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B-288 The Beginning of the End: AGO2 Protein Identified and Validated as a Novel Biomarker for Multi-cancer Diagnosis Through Bioinformatics Analysis and Immunoassay

A. Hashmi,[a] G. Hutvagner,[b] and S. Sidhu[c]
[a]University of Technology/NSW Health Pathology, Sydney, Australia
[b]University of Technology Sydney, Sydney, Australia
[c]Kollings Research Institute, Sydney, Australia

BACKGROUND: Despite significant progress in cancer research, the complexity and heterogeneity of the disease still pose major challenges to accurate diagnosis and effective treatment. Recent advancements in biomedical technologies have led to the identification of reliable potential cancer biomarkers. In this sense, the link between microRNAs (master regulators of gene expression) & cancer is well-established, but there has been little research on the microRNA machinery itself. We aim to investigate whether changes in the expression of genes & proteins involved in the miRNA pathway can be used for multi-cancer detection.

METHOD: We analyzed RNASeq data from the TCGA (The Cancer Genome Atlas) and GTEX (The Genotype-Tissue Expression) projects to compare the expression of core components in the miRNA biogenesis pathway, including AGO2, DGCR8, XPO5, RAN, DROSHA, DICER, and TARBP2, in normal and tumorous samples across 22 tissue types, including adrenocortical, AML, breast, colon, lung, liver, esophageal, prostate, pancreas, stomach, thyroid, rectum, uterus and ovarian cancer. We accessed and analyzed the TCGA and GTEx datasets using the UCSC Xena Browser. We also measured the protein concentrations of all these microRNA regulators in 15 normal adrenal cortex, 15 benign adenoma, and 15 adrenocortical cancer tissue homogenate samples using commercial ELISA kits. The Human Protein Argonaute-2 (EIF2C2) ELISA Kit-AE45910HU (Abebio-Co.Ltd) was used for the assay procedure, which was performed according to the manufacturer's instructions. Statistical analysis was performed using GraphPad Prism, Version 9 (GraphPad Software, CA, USA). A *P*-value of less than 0.05 was considered statistically significant.

RESULTS: Our RNASeq analysis results showed that among all microRNA regulators, AGO2 is most highly significantly over-expressed in samples derived from cancer patients compared with normal controls ($P < 0.05$). In addition, we analysed the protein expression of AGO2 in adrenocortical tissue homogenate samples. Our results demonstrated that the protein expression of AGO2 in adrenocortical carcinoma samples was significantly higher than in normal adrenal cortex and benign adrenocortical tumour samples ($P < 0.001$).

CONCLUSION: Our study highlights the potential role of Argonaute 2 protein (AGO2) in cancer development and progression. AGO2 is a key component of the RNA-induced silencing complex, which regulates gene expression. Our findings show that AGO2 is overexpressed in cancer samples compared to normal controls across a range of cancer types. This suggest that AGO2 could be used as a promising marker for the development of more accurate and specific methods for cancer diagnosis, in combination with other markers. Furthermore, the potential for using AGO2 protein expression in serum samples as a non-invasive diagnostic tool is a promising area for future research. This could be achieved through automated immunoassay, making it a practical diagnostic tool for use in routine clinical practice.