ANTIBACTERIAL ACTIVITY OF LOW BRANCHED ANIONIC BIOSURFACTANTS PREPARED FROM PALM KERNEL OIL DERIVED OCTYL-DECYL ALCOHOL

Jia Hui Chia¹, Siang Yin Lee², Dinesh Kumar Chellappan³, Li Li Chan⁴, Yun Khoon Liew⁵

¹Department of Pharmaceutical Chemistry, School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Technology and Engineering Division (BTK), RRIM Sungai Buloh Research Station, Malaysian Rubber Board (MRB), Sungai Buloh, 47000 Selangor, Malaysia
³Department of Life Sciences, School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
⁴Department of Pathology, School of Medicine, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nosocomial infections are one of the major causes of death and they are a significant burden for both patients and public health. Cross-infections through contaminated hands of healthcare personnel are the most common transmission route of nosocomial infections. The use of antibacterial coatings and synthetic surfactants as antibacterial agents has been adopted to inhibit bacteria colonisation and adhesion. In recent decades, biosurfactants have gained great interest as a sustainable and greener alternative in comparison with their synthetic analogues due to their appealing properties and eco-friendly characteristics. The aim of this study was to explore the antibacterial activity of two low branched anionic biosurfactants prepared from palm kernel oil derived octyl-decyl alcohol, AS Alc 1 and AS Alc 2 against various targeted bacteria. In this study, the antibacterial activity of AS Alc 1 and AS Alc 2 was screened on the targeted Gram-positive and Gram-negative bacteria. Characterisation of the low branched anionic biosurfactants by using Fourier-transform infrared spectroscopy revealed that the synthesised biosurfactants were of similar structure and they contained carbonyl group as indicated by the absorption peak at 1736 cm⁻¹ and hydroxyl group as indicated by the absorption peak at 3419 cm⁻¹ for AS Alc 1 and 3394 cm⁻¹ for AS Alc 2. Agar dilution susceptibility testing technique was employed to determine the antibacterial activity of the two biosurfactant samples. Results from this study showed that AS Alc 1 and AS Alc 2 slightly reduced the growth of Streptococcus mutans ATCC 25175 and Enterococcus faecalis ATCC 29212. At this stage, the findings are still inconclusive for the strength of both tested biosurfactants in reducing the growth of S. mutans and E. faecalis. However, this study indicates clear evidence that both biosurfactants lack of antibacterial activity against the tested Gram-negative bacteria.
IN SILICO INHIBITION OF SELECTED NATURAL COMPOUNDS AGAINST ATP CITRATE LYASE (ACLY) IN HUMAN BREAST CANCER CELL LINES

Vivian Chong, Shamala Salvamani
Division of Applied Biomedical Science and Biotechnology, School of Health Sciences, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Cancer imposes a serious burden on public health and the treatment and curing processes for cancer are still scientifically challenging. Breast cancer is the most common cancer in females in Malaysia, comprising of 32.9% of cancer cases in 2020. The most common treatment option for cancer is chemotherapy. However, this comes with side-effects like fatigue, hair loss and weakened immune system, disrupting patients’ quality of life. 80% of the total world’s population relies on herbal medicine for their primary health needs. Natural compounds possess anti-inflammatory, anti-metastatic, anti-proliferative, anti-angiogenic and anti-cancer properties in breast cancer, which are safe, effective, and economical. ATP citrate lyase (ACLY) is a cytosolic enzyme responsible for acetyl-CoA synthesis. Acetyl-CoA is involved in biosynthetic pathways, like lipogenesis, and acetylation reactions that modify proteins like histone acetylation. Researchers found that ACLY inactivation suppressed cancer viability and inhibited cancer growth. Hence, ACLY might be a potential biomarker and an effective therapeutic target for cancer. Can selected natural compounds inhibit enzyme ACLY in human breast cancer cells? This study aimed to identify potential inhibitors of metabolic enzyme ACLY via in silico docking.

The drug likeness of the natural compounds from Universal Natural Product Database (UNPD) was filtered based on the Lipinski’s Rule of Five. The crystal structure of the enzyme ACLY was obtained from Protein Data Bank (PDB ID: 3MWD). Virtual screening of compounds was done using AutoDock Vina via PyRx 0.8 software. The ADMET properties of the Hit compounds were then analysed.

A total of 17,150 drug like natural compounds were identified. Molecular docking and ADMET analysis are to be evaluated.

We hope to have new findings on the anti-metabolism and lipogenic regulated pathway of natural compounds on cancer cell line, and high potential in identification of natural substance as an anticancer agent or adjuvant in breast cancer therapies.
[PPD3]

IDARUBICIN EFFECTS ON CYTOTOXIC T-CELL (CTL)-RESISTANT NASOPHARYNGEAL CARCINOMA (NPC)

Hui Jun Pee¹, Chee Onn Leong¹,²
¹Department of Pharmacy, International Medical University, 126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University, 126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nasopharyngeal carcinoma (NPC) is the presence of malignant neoplasm of the epithelium in the mucosal lining of the nasopharynx where the tumours are located at the pharyngeal recess in the nasopharynx. Radiotherapy and chemotherapy are the main treatment for nasopharyngeal carcinoma (NPC), and with the addition of chemotherapy to radiotherapy, the overall survival rate is increased. The treatment of cytotoxic T-cell resistant NPC remains poor. Therefore, identifying a drug which could further reverse CTL-resistance is a promising therapeutic strategy for the novel therapies of NPC. Idarubicin is a semi-synthetic anthracycline analogue used to treat several human neoplasms. Anthracyclines, quinone-containing antibiotics, are widely used in anticancer chemotherapy for the treatment of solid tumours and haematological malignancies including lymphomas, acute lymphocytic as well as myelocytic leukaemia. Anthracyclines are cell cycle-nonspecific, produce free radicals and carry out the cytotoxic actions. Several mechanisms of anthracyclines exert antitumour effects, including intercalation between base pairs forming idarubicin-DNA complex that inhibit DNA biosynthesis, inhibition of topoisomerase II by stabilising the DNA-topoisomerase II complex and induction of apoptosis resulting in DNA damage. Polymerase activity will also be inhibited by idarubicin which will affect the regulation of gene expression, and DNA damage due to the production of free radicals. Whole genome-wide transcriptomic analysis was used to identify gene signature that is associated with CTL-resistant in C666 NPC cells. The purpose was to find out what are the drugs that can reverse or have a negative correlation with the gene signature. The CTL summary data of connectivity map were sorted from the lowest connectivity score to the highest. From the Connectivity Map, 20 drugs were found which have a connectivity score of less than or equal to -80. The drugs that have the negative score were chosen because negative score indicates the drug will reverse the CTL resistant NPC cells. Idarubicin has a score -87.47, which is one of the drugs which could be further investigated to reverse CTL-resistance.
[PPD4]

EFFECT OF RESVERATROL ON CYTOTOXIC T-CELL (CTL)-RESISTANT NASOPHARYNGEAL CARCINOMA (NPC)

Celestine Ang1, Chee Onn Leong1,2
1Department of Pharmacy, International Medical University,
126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
2Institute for Research, Development & Innovation, International Medical University,
126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Resveratrol (trans-3,4',5-trihydroxystilbene) is a natural polyphenolic phytoalexin that can be found in fruits such as grapes where it is synthesised in response to fungal infections and trauma. Studies had shown that resveratrol possesses cancer-chemo-preventive activity that inhibits the development and progression of cancer in several cancer types such as colorectal and breast cancers. This is achieved by enhancing the oxidation phosphorylation that increases the energy production mediated by mitochondria to reduce the release of free radicals into the healthy cells. In cancer cells, the function of their mitochondria is reduced, and the tumour cells rely on anaerobic glycolysis to generate energy. This research attempts to determine whether resveratrol is able to reverse the tumour-intrinsic immune resistance to CTL-mediated cytotoxicity in NPC cells. To identify the differentially regulated genes (DEGs), the cut-off points were set at log 2-fold change, where ≥ 2 as up-regulated genes and ≤ 2 as down-regulated genes. Based on the transcriptomic analysis, a total of 372 DEGs were identified where 70 are up-regulated and 302 are down-regulated genes in CTL-resistant cells. After performing connectivity map (Cmap) by inputting the list of CTL-resistant NPC genes into the database, a total of 20 drugs with negative connectivity score of ≤ -80 were discovered. Resveratrol was one of the 20 drugs discovered to possess the potential to reverse the CTL-resistant genes with connectivity score of -95.17. Hence, resveratrol could be further investigated to reverse the CTL-resistance as it could provide benefits for the intended population.
RAMAN IMAGE-GUIDED NANO-DRUG DELIVERY FOR PRECISE DIAGNOSIS AND TREATMENT OF RHEUMATOID ARTHRITIS

Bo Cao, Yongming Zhang, Zeyu Xiao
Department of Pharmacology and Chemical Biology, Institute of Medical Sciences, Shanghai Jiao Tong University School of Medicine, 280 South Chongqing Road, Shanghai, China, 200025

Rheumatoid arthritis (RA) is a chronic autoimmune disease that can lead to joint destruction and disability. Because of the unknown pathogenic mechanism, real-time detection of the pathological progression is still a significant challenge. Early recognition and treatment of RA is essential for achieving effective therapeutic outcome. As a high sensitivity optical imaging technique, Raman molecular imaging is a promising strategy for the effective diagnosis and treatment guidance of RA.

Herein, the first Raman technology-mediated innovative nanotherapeutic particle (MTX-PNPs) for RA was constructed for real-time disease course monitoring and efficient drug delivery therapy. Molecular B (found by our laboratory) is used to provide high-intensity Raman signals and enable early diagnostic imaging of RA, while MTX is a drug molecule for the treatment of RA. When RA develops, a large number of MMP2/9 enzymes will be secreted and aggregated in the corresponding joints. The drug molecules will be released through the response mechanism of the enzymes and peptides, thus completing the treatment of RA.

The MTX-PNPs were demonstrated to have strong Raman spectral signatures, good biocompatibility and excellent arthritis enrichment responsiveness. Remarkably, early experiments have successfully demonstrated that the nanoparticles enable real-time monitoring of inflammatory signals. Therefore, as the first application of Raman technology in RA, this real-time imaging strategy will bring new hope for RA treatment and therapeutic monitoring.
THE ROLE OF TENIPOSIDE IN KILLING CYTOTOXIC T-CELL RESISTANT NASOPHARYNGEAL CARCINOMA CELLS

Li Han Chang¹, Chee Onn Leong²

¹Faculty, Postgraduate and BioMed Science Research, International Medical University,
126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

²Institute for Research, Development & Innovation, International Medical University,
126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nasopharyngeal carcinoma (NPC) is the 4th most common cancer in Malaysia. The process of immune evasion and tumour microenvironment suppression plays a crucial role in causing the NPC cells to be inherently resistant to cytotoxic T-cell (CTL) and therefore resistant to conventional therapies. Teniposide was known to induce immunogenic cell death and enhance anti-tumour immune response. This study aimed to investigate whether teniposide is able to reverse the CTL-resistant and kill the NPC cells.

To identify the differentially regulated genes between C666 parental and CTL-resistant NPC cells, gene expression with log2 fold change ≥ 1 was considered as up-regulated genes while log2 fold change ≤ -1 was considered as down-regulated genes. Transcriptomic and gene expression data were overlayed onto Reactome analysis to assess the likelihood that the pathway is relevant to the study. The 372 differentially regulated genes were queried against the connectivity map (CMap) in CLUE data library, considering a connectivity score of less than – 80 as hits. Teniposide was screened across the panel of parental and CTL-resistant cell lines. The cell viability and half-maximal inhibitory concentration (IC50) of teniposide were investigated in both cell lines by using methyl thiazolyl tetrazolium (MTT) assay.

A total of 70 up-regulated genes and 302 down-regulated genes were identified. 7 pathways were found to be significant enriched in the pathway enrichment analysis, including interleukin and chemokine signalling. Connectivity mapping analysis with this signature of 372 genes identified 20 candidate compounds, including teniposide, with a negativity score of -89.86. Teniposide exhibited lower IC50 in the CTL-resistant cells in comparison with the parental cells. The results suggested that CTL-resistant cells were more sensitive to teniposide compared to the parental cells, with significant difference at 1.5 and 12.5 uM concentrations.

This study demonstrates the potential of teniposide as a therapeutic option against CTL-resistant nasopharyngeal cancer.
EFFECTS OF IRINOTECAN ON TARGETING TUMOUR-INTRINSIC IMMUNE RESISTANCE TO CYTOTOXIC T-CELL (CTL)-MEDIATED CYTOTOXICITY IN NASOPHARYNGEAL CARCINOMA (NPC)

Jing Yee Yim¹, Chee Onn Leong²

¹Faculty, Postgraduate and BioMed Science Research, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nasopharyngeal carcinoma is a rare cancer that occurs at the head and neck area, also known as an Epstein-Barr virus associated malignancy endemic in a few places throughout the world. Researchers have investigated the possibility of using the immune system to trigger an anti-tumor immune response. Tumors have been observed often poorly immunogenic for both humoral and T cell-mediated responses. Hence, there are many improvements in the study of the molecular biology and treatment of nasopharyngeal carcinoma. In these studies, irinotecan was used to further investigate whether it is able to reverse the Cytotoxic T-cell Lymphocytes resistance as designed for appropriate treatment towards nasopharyngeal carcinoma.

In these studies, differentially expressed genes were identified from the transcriptomic analysis based on the criteria where the value of Log2FC < -2 or > 2 and p-value <0.01 to get the specific hit candidates which could be used to further studies in the connectivity map. Therefore, to reverse the Cytotoxic T-cell Lymphocytes resistance, the connectivity score of the hit candidates was required to be less than -80. Besides that, methyl thiazolyl tetrazolium assay to determine cell viability was quantified spectrophotometrically at wavelength of 570 nm with the reference wavelength of 630 nm by using Tecan Infinite® F200 Microplate Reader and the half-maximal inhibitory concentration was obtained from the dose response curve.

Irinotecan was obtained based on the results of CLUE platform which had the connectivity score -83.01. The half maximal inhibitory concentration of irinotecan was determined by dose response curve with the value 2.909, as well as it had the p-value of 0.001 which fulfilled the criteria of P-value <0.05; hence it showed a significant difference in the Cytotoxic T-cell Lymphocytes resistant response.

Irinotecan exhibits anticancer properties in the reversing of CTL resistance of nasopharyngeal carcinoma.
[PPD8]

EFFECT OF AZACITIDINE ON CYTOTOXIC T-CELL (CTL)-RESISTANT NASOPHARYNGEAL CARCINOMA (NPC)

Charissa Cheah¹, Chee Onn Leong¹,²

¹Department of Pharmacy, School of Pharmacy, International Medical University, 126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University, 126 Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nasopharyngeal carcinoma (NPC) belongs to a type of head and neck cancer with poor survival rate. Conventional treatments available are chemotherapy and radiotherapy. However, several drawbacks are associated with the conventional treatments such as resistance developed and local recurrence of NPC. This review attempts to determine whether azacitidine is effective in reversing tumour-intrinsic immune resistance to CTL-mediated cytotoxicity in NPC cells. In identifying the differentially regulated genes (DEGs) between C666-1 parental and CTL-resistant cells, the cut-off point was based on log 2 fold change, where ≥ 2 as up-regulated genes and ≤ 2 as down-regulated genes. Based on the whole genome-wide transcriptomic analysis, there are a total of 372 DEGs, in which 70 are up-regulated genes and 302 are down-regulated genes in CTL-resistant cells. Then, the CTL-resistant cells were queried against the Connectivity Map (CMap), a database that has gene profiles of 20,000 compounds. The purpose was to identify the drug that had a negative connectivity score as a negative score indicates the drug is able to reverse CTL-resistant cells. From the CTL summary data, there were 20 drugs identified that were able to reverse CTL-resistant cells, in which they had a connectivity score of less than or equal to -80. As a result, azacitidine was chosen for our research because it has a score of -83.75.
THE ROLE OF ETOPOSIDE IN KILLING CYTOTOXIC T-CELL (CTL)-RESISTANT NASOPHARYNGEAL CARCINOMA (NPC) CELLS

Jia Hao Tan¹, Chee Onn Leong²

¹School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Nasopharyngeal carcinoma is endemic in Southeast Asia and is highly associated with persistent Epstein-Barr virus latent infection. Tumour promotes the formation of a highly immunosuppressive microenvironment which leads to cancer evasion from the host immune response. In the past two decades, Epstein-Barr virus specific cytotoxic T lymphocytes have successfully treated lymphoproliferative disorders. However, the recurrent nasopharyngeal carcinoma treatment becomes more challenging as it is resistant to upfront therapy. Most studies reported using a combination of etoposide to make cancer cells sensitive to apoptosis. Therefore, this study aimed to investigate whether etoposide can overcome cytotoxic T-lymphocytes resistance in nasopharyngeal carcinoma.

Connectivity Map computational drug repositioning algorithm was used to identify the candidate drugs which can potentially reverse the gene expression profile of cytotoxic T lymphocytes resistance. Drug candidates with significant negative connectivity scores (≤ -80) were further investigated. In addition, the up-regulated and down-regulated genes of cytotoxic T lymphocyte resistant nasopharyngeal carcinoma cells were put into the Reactome pathway database to perform pathway enrichment analysis. The screened candidate drug was used to treat both parental and cytotoxic T lymphocyte resistant cell lines. The cell viability of etoposide was investigated in both cell lines through the methyl thiazolyl tetrazolium assay. Lastly, Microsoft Excel was used to perform the statistical analysis and identify the half-maximal inhibition of etoposide.

A total of 70 up-regulated genes and 302 down-regulated genes were identified in cytotoxic T lymphocytes resistant nasopharyngeal carcinoma cells according to transcriptomic analysis. Based on Reactome pathway analysis, there are seven pathways which were significant enriched (p-value < 0.01) in cytotoxic T lymphocyte-resistant nasopharyngeal carcinoma. Etoposide is chosen for further investigation after comparing with other drug candidates as its connectivity score is -93.48. Etoposide exhibited lower half maximal inhibition in cytotoxic T lymphocyte-resistant cell lines.

Etoposide demonstrated potential killing properties against cytotoxic T lymphocyte-resistant nasopharyngeal carcinoma.
EXTRACTION OF CRUDE FLAVONOIDS FROM GREEN TEA LEAVES OF CAMELIA SINENSIS TO INVESTIGATE THEIR NEUROPROTECTIVE EFFECT COMPARED WITH PURE FLAVONOID, EGCG, BY MODIFYING GENE EXPRESSION IN PARKINSON’S DISEASE

Hiu Laam Christy Sit\(^1\), Zhao Yang\(^2\)
\(^1\)Faculty of Medicine, University of New South Wales, High St Kensington, NSW 2052, Australia
\(^2\)School of Chinese Medicine, Hong Kong Baptist University, 224 Waterloo Rd, Kowloon Tong, Hong Kong

The prevalence of neurodegenerative diseases, for instance Parkinson’s Disease (PD), has increased by more than 50% in the past five years. Pharmaceutical therapy-induced adverse effects remain unresolved, thus finding one has become a growing area of interest. Small molecules in ongoing clinical trials demonstrates promise. This project investigates on the extraction of crude flavonoids from green tea leaves with pure EGCG (a small molecule in green tea) as a control, to assess its anti-neuroinflammatory effects in Parkinson’s Disease.

A literature review and pilot study on extraction methods of flavonoids, importance of temperature in the degradation of flavonoids, decaffeination and the type of column chromatography were conducted. Combined extraction methods were used, with organic solvent extraction, reverse-phase column chromatography with AB-8 macroporous resin and ultrasound assistance. HPLC and NMR spectroscopy were used to detect the presence of flavonoids in the extracted green tea. The extracted flavonoids and pure EGCG sample (1µM, 10µM, 100µM) were used on \(\alpha\)-synuclein (key protein involved with PD pathology) stimulated RAW264.7 mice macrophage cells and put into qRT-PCR to detect the gene expression of IL-6, TNF-\(\alpha\) (pro-inflammatory cytokines) and IL-10 (anti-inflammatory cytokine).

It was concluded that EGCG was present in the crude extract in high amounts. However, the purity of flavonoids was low due to the lack of decaffeination and repetition of column chromatography. In the qRT-PCR, the pure EGCG sample suppressed the production of IL-6 and TNF-\(\alpha\) and increased IL-10 production, demonstrating that EGCG could have neuroprotective effects, in concordance with previous studies. The crude flavonoids extracted from green tea had anti-inflammatory effects at low concentrations (1µM), but the surge in gene expression at higher concentrations (10 and 100µM) suggested cytotoxicity. Likely explanations include low therapeutic working range of flavonoids, extract impurity and synergistic effects between flavonoids, which could point directions to future research.
CANCER GENOMIC DATABASES ANALYSIS OF IKK ALPHA AS POTENTIAL TARGET FOR KIDNEY RENAL CLEAR CELL CARCINOMA

Kerry Pui Yi Lee¹, Chee Onn Leong², Ling Wei Hii¹, Wei Meng Lim¹

¹School of Pharmacy, International Medical University,
126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University,
126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Kidney Renal Clear Cell Carcinoma (KIRC) is the most common type (75%) of kidney cancer with high mortality rate. CHUK (IKKα) is a homodimer complex and it is encoded by the CHUK gene. IKKα is mainly activated in the non-canonical pathway of NF-κB pathway. Studies have shown that the IKKα homodimer is mainly involved in cancer development. The aim of this novel study was to validate whether CHUK could be a potential target for pharmacological treatment approach in KIRC.

In this study, CHUK gene alteration, mRNA and protein expressions in all TCGA cancers and Kidney Renal Clear Cell Carcinoma (KIRC) were investigated by using the cBioPortal. Survival analysis between CHUK altered and unaltered groups was done using Kaplan Meier Survival curve. mRNA expression data of KIRC was extracted from Genome Data Analysis Centre (GDAC) Firehose database.

The alteration frequency of CHUK gene in all 32 types of TCGA cancers is 1.5%. No CHUK gene alteration was observed in KIRC. CHUK mRNA expression was found to be significantly downregulated in KIRC (Fold difference: 0.61, p-value: 9.10E-25). Patients with high CHUK expression in KIRC (CHUK: EXP>=1) have a better survival outcome, while patients with low CHUK expression in KIRC (CHUK: EXP<=-1) have a poorer survival outcome. It was observed that when CHUK expression is altered, other mRNA and proteins gene expressions are altered as well.

In summary, CHUK gene is not commonly altered in KIRC. All p-values of the survival outcomes of KIRC are not statistically significant (p>0.05). Findings showed that the alteration of CHUK in KIRC is not prominent. To date, the correlation of the over and under expression CHUK and other mRNA and protein genes in KIRC is not well established. Hence, the lack of supportive connect limits the use of CHUK as a molecular target in KIRC.
CANCER GENOMIC DATABASES ANALYSIS OF IKKa (INHIBITORY KAPPA B KINASE ALPHA) AS POTENTIAL TARGET FOR STOMACH ADENOCARCINOMA

Sin Wei Ng¹, Chee Onn Leong², Ling Wei Hii¹, Wei Meng Lim¹

¹School of Pharmacy, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia
²Institute for Research, Development & Innovation, International Medical University, 126, Jalan Jalil Perkasa 19, Bukit Jalil, 57000 Kuala Lumpur, Malaysia

Stomach cancer is one of the most common causes of cancer death worldwide in the past few years. 95% of stomach cancers are stomach adenocarcinoma. NF-κB pathway is found to be associated with the carcinogenesis of stomach cancer due to the regulation of chemokines, anti-apoptotic factors, growth factors, metalloproteinase and cell cycle regulators. IKKa which is encoded by the CHUK gene has been a novel drug target for cancer treatment due to its critical role in the NF-κB pathway. This study aimed to investigate the IKKa (CHUK) gene alteration and expression in 32 cancer types including stomach cancer. Survival analysis was analysed using the Kaplan-Meier curve and the difference between groups was compared using log-rank p-value. Data from cBioPortal was used to extract the genomic and clinical data of 32 cancer types. The mRNA expression data of the cancer was collected from the Genome Data Analysis Center (GDAC) Firehose platform. In the studies of 32 cancer types, 161 out of 10,953 (1%) patients had altered CHUK gene. The survival outcome for both the altered CHUK gene group and the unaltered group was not significantly different (log-rank p>0.05). Results showed 35 stomach adenocarcinoma patients had a higher CHUK gene expression in their tumour samples compared to their normal samples (fold difference = 1.32; p=0.0001). The survival analysis included 57% and 8% of stomach adenocarcinoma patients with a higher and lower CHUK gene expression respectively and their survival outcomes were not significantly different (log-rank p>0.05). The clinicopathological characteristics and the differentially expressed genes (DEGs) which correlated with CHUK gene expression were identified. In this study, IKKa was shown to be differently expressed in stomach adenocarcinoma but the impact of its expression in the patients' survival outcome was not substantiated. The clinicopathological characteristics and the DEGs showed the significance of the CHUK gene in cancer settings.