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**PO-435** **PROTEOMIC CLASSIFICATION OF TRIPLE NEGATIVE BREAST CANCERS**

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**Introduction** Triple negative (TN) breast cancer is an aggressive form of breast cancer for which no targeted treatment currently exists. The identification of potential therapeutic targets is hampered by the heterogeneity observed among TN breast cancer tumours. The aim of the present study is therefore to classify TN cancer. Earlier studies have classified TN breast cancers mainly based on transcriptomic and genomic data. Proteins play a major role in cellular functions and could give important clues for therapeutic development. The originality of this work was therefore<sup>1</sup> the use of proteomic data for the classification and<sup>2</sup> taking into account protein variability in the classification. This enabled us to study not only the protein expression, but also protein activation, by analysing protein phosphorylation.

**Material and methods** We analysed two datasets of TN breast cancer samples that were both part of the Rational Therapy for Breast Cancer (RATHER) consortium (www.ratherproject.com). First, TN breast cancer tumour samples collected from patients in the Netherlands Cancer Institute (NKI), Amsterdam (n=64). Second, TN breast cancer tumour samples collected from patients at the Addenbrooke's Hospital, Cambridge, UK (n=31). Protein expression was measured for 116 proteins using Reverse Phase Protein Arrays. The NKI dataset served as the training set and the Cambridge dataset served as the validation set. Unsupervised classification methods were applied to the training set and differential analyses for the identified groups were applied at protein, transcriptome and clinical levels.

**Results and discussions** Two TN groups were identified in the training set. Each group was characterised by a specific set of proteins. The groups were robust to protein subsampling, *i.e.* they did not change if a part of the proteins were removed from the analysis. Importantly, the same two groups were found in the validation set, confirming the biological relevance of the two groups. Eighteen proteins were found to be crucial for identifying the two groups. Among these 18 proteins, eight were phosphorylated (*i.e.* 45%, compared to 32% in the original dataset).

**Conclusion** Our results stress out the importance of including proteomic data in TN breast cancer classifications. In order to better understand the underlying molecular mechanism in TN breast cancer, we now plan to study the relations between genomic, transcriptomic and proteomic data for the two identified TN groups.

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**PO-436** **DOSE-DEPENDENT RELATIONSHIP BETWEEN METFORMIN AND THE OCCURRENCE OF COLORECTAL CANCER AMONG TAIWANESE PATIENTS WITH TYPE 2 DIABETES**

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**Introduction** Increasing evidence suggests that metformin may be beneficial in the primary prevention of colorectal cancer (CRC) and a dose-response relationship has been reported. However, a long-term epidemiologic observation between treatment period, cumulative dose, and intensity of metformin and CRC is rarely reported. The aim of this study is

**Material and methods** The dataset used for this nationwide population-based study is a cohort of 1,000,000 subjects randomly sampled from individuals enrolled in the Taiwan National Health Insurance system. The subjects with newly diagnosed type 2 diabetes mellitus (DM) between 1997 and 2007 were enrolled. A statistical algorithm, including the demographic data, treatment period, cumulative dose and intensity of metformin use, was compared between patients developing CRC and those without CRC.

**Results and discussions** 47 597 subjects were included in this study. The mean follow-time was 7.17±3.21 years. After adjustment, the utilisation of metformin was an independent protecting factor of CRC development (p<0.001). Although the protecting ability of for CRC development reduced during long-term therapy, the risk of developing CRC decreased progressively with either the higher cumulative dose or the higher intensity of metformin use (both p<0.001).

**Conclusion** This study revealed that the use of metformin significantly decreased the risk of CRC development in a dose-dependent manner in patients with type 2 DM in Taiwanese population. However, a gradual decline in medication adherence may reduce the protecting ability of metformin for CRC development during long-term therapy.

**PO-437** **DRUG AND RADIO SENSITIVITY PROFILE OF A PRIMARY CTC CELL LINE DERIVED FROM A PATIENT WITH METASTATIC NEUROENDOCRINE TUMOUR OF THE DISTAL OESOPHAGUS**

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**Introduction** Circulating Tumour Cells (CTCs) are important biomarkers in many solid tumours including gastroesophageal cancer. Cultures derived from CTCs provide many potential benefits, including an *in vitro* model to assist selection of systemic treatment for personalised treatments. This study aimed to determine the sensitivity of a CTC derived primary culture to commonly used chemotherapeutics and radiation.

**Material and methods** RFCTC is the first described long term primary CTC culture derived from a patient with a metastatic, high-grade neuroendocrine tumour of the distal oesophagus. The *in vitro* chemo sensitivity of RFCTC to 7 different cytotoxic drugs alone and in fixed ratio dose combination was determined using standard cell proliferation assays, and reported as IC<sub>50</sub> ±SD or Combination Indices (CI) as determined using median-effect analysis (CalcuSyn software, Biosoft, UK). The sensitivity of the cells to radiation with drug pretreatment was also investigated using clonogenic survival as the radiobiological endpoint. Cells were exposed to 2 Gy X-