressed by tumors in HNSCC
• Determine potential biomarkers for earlier detection, potential therapies and prediction of patients’ survival

Methods
The HNSCC patients were recruited to the study in the Greater Poland Cancer Centre in 2010. Oral cancer and normal epithelium tissue taken at a minimum of 2 cm distal from the tumors’ margins from 41 patients were used for analysis by Cancer Pathway Finder array and followed with real-time PCR.

Results
Analysis indicated up-regulation of 11 genes including KRT14, ALCY, MCM2, SKP2, STMN1, CDC20, SNAI2, MKI67, SLCA1, BCLL11, IGBP3 (P<0.05) suggesting altered regulation of cell cycle, cell senescence, apoptosis and hypoxia. Five years patient follow-up survival analysis indicated that SKP2, KRT14, FOXC2, Acly, PFG, OCLN, CDH2, LDHA, VEGFC, BCLL11, CA9 genes expression was significantly associated with survival of the patients.

Conclusion
Our data indicate that there is significant activation of several cellular pathways in tumor tissue that should be further investigated. Importantly, observed significant association between the expression of SKP2, KRT14, FOXC2, Acly, PFG, OCLN, CDH2, LDHA, VEGFC, BCLL11, CA9 and survival indicate that the level of the expression of these genes in tumor tissue may predict the survival of the patient.

Table 1: RT® Profiler™ PCR Array Human Cancer PathwayFinder™ (PAHS-0332 )

| Gene                | Exp(coef) | se(coef) | z   | Pr(>|z|) |
|---------------------|-----------|----------|-----|----------|
| KRT14               | 2.20E-01  | 4.97E-01 | 4.50E+00 | 1.45E+01 |
| FOXC2               | 1.70E+00  | 5.99E+00 | 2.14E-01 | 0.9602   |
| CDC20               | 6.58E-03  | 6.39E-01 | -2.843 | 0.0061   |
| SNAI2               | 3.68E+01  | 7.43E+00 | 0.9602  | 0.3334   |
| BCL2L11             | -9.25E-01 | 6.58E-03 | 0.402407 | 0.6897   |

Conclusions
1. Human Cancer PathwayFinder™ analysis in selected 5 patients indicated alterations of the expression level in 22 genes
2. Analysis of all 41 patients confirmed statistically significant changes of 10 genes only
3. Cox proportional hazard model showed that lack of statistical differences between normal and tumor tissue does not exclude the gene as a potential biomarker for patients recovery and tumor aggressiveness
4. Difference in the expression of SKP2 between normal and tumor tissue is associated with survival indicating the greater the expression in tumor tissue relative to normal tissue the higher is the risk of death
5. ETS2, cell senescence gene is negatively associated with survival- lower expression equal higher chance of death
6. Altered expression of KRT14, FOXC2, ALCY, PFG, OCLN, CDH2, LDHA, VEGFC, BCLL11 and CA9 predict survival

Acknowledgement
Research reported in this presentation is supported by National Institute on Aging of the National Institutes of Health under award number RO1AG033229.