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Differential expression of KLF1 in family studies and their role in globin gene switching

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Introduction: Kruppel like factor 1 (KLF1) also known as the 'Master regulator of erythropoiesis' is located on the short arm of chromosome KLF1 activates a diverse set of genes that have an important role in the regulation of key pathways such as erythropoiesis, cell membrane and cytoskeleton. To date over 65 molecular variants have been recorded. Their haematological phenotypes range from the clinically unremarkable In(Lu) type of Lu(a-b-) blood group, variability in the HbA2 levels, congenital dyserythropoietic anaemia (CDA) and in most extreme cases hydrops foetalis secondary to profound anaemia. In 2010 sequencing revealed a nonsense mutation in KLF1 in a large Maltese family with hereditary persistence of foetal haemoglobin (HPFH). The p.K288X mutation was found to ablate the DNA binding domain of the key erythroid transcription factor.

Methods: We explored the occurrence of additional KLF1 mutations with genotype – phenotype associations among a large number of cases, all from Malta with a borderline HbA2 but without ? globin gene mutations and other ? thalassaemia heterozygotes from the Malta Biobank and the Thalassaemia Clinic. Sequencing of the KLF1 gene was carried out. To study the promoter mutations in the KLF1 gene Dual- Luciferase reporter assays were performed on HEK293T cells and K562 cells transfected with the pGL4.10 vector containing either the wildtype promoter or the mutant promoter. This was followed by Electromobility Shift assays.

Results: Four-hundred and twenty six subjects were collected. After sequencing of the KLF1 gene we identified 5 other families with the p.K288X mutation together with other nucleotide variants, six of which were in the KLF1 promoter. In both cell lines dual-luciferase assays showed a statistically significant difference between cells transfected with the wildtype KLF1 promoter and cells transfected with 7 different KLF1 promoter mutations. Electrophoretic Mobility Shift Assays on nuclear extracts further show DNA:Protein binding evidence and are currently being investigated

Conclusion: This data further highlights the importance of KLF1 function in globin gene control and demonstrate the importance of KLF1 sequencing in patients with haematological features resembling ?-thalassaemia

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Surviving with cancer and thromboembolism

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Introduction: The aim of the study was to calculate the mortality rate of adult patients with solid malignancies receiving chemotherapy on an in-patient and out-patient basis at Sir Anthony Mamo Oncology Centre (SAMOC). The prevalence of thromboembolic events in these patients was studied and the effect on the mortality rate was analysed.

Methods: Study population included all 414 patients who were reviewed for treatment administration at SAMOC during the first three weeks of August 2017. Patient electronic and paper records were reviewed from date of cancer diagnosis to the third week of August 2017 to look for thromboembolic events. The number of deceased patients by 20th July 2018 was documented.

Results: 30.4% (n = 126) of patients investigated were deceased by the end of study, 27.0% (n=34) of whom were dead within 1 year of cancer diagnosis. 55.6% (n=69) were deceased within 2 years of diagnosis, while 88.9% (n=112) were dead within 5 years of diagnosis. 14.0% (n=58) of patients recruited developed a thromboembolic event, 15.5% (n=9) of whom had multiple events. 65.5% of these patients (n=38) developed a thromboembolic event within 1 year of diagnosis. More than half of patients (55.3% i.e. 21 out of 38 patients) who developed a thromboembolic event within one year of diagnosis were dead by the end of the study.

Conclusion: This study highlights the increased mortality rate associated with thromboembolism in the setting of solid malignancies.

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The use of neoadjuvant chemoradiotherapy in rectal cancer - a local experience

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Introduction: Neoadjuvant chemoradiotherapy (CRT) is the standard treatment for locally advanced rectal cancer (LARC). It has been shown to improve tumour resection rate and reduce local recurrence rate.

Methods: The number of patients diagnosed with LARC and treated with neoadjuvant CRT between 2012 and 2017 were identified through the Radiotherapy Department. Patients who were treated with neoadjuvant short course RT were excluded. Demographic and clinical data was collected. The TNM classification (7th edition) was used to stage the cohort. Risk stratification was done according to the European Society for Medical Oncology (ESMO) guidelines for rectal cancer published in 2017. The Rectal Cancer Regression Grade (RCRG) was used to classify histological response. RCRG 1 and 2 were