no cessation instructions. Ten patients with mechanical valves (90.9%) knew about possible pre-operative heparinisation. Thirty-four patients (70.8%) with other indications were aware of possibly stopping warfarin pre-operatively. Around 62.7%, 76.7% and 52.5% knew about interactions with food, alcohol and other medicines respectively. Only 40.6% of respondents were aware of potential bleeding with concomitant use of non-steroidal anti-inflammatory drugs. In cases of significant blood loss, 16.9% of patients were not aware that they need to seek medical help. Four women started warfarin at an age less than 55 – three had not been informed of the potential teratogenicity. Regular bloodletting disrupted patients' life in 32.2% of cases. Thirty-four patients without mechanical valves consider switching to direct oral anticoagulants, but only seven accepted the current prices. Most patients learnt about warfarin from doctors (69.5%).

Conclusion: Some lacunae in patients' knowledge exist regarding drug interactions, risk of bleeding with NSAIDs, and teratogenicity. Patient education can improve, but the various possible ways to address this need to be evaluated.

P8.24

Colorectal screening: will raising the "positive test" cut-off decrease cancer pickup?

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Introduction: Colorectal cancer is one of the most prevalent carcinoma in Malta, which can be successfully treated if detected in its early stages. In 2012, a screening program was introduced, making a percentage of the Maltese population (aged 60-64), eligible to undergo colo-rectal screening. Out of the total population eligible, the uptake is low at 20%. A faecal immunochemical test (FIT) level of more than 100µg Hb/g faeces is considered positive and subjects are then referred for Colonoscopy; with findings varying from polyps, neoplasia or benign pathology to normal. This is a retrospective study looking into the local scenario to see whether the FIT level correlates with specific pathology and to investigate whether raising the cut-off level for FIT to 600µg Hb/g faeces would be safe. Data collected by the CRCS unit was analysed for the study period. Out of a total of 16,563 FIT tests carried out in 2017, 24 cohorts where diagnosed with colorectal carcinoma, out of which, 9 cohorts had FIT levels of less than 600µg Hb/g faeces. This study determined that raising the cut-off level to 600µg Hb/g faeces would have missed almost 40% of cancers as well as 25% percent of high grade dysplastic polyps in this cohort.

Conclusion: In conclusion this study confirms that while FIT is a useful test to identify subjects that might be harbouring colorectal cancer in the general population as means of a screening test, it is not very specific. Hence, raising the cut off level would significantly reduce the sensitivity of this test.

P8.25

The role of *FLVCR1* isoforms on inter-erythrocytic distribution of human foetal haemoglobin

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Introduction: We sought to expand the genetic repertoire underlying the developmental switching of gto bglobin genes with haematological and molecular exploration among two families from Malta with the *KLF1* p. K288X truncation. The data revealed competitive inter-play between KLF1 and FLVCR1 isoforms on BCL11A that acted on the inter-erythrocytic distribution of Hb F among F-Erythrocytes, the MC-HbF of adults.

Methods: HbF concentration, expressed as the percentage of total haemoglobin was determined with the Bio-Rad VARIANT™ Haemoglobin Testing System (Bio-Rad Laboratories, California, USA). F-Erythrocytes were quantified by flow cytometry on a BD FACSCalibur™ cytometer (Becton Dickinson Biosciences, California, USA) The cMC-Hb.F was confirmed by semi-automated quantitative imaging immuno-cytometry (qMC-Hb.F) that gave a mean value of 6.2 pg ranging from 3.0 to 9.8 pg in the KLF1± heterozygotes. Human erythroid progenitor cells (HEPs) were cultured from samples of ten family members and allowed to differentiate for two days. Cells were classified morphologically by microscopy and counted with an electronic cell counter (CASY-1, Schärfe System). Lentiviral transfection of buffy coat HEPs was conducted using clones obtained from The RNAi Consortium (Sigma-Aldrich, St.Louis)

Results: The two families from Malta segregated a unique truncation mutation of the *KLF1* locus such that the protein product was inactivated and expressed HbF over a broad range of 230 - 2480 mg/dL in peripheral blood. Non-linearity between the HbF (mg/dL) and the F-Erythrocyte numbers ($N.10^{12}$/dL) suggested independent gene control of the inter-erythrocytic distribution of the HbF calculated as the Mean Corpuscular HbF or cMC-HbF (0 – 9.2 pg) The cMC-HbF correlated well with direct immune-cytometric quantification (qMC-HbF) Bio-Informatic studies with exome sequences from both families revealed a strong connection between the cMC-HbF and a new mutation in *FLVCR1* (p.F473L; SIFT -5.37; Polyphen 0.029). *FLVCR1* is a known Haeme transporter producing two isoforms. FLVCR1a is plasma membrane bound and FLVCR1b is bound to the mitochondrial membrane. *In vitro* transcriptomics and knockdowns

showed that the *FLVCR1* mutation decreased the output of BCL11A independent of KLF1 and it shifted the relative amounts of the two isoforms with increasing cMC-HbF.

Conclusion: The interplay between the two FLVCR1 iso-forms could regulate intra-cellular concentration of Haeme and the total rate of translation with differential effects on specific messengers depending on the strength of the translation initiation complex. These data widen the understanding of globin gene switching and the possibilities of therapeutic intervention to increase Hb F levels in human haemoglobinopathies through alternative pathways.

P8.26

Cancer incidence and annual mean exposure to PM10: the case of Malta

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Introduction: Air pollution is a risk factor for several pathologies and of concern for Public Health. Predictions for its future projections in various localities provide no halcyon scenarios. Particulate Matter with a diameter 2.5 - 10 μm (PM10) has been associated with increased pulmonary, cardiovascular, cancer mortality and morbidity. However, from the plethora of other air pollution agents, whether PM10 could be utilized as an outdoor air pollution (OAP) indicator that could possibly contribute to the onset of cancer (Ca) is less clear. The current study aimed to evaluate the effects of annual average PM10 concentration on overall Ca incidence and on specific other types of Ca incidence for the inhabitants of the Maltese islands.

Methods: The database of PM10 annual average concentration for the islands of Malta from the European Environmental Agency (EEA, European Union, 2018 was utilized. Data for the years 2007, 2008, 2009, 2010, 2011, 2012, 2013, 2014, 2015 was obtained. The PM10 annual average concentrations comprised contributions from urban traffic, Sahara dust and sea salt trapping, all within the sea breeze phenomenon system. Population data was sourced from the EUROSTAT Statistics Database (EUROSTAT, © European Union, 2018) for the years 2000-2015. Data on Ca Incidence was extracted from the European Cancer Information System (ECIS - European Cancer Information System, European Union, 2018). The years available were 2000, 2001, 2002, 2003, 2004, 2005, 2006, 2007, 2008, 2009, 2010, 2011, 2012, and 2013. Data on incidence for Lung Ca, Non-Hodgkin Lymphoma, Hodgkin Lymphoma, Leukemia, Breast Ca in females and Lymphocytic Leukemia was obtained. We had the World Age Standardized Rates ASR (W) for the population, by gender. The initial analysis involved eyeballing of trends in Ca incidence and PM10 annual average levels in Malta. There seemed to be a rise in PM10 concentration corresponding to rises in Ca incidence overall and lung Ca incidence specifically. In order to formally test for correlation between PM10 annual mean concentration and Ca incidence, analysis of Ca incidence data in relation to PM10 was carried out using the Spearman correlation test on SPSS v.24. Analysis was repeated with a time delay for 0, 1, 2, 3, 4 and 5 years.

Results: This study showed that exposure to PM10 alone was linked to a rise in Ca incidence, particularly for haematological Ca. Furthermore, this was evident with specific time lag.

Conclusion: These findings support the hypothesis that PM10 may be linked to the onset of Ca, possibly by suppressing immune response systems, indicating a possible new role for pollution exposure in Ca and/or disease susceptibility. However, the immune system has complex and multifunctional defense mechanisms and more work needs to be done to assess the significance of this finding. This study suggests that air pollution is an important research area for health outcomes that should be investigated furthermore.

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P8.27

Leucocyte and platelet activation in patients with *BCR-ABL* negative myeloproliferative disorders

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Introduction: Polycythaemia vera, essential thrombocythaemia and primary myelofibrosis are BCR-ABL negative myeloproliferative disorders characterised by the overproduction of mature blood cells. MPD patients have a high risk of suffering from thrombotic episodes, the pathogenesis of which is thought to arise in part from the overproduction and overactivation of blood cells.

Methods: Flow cytometry was used to assess the degree of platelet, neutrophil and monocyte activation using the activation markers P-selectin, leucocyte alkaline phosphatase and CD11b. The microparticle (MP) procoagulant activity was quantified using a functional enzyme linked immunosorbent assay. Several parameters were also extracted from a complete blood count.

Results: P-selectin, LAP, MP activity and all CBC parameters investigated except for the monocyte count were higher in MPD patients than in controls. PV patients had increased monocyte CD11b when compared to ET patients, as observed in *JAK2*+ patients when compared to *JAK2*-. The MP procoagulant activity was higher in patients taking aspirin only when compared with patients taking cytoreductive therapy with aspirin. The MP procoagulant activity was also significantly higher in intermediate-risk ET patients than in high-risk ET patients.

Conclusion: MPD patients have increased production and activation of leucocytes and platelets when compared to controls; this could possibly play a role in the increased thrombotic risk. PV and *JAK2*+ patients had increased monocyte activation when compared to ET and *JAK2*-