Analysis of driver gene mutations in oesophageal squamous cell carcinoma

Hendrina Shipanga, Denver Hendricks and M. Iqbal Parker

Division of Medical Biochemistry and Structural Biology, Department of Integrative Biomedical Sciences and IDM, Faculty of Health Sciences, University of Cape Town, South Africa.

Introduction: Oesophageal cancer is the sixth cause of cancer related deaths worldwide and over 80% of the Oesophageal Squamous cell carcinoma (OSCC) cases and deaths worldwide occur in less developed regions. Sub-Saharan Africa is one of the two high risk areas for OSCC. OSCC is the most common cancers in males and second most common in females in South Africa.

This study investigated driver gene mutations and potential biomarkers associated with OSCC in South African patients.

Methodology: Normal and tumour DNA were isolated from OSCC patient biopsies and subjected to Whole Genome Sequence (WGS) analysis to characterize OSCC mutations in South Africa. Non-synonymous mutations and indels identified were used to investigate the impact of genomic mutations in OSCC. Currently ongoing validation studies are being carried out and functional studies to investigate the biological role of the genes of interest in OSCC development.

Results: In addition to insertions and deletions (indels) and copy number variations (CNVs), WGS yielded a total of 173869 single nucleotide variations (SNVs) and 433 driver SNVs. Among the 28 genes identified to be significantly mutated were CDKN2A, TP53, PIK3CA, NFE2L2, FBXW7, KMT2D, KMT2C, FAT1, FAT2, NOTCH1, NOTCH3. CDKN2A mRNA was
not detected in OSCC cell lines investigated in this study. In biopsies, CDKN2A mRNA levels were significantly elevated in 5/15 tumour samples; and significantly downregulated in 5/15 tumour samples. PIK3CA was variably expressed among the cell lines while it was significantly higher in 10/15 tumour samples.

Discussion and conclusion: The results of this study are important because there is not much published information on the nature of the alterations associated with oesophageal cancer in Africa. These studies will have important implications for the diagnosis and treatment of oesophageal cancer in Africa.

References:

Ferlay, J., Soerjomataram, I., Dikshit, R., Eser, S., Mathers, C., Rebelo, M., Parkin, D. M., Forman, D., & Bray, F. (2015). Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. International Journal of Cancer, 136(5), E359-E386.

Parkin, D. M., Bray, F., Ferlay, J., & Pisani, P. (2005). Global cancer statistics, 2002. CA: ACancer Journal for Clinicians, 55(2), 74-108.

Keywords: Oesophageal Squamous Cell Carcinoma, driver gene mutations, OSCC,biomarkers, whole genome sequencing