92. SELF-SAMPLING VERSUS PHYSICIAN SAMPLING FOR CERVICAL CANCER SCREENING; THE AGREEMENT OF CYTOLOGICAL DIAGNOSES

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Background: The major problem with cervical cancer screening in countries which have no organized national screening program for cervical cancer is sub-optimal participation. Implementation of self-sampling method may increase the participation of women to screen for cervical cancer.

Aims: To determine the agreement of cytological diagnoses made on samples collected by women themselves (self-sampling) versus cytological diagnoses made on samples collected by physicians (Physician sampling)

Methods: We invited women volunteers to undergo two procedures; cervical self-sampling using the Evalyn brush and physician scraping using Cervex brush. They women were shown a video presentation on how to take their own cervical samples before the procedure. The samples taken by physicians were taken as per routine testing (Gold Standard). All samples were subjected to Thin Prep monolayer smears. The diagnoses made were according to the Bethesda classification. The results from the two sampling methods were analysed and compared.

Results: A total of 367 women were recruited into the study. Thin Prep smears by physicians were better in terms of volume and variety of the cells seen. There is significant good agreement of the cytological diagnoses made on the samples from the two sampling methods with the Kappa value of 0.568 ($p=0.040$). The Thin Prep smears by self-sampling method were better in detecting microorganisms.

Conclusion: This study shows that samples taken by women themselves (self-sampling) and physicians sampling had good cytology agreement. Self-sampling could be the method of choice in countries in which the coverage of women attending clinics for screening for cervical cancer is poor.

93. INHIBITORY EFFECTS OF MALAYSIAN TUALANG HONEY AND AUSTRALIAN/NEW ZEALAND MANUKA HONEY IN MODULATING EXPERIMENTAL BREAST CANCERS INDUCED BY *N-METHYL-N-NITROSOUREA* (MNU): A COMPARATIVE STUDY

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Introduction: Several studies have shown that honey being rich in sugars, polyphenols and flavonoids exhibits anticancer properties. Most studies were done on cancer cell lines, only a few studies were done *in vivo*.

Aim: To study the inhibitory effects of Malaysian Tualang honey and Australian/New Zealand Manuka honey on

experimental breast cancers induced by carcinogen; *N-methyl-N-nitrosourea* (MNU) in rats.

Methods: Forty female Sprague-Dawley rats were randomly divided into 4 groups with 10 animals each ($n=10$); Group 1 did not receive MNU and did not receive honey (Negative Control); Group 2 received MNU but not honey (Positive Control). Groups 3 and 4 were fed orally with 1.0 g/kg body weight of Tualang and Manuka honeys daily from day 0 of the experimentation. Cancer induction using MNU was done on the 7th day and development of mammary cancer masses was charted. All rats in all groups were given rat chowder ad-lib. The rats in group 3 and 4 continued to receive honey until the 120th day when they were sacrificed. The tumors were harvested for gross and histopathological examinations.

Results: The total number of tumors developed in all groups was 72; 39 (control) + 22 (TH) and 11 (MH). The mean number of tumors developed per rat in groups 2, 3 and 4 was, 4 ± 1.56 , 3 ± 1.41 , and 2.66 ± 2.25 respectively. The groups 2, 3 and 4 showed mean tumor size 2.43 ± 2.75 , 0.88 ± 0.95 and 0.81 ± 1.29 cm³ respectively. The number and size of tumors developed in treatment was smaller compared to non-treated control group ($p<0.05$). Honeys were found to reduce the number of tumor masses, and tumor size. Histopathological grading revealed that majority of TH and MH treated group tumors were of grade 1 and 2; TH Grade 1=9/22 (40.90%), TH Grade 2=9/22 (40.90%), TH Grade 3=4/22 (18.18%); MH Grade 1=8/11 (72.72%), MH Grade 2=3/11 (27.27%), MH Grade 3=0/11 (0%) compared to the control; grade1=7/39 (17.94%), grade2=10/39 (25.64%), grade 3=22/39 (56.41%).

Conclusion: Tualang and Manuka honeys have an inhibitory effect on breast carcinogenesis in rats when given one week prior to tumor induction. Manuka honey seems more effective to modulate breast cancer carcinogenesis compared to Tualang honey.

94. TARGETED DISCOVERY AND VALIDATION OF PLASMA BIOMARKERS OF PARKINSON'S DISEASE

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Despite extensive research, an unmet need remains for protein biomarkers of Parkinson's disease (PD) in peripheral body fluids, especially blood, which is easily accessible clinically. The discovery of such biomarkers is challenging, however, due to the enormous complexity and huge dynamic range of human blood proteins, which are derived from nearly all organ systems, with those originating specifically from the central nervous system (CNS) being exceptionally low in abundance. In this investigation of a relatively large cohort (~300 subjects), selected reaction monitoring (SRM) assays (a targeted approach), were used to probe plasma peptides derived from glycoproteins previously found to be altered in the CNS based on PD diagnosis or severity. Next, the detected peptides were interrogated for their diagnostic sensitivity and specificity, as well as the correlation with PD severity as determined by the Unified Parkinson's Disease Rating Scale (UPDRS). The results revealed that 12 of the 50 candidate glycopeptides were reliably and consistently identified in plasma samples, with three of them displaying significant differences among diagnostic groups. A combination of four peptides (derived from PRNP, HSPG2, MEGF8, and NCAM1) provided an overall area under curve (AUC) of 0.753 (sensitivity: 90.4% and specificity: 50.0%). Additionally, combining

two peptides (derived from MEGF8 and ICAM1) yielded significant correlation with PD severity, i.e., UPDRS ($r=0.293$, $p=0.004$). The significance of these results are at least two-fold: (1) it is possible to use a targeted approach to identify otherwise very difficult to detect CNS related biomarkers in peripheral blood, and (2) the novel biomarkers, if validated in independent cohorts, can be employed to assist with clinical diagnosis of PD as well as monitoring disease progression

95. COMBINATION OF HPV E6/E7 AND HTERT MRNA REAL-TIME RT-PCR ASSAY FOR DIAGNOSING HIGH GRADE CERVICAL LESIONS AND MALIGNANCY

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Background: The Real-HPV-E6/E7 mRNA[®] multiplex RT-qPCR assay (M&D, Wonju, Republic of Korea) has been developed and evaluated. Human telomerase reverse transcriptase (hTERT) is also considered as complementary marker that may provide criteria in high grades of cervical lesions.

Aims: In this study, HPV E6/E7 oncogene and hTERT are detected by Real-HPV-E6/E7 mRNA[®] multiplex RT-qPCR and Real-hTERT mRNA[®] RT-qPCR assay (M&D), respectively.

Methods: A total of 545 patients including 18 squamous cell carcinoma, 21 HSIL, 17 ASC-H, 101 LSIL, 100 ASC-US, and 288 normal cytology samples, were enrolled and analyzed. 39 samples were confirmed in histological diagnosis.

Results: The positive rates of HPV E6/E7 mRNA RT-qPCR assay were 94.4%, 95.2%, 82.4%, 46.5%, 25.0%, and 1.1% in SCC, HSIL, ASC-H, ASC-US, LSIL, and normal samples, respectively. Relative hTERT mRNA expression levels were able to distinguish high grade and low grade of cervical lesion significantly ($p<0.001$). Notably, 5 high grades of cervical samples ($\geq$ HSIL) were not detected by HPV E6/E7 mRNA real-time RT-PCR assay, but those samples were high relative expression levels with hTERT mRNA real-time RT-PCR assay.

Conclusions: For predicting the outcomes of cervical intra-epithelial neoplasia (CIN) 1 or CIN 2 patients, the combined use of HPV E6/E7 and hTERT mRNA RT-qPCR assay could be a significantly complementary approach for diagnosing high grade cervical lesions because of the hTERT mRNA expression levels highly increased in cervical cancer and which was very low in low grade cervical lesions and normal tissues.

96. IMMUNOTACTOID GLOMERULOPATHY WITH IGM POSITIVITY AND ASSOCIATED IGM PARAPROTEIN

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Introduction: Fibrillary glomerulonephritis is characterised by the glomerular deposition of randomly arranged non branching fibrils which differ from amyloid fibrils in size (typically 16-24nm in diameter as compared with 7-10 nm for amyloid) and lack of reactivity with congo red histochemistry. Immunotactoid glomerulopathy, widely but not universally considered distinct from fibrillary glomerulonephritis, is distinguished by deposition of immunoglobulin organised as microtubules, which typically measure >30 nm diameter. The diagnosis of each relies on electron microscopic identification of the glomerular deposits.

Case report: A 77 year old woman was admitted for investigation of nephrotic syndrome (proteinuria 3.1 g/24 hours). A renal biopsy showed a mesangiocapillary glomerulonephritis, IgM positivity on direct immunofluorescence and lambda light chains, and trace positivity with C1q. There was no positivity with IgG, IgA, C3 and kappa light chains. Electron microscopy showed glomerular deposition of microtubules with a diameter of 34 nm. She was found to have an IgM lambda paraprotein and diagnosed with IgM MGUS.

Discussion: Immunotactoid glomerulopathy is a rare entity occurring one tenth as frequently as fibrillary glomerulonephritis,¹ tends to occur in older patients, who typically present with nephrotic syndrome, and is often secondary to an underlying cause such as a lymphoplasma-cytic disorder. The most common light microscopic pattern is mesangiocapillary, and direct immunofluorescence is typically positive for IgG, with variable positivity of the other immunoreactants. As seen in our case, IgM positivity is unusual, and is not reported without concurrent IgG positivity.

Reference

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97. CONGENITAL PULMONARY AIRWAY MALFORMATION – A STUDY OF 2 CASES

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Introduction: Congenital pulmonary airway malformation (CPAM) or also called congenital cystic adenomatoid malformation (CCAM) is a rare developmental anomaly occurring in early childhood by the age of 2 years. It is associated with stillbirth and neonatal distress. There are 5 subtypes which have been described of which type 1 and 2 are the most common. We present two cases of CPAM.

Case 1: A 5 month old baby was brought to the pediatric outpatient with complaints of noisy breathing and failure to gain weight. Contrast enhanced computed tomography (CECT) revealed congenital cystic adenomatoid malformation - type II of the left lung. Left thoracotomy with left lower lobectomy performed under general anaesthesia. Grossly, the specimen showed solid areas and cystic spaces filled with papillary excrescences. Microscopy revealed dilated cystic spaces lined by a layer of cuboidal cells filled with papillae composed of