POTENTIAL ANTIOXIDATIVE EFFECTS OF PLATINUM NANOPARTICLES IN HYDROGEN PEROXIDE TREATED HUMAN LUNG EPITHELIAL CELLS

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Oxidative stress plays an essential role in the normal regulation of various cellular physiological processes. It is known to contribute to the pathogenesis of lung cancer as the leading cause of cancer worldwide. While platinum-based chemotherapy has been the standard of care in advanced lung cancer, we hypothesised that platinum nanoparticles (PtNPs) can play a role in reversing oxidative stress in human A549 epithelial lung cell lines. Hydrogen peroxide (H$_2$O$_2$) induces oxidative stress in cells and the role of PtNPs was determined to lower the capacity in metabolising H$_2$O$_2$. The oxidative status was assessed through antioxidant enzyme activity and DNA damage was qualitatively and quantitatively measured through comet assay. Even though the antioxidant capacity of the PtNPs was found to be significantly lower than ascorbic acid through the ferric reducing antioxidant potential (FRAP) assay, the scavenging of free radical activity of PtNPs is still durable at high concentrations. PtNPs were found to be able to reduce H$_2$O$_2$-induced DNA damage significantly by increasing antioxidant enzyme activity such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAS). Hence, PtNPs could be a promising antioxidant in the treatment of oxidative stress-related conditions, specifically lung cancer.
CAN CLINICAL PREDICTIVE RULES REDUCE UNNECESSARY BLOOD CULTURES IN THE EMERGENCY DEPARTMENT?

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Due to the high mortality associated with bacteraemia, blood cultures are often ordered liberally contributing to increased costs and unnecessary exposure to antibiotics. Clinical predictive rules (CPRs) can guide clinicians in taking blood cultures such as the Systemic Inflammatory Response Syndrome (SIRS) criteria and Shapiro’s rule. Employing these rules may decrease blood cultures while retaining true positive cases of bacteraemia. Is SIRS criteria or a modified Shapiro’s rule better at reducing the number of blood cultures while retaining high sensitivity?

Retrospective study of electronic medical records of patients who had a blood culture taken at a Sydney tertiary emergency department from Jan to Dec 2020 was performed. The primary outcome was true bacteraemia, defined as a culture with pathological bacterial growth. Cultures were categorised as either true positives, contaminated or true negatives. Contaminated cultures were identified based on presence of contaminant organisms or if the treating team deemed the culture as contaminated. True positive patients were compared to a randomly selected control group of negatives in a 1:3 ratio. Clinical information from these patients was collected and then appraised against the CPRs.

For Jan to March 2020, 1,035 blood cultures were collected, of which 136 were true positive for bacteraemia, 11 were contaminated and the remainder negative. Of the true positives, 90 (90%) and 97 (97%) patients met SIRS criteria and Shapiro’s rule respectively and of the randomly selected 401 negative patients, 277 (69%) and 271 (67.5%). If the rules had been applied, 10 and 3 bacteraemic patients would have been missed using SIRS criteria and Shapiro’s rule respectively, while cultures collected from 123 and 129 patients would have been avoided.

The modified Shapiro’s rule is useful for determining blood culture collection as it has high sensitivity, avoiding unnecessary collection of blood cultures.
CANCER GENOMIC DATABASES ANALYSIS OF IKK ALPHA AS POTENTIAL TARGET FOR BREAST INVASIVE CARCINOMA

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Inhibitory-κB kinase (IKK) α has been characterised by its critical role in various major cellular processes including immunity, inflammation, and cancer as the key intermediate in nuclear factor-κB (NF-κB) signalling pathway. In recent breast cancer studies, IKKα was found to promote tumorigenesis and associated to worse survival outcome in specific breast cancer subtype when being highly expressed, representing an attractive therapeutic target or prognostic marker to be explored. CHUK is the gene that encodes IKKα. In this study, bioinformatics analysis was performed on the CHUK alteration rate, survival and expression on human cancer and breast invasive cancer in public available cancer genomic datasets and we also explored the potential hub gene that was correlated to the CHUK expression in breast invasive carcinoma.

cBioPortal for Cancer genomic, was used as the main data visualisation platform to identify the CHUK alteration and survival value. The Cancer Genome Atlas (TCGA) studies' datasets were selected for the coverage of population genomic profile in human cancer and breast cancer. Expression analysis and hub gene identification were done by manual data mining using Microsoft excel on raw TCGA dataset and mRNA and protein expression data of the differentially-expressed-gene (DEGs) based on CHUK mRNA expression.

CHUK gene alteration rate was 1.5% out of 10,953 samples in human cancer, and 1.1% of 996 samples in breast invasive carcinoma. The prognostic value of CHUK was not statistically significant in both. Significant upregulated CHUK expression was found in breast invasive carcinoma. A total of 21 and 15 potential hub genes based on mRNA and protein expression respectively were identified in this study.

To conclude, CHUK does not show prognostic value across the data in public cancer genomic datasets in human cancer and breast invasive carcinoma. This study provides a set of potential hub genes in breast invasive carcinoma correlated to CHUK expression.
CANCER GENOMIC DATABASES ANALYSIS OF IKK ALPHA AS POTENTIAL TARGET FOR LUNG ADENOCARCINOMA

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Lung Adenocarcinoma (LUAD) is one of the most prevalent cancer types in Malaysia and accounts for the most frequent cause of cancer-related death in the country. Different genes or proteins were found to have significant roles in promoting cancer cell growth of LUAD. Inhibitor-κB kinase α (IKKα) is one of the proteins which was found to play significant roles in tumor progression of LUAD. IKKα protein is encoded by CHUK. The research objectives were to investigate CHUK gene alteration and gene expression in LUAD and the association with clinicopathological characteristic of tumor.

The research was performed by conducting analysis using online cancer genomic database. The Cancer Genome Atlas (TCGA) database was used as a data source. The data were obtained from Genome Data Analysis Centre (GDAC) firehose and cBioPortal for cancer genomics.

Research results showed that the frequency of overall CHUK gene alteration in 32 TCGA cancer projects was only 1.5% whereas in LUAD-TCGA project it was 1.6%. The associations between CHUK alteration and survival outcomes of overall cancer and LUAD were not significant. The gene expression analysis showed CHUK gene expression was significantly upregulated in LUAD. However, its association with survival outcomes was not significant. The correlated differentially expressed mRNA/protein-encoded gene of other genes were ranked according to its Log₂ Fold-change difference and reviewed by current available literature. Most of the correlated genes were involved in the disease progression of LUAD.

The research found that the results supporting IKKα as potential target is limited. However, other differentially expressed genes that correlated with differentially expressed CHUK gene expression may serve as potential targets and require further validation by future research.