ImmunoTools *FlowISiAM* Award 2026

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Identification of Redox Biomarkers for Diagnosis, Prognosis, and Disease Monitoring in Head and Neck Cancer

Background

Head and neck cancer (HNC) encompasses a diverse group of malignancies arising from the epithelial lining of the oral cavity, pharynx, larynx, nasopharynx, and sinonasal tract. The majority of cases are histologically squamous cell carcinomas, representing a substantial global health burden, particularly in Southeast Asia. In Malaysia, HNC ranks among the three most prevalent cancers **[1, 2]**. Despite significant advances in surgery, radiotherapy, and chemotherapy, patient survival remains limited, largely due to late-stage presentation and high rates of recurrence. At present, reliable biomarkers for early detection, prognostic stratification, and disease monitoring are lacking **[3]**, underscoring a critical unmet need for minimally invasive strategies that accurately reflect tumour biology and disease progression.

The development and progression of HNC are strongly influenced by lifestyle, environmental, and viral factors. Chronic exposure to tobacco and alcohol induces genomic instability and mucosal damage, while viral infections, including Human papillomavirus and Epstein–Barr virus, contribute to subtype-specific pathogenesis **[4]**. These exposures drive persistent inflammation and oxidative stress within the tumour microenvironment, promoting DNA damage, metabolic reprogramming, and malignant transformation **[5]**.

Recent research highlights the potential of circulating biomarkers that capture tumour metabolism, apoptosis, and redox regulation. Transketolase-like protein 1 (TKTL1) reflects enhanced glycolytic metabolism characteristic of the "Warburg effect," supporting tumour proliferation and survival, whereas DNaseX (Apo10) indicates dysregulated apoptosis and the ability of malignant cells to evade programmed cell death **[6]**. Both biomarkers are detectable in circulating immune cells, offering a minimally invasive window into tumour biology. Circulating monocytes and macrophages, defined by CD14 and CD16, play pivotal roles in tumour–immune interactions, and changes in their distribution or activation reflect systemic inflammation and immune dysregulation **[7]**. Additional ROS-sensitive markers such as CD95, CD38, CD71, and CD56 capture oxidative stress–mediated functional alterations, providing an integrated view of tumour metabolism, apoptosis, and redox processes **[8-12]**.

This study aims to identify and characterise circulating biomarkers in HNC by exploring the interplay between redox balance, immune cell phenotypes, and tumour metabolic activity. By integrating metabolic, apoptotic, and ROS-sensitive immune markers, we aim to develop a novel, minimally invasive strategy to enhance early detection, refine prognostic stratification, and guide personalised therapeutic interventions. Establishing robust biomarker frameworks could transform clinical management and improve patient outcomes in HNC.

Experimental Design

Peripheral blood samples will be collected from HNC patients enrolled at **PKTAAB-USM** and analyzed using the *FlowISiAM* AT-test and ImmunoTools *AMANDUS-ReIMPACT* platform (Redox, Immune, Metabolic Profiling for Advanced Cancer Tracking). Ethical approval and written informed consent will be obtained prior the blood collection. Approximately 3 mL of whole blood will be collected in EDTA tubes longitudinally from two cohorts with complete

sampling sessions: (i) a pre-treatment cohort and (ii) a treatment cohort, with collections performed at pre-treatment, during treatment, and after treatment or at recurrence.

The *FlowISiAM* AT-test will quantify TKTL1 (glycolytic metabolism) and DNaseX (Apo10) (apoptosis dysregulation) in circulating monocytes and macrophages. Alterations in these biomarkers may indicate early metabolic reprogramming, malignant transformation, or imminent disease progression.

The ImmunoTools *AMANDUS-ReIMPACT* panel will characterise immune cell subsets and activation status using CD14, CD16, CD95, CD38, CD71 and CD56, with a focus on ROS-sensitive markers. Changes in these populations will reveal oxidative stress–driven immune dysregulation and tumour–immune interactions. Biomarker profiles will be correlated with clinical parameters, treatment response, and progression-free survival to identify predictive signatures of recurrence, therapy resistance, or poor prognosis.

Expected Outcomes

This study is expected to identify circulating biomarkers reflecting tumour metabolism, apoptosis, and oxidative stress in HNC and to characterise immune cell phenotypes linked to redox imbalance. The integration of these markers will enable the development of minimally invasive biomarker panels for early detection, prognostic stratification, and therapeutic monitoring. Ultimately, this framework has the potential to translate into clinical practice, guiding personalised interventions, anticipating disease progression, and improving the overall management and outcomes of patients with HNC.

Collaboration Plan

The studies will be conducted with collaborative support from ImmunoTools and partner INVIGATE. The collaboration will provide antibodies and reagents for establishing the *FlowISiAM* platform, together with technical training, protocol and know-how transfer, and guidance on biomarker-specific antibody selection. Partners will support assay development (e.g., *FlowISiAM* AT-test, ImmunoTools *AMANDUS-ReIMPACT* platform), data analysis, and integration into the ImmunoTools *FlowISiAM* network. This partnership aims to facilitate international research funding opportunities and the future development of HNC testing kits.

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ImmunoTools *FlowISiAM* AWARD for

Rabiatul Basria S. M. N. Mydin and **Muhamad Yusri Musa** includes

antibodies for *FlowISiAM*, know how transfer and protocol, support regarding selection of specific antibodies against some specific biomarkers from INVIGATE, engagement regarding development of specific *AMANDUS-ReIMPACT*, and expert assistance in evaluating the results obtained, and integration into the ImmunoTools *FlowISiAM* network.