Comments on "Transcriptional profiling of oral squamous cell carcinoma using formalin-fixed paraffin-embedded samples" by Saleh et al., Oral Oncol 46 (2010) 379-386 Reply

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Content:

Dear Editor,

We thank Rentoft and colleagues for commenting on our paper “Transcriptional profiling of oral squamous cell carcinoma using formalin-fixed paraffin-embedded samples”, and agreeing that formalin-fixed paraffin embedded (FFPE) tissue specimens can be used for gene expression studies using microarrays, to identify genes that are significantly involved in oral carcinogenesis. The similarities and high concordance between the study by Rentoft et al. [1] and ours [2] is comforting and clearly supports the use of FFPE tissues in such experiments. More importantly, these studies act as independent validation for one another and strongly suggests that genes that were found to be up- or down-regulated in oral squamous cell carcinoma (OSCC) do indeed play a role in these cancers and therefore warrant further investigation to determine their utility as biomarkers and therapeutic targets for OSCC. We wanted to point out however, that the similarities between these 2 studies are not completely unexpected despite previous reports highlighting that the concordance between microarray studies are hard to achieve [3]. The main disparities between datasets from microarray experiments have been attributed to the use of different microarray platforms and the heterogeneity of the tissue specimens that were used [4] and [5]. Indeed, many microarray studies reported for the head and neck, used tissues from several distinct areas which have been reported to be genetically heterogeneous, and associated with different aetiologies [6] and [7]. Given that both our studies used the DASL assay and tissues from the oral cavity (albeit from different sites-explained further below) the consistency of the genes that were identified should not come as a complete surprise. However, it is still intriguing that the similarities between these two studies were so close despite previous reports indicating that there are distinct differences between oral cancers associated with different aetiology [8] and [9], and reports describing the distinct genetic differences between subsites of the oral cavity [10], [11] and [12]. Our previous study describing the differences in gene-expression patterns between oral cancers associated with betel quid chewing and smoking demonstrated that despite the differences seen, genetic changes common to all the cancers were also observed suggesting that there are core events and pathways that are important regardless of the aetiology or site of the cancer [8]. Consistently, upon close examination of the genes that are most differentially expressed between our study and that of Rentoft et al. [1] 5 of the top 10 over-lapping genes most differentially expressed were matrix metalloproteinases, whilst other genes include IL-8, CXCL-9 and BCL2A1, genes that were consistently up-regulated in many other microarray studies of the head and neck independent of the subsites of cancer [8], [12], [13] and [14]. An unprecedented large overlap of genes between our study [2] and that of Rentoft and colleagues [1] may also be due to the smaller number of genes on

the arrays that were used in these studies (502 genes), and that these genes were pre-selected based on their involvement in cancer development, whereas the majority of previous studies used platforms consisting of larger arrays and hence could capture much more of the heterogeneity typically observed in cancers. More recently, Illumina launched its whole genome DASL assay and it would be interesting to see if the similarities between buccal and tongue cancers still prevails. In conclusion, increasing number studies including the 2 compared here, strongly supports the use of FFPE tissues for gene expression studies using microarrays. The development of new technologies and statistical methods that addresses the challenges associated with using FFPE tissues, combined with the clinical information available with these specimens, will indeed facilitate the identification and discovery of clinically relevant gene signatures and biomarkers and therapeutic targets to improve the management of cancers in general.

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