establish links between molecular subtypes of AML and responsiveness to identified cell differentiating therapies.

**Material and methods** Our approach is to explore drug-induced cell differentiation in primary samples from AML patients and genetically engineered AML mouse models using high-throughput flow cytometry. Specifically, we characterise samples by their expressed cell differentiation-related cell surface markers with and without drug treatment to identify compounds capable of inducing cell differentiation *ex vivo*. The primary AML patient samples are also profiled by exome- and RNA-sequencing.

**Results and discussion** Preliminary results with a Flt3/Npm1 – mutated mouse model suggest that several compounds elicit cell differentiation-state specific responses, some of which could be indicative of a dynamic shift towards cell differentiation. For example, treatment with mTOR-kinase inhibitors sapanisertib and vistusertib resulted in a concentration dependence. For example, treatment with mTOR-kinase inhibitors sapanisertib and vistusertib resulted in a concentration dependent increase of differentiating cells marked by CD11b expression and decrease of stem cells marked by CD34 expression.

**Conclusion** We have established a high-throughput flow cytometric screening platform to identify drugs that are able to induce differentiation in primary AML samples and genetically engineered mouse models of AML. By integrating drug response data with genetic background information from samples we aim to reveal novel genotype-phenotype relationships in the level of cell differentiation that could eventually be translated into clinically relevant biomarkers and treatment options for AML patients.
Results and discussions We corroborate that CMS1 and CMS4 subtypes showed higher levels of immune and stromal infiltration than CMS2-3 subtypes. Several CD molecules have been found to be under-expressed in tumour vs. normal tissues that have a protective effect. Interestingly, when stratifying by subtypes, they showed the better accuracy discriminating between good and poor prognosis patients in the CMS4 subtype. Significant functions associated with higher expression of those molecules are IGA production, IL12 pathway, TCR pathway and PD1 signalling among others; thus suggesting an immune modulation of the microenvironment that leads to a better prognosis.

Conclusion The CMS4 subtype has usually higher risk of relapse compared to other subtypes. However, segregating the group using specific immune biomarkers is able to identify patients with the significantly better survival.

PO-517 PROTEIN PROFILING IN COLORECTAL CANCER: FROM BIOLOGICAL MAPPING TO FUNCTIONAL VALIDATION

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Introduction Colorectal cancer (CRC) is one of the most prevalent malignancies and contributes to significant cancer-related deaths worldwide. Despite commonly asymptomatic with 5 year survival rate of 90% at the early stage of disease, extremely low survival rate was reported for late stage diagnosis with metastasis. Therefore, there is an immense urgency for reliable biomarkers to aid in the early diagnosis of CRC and to assist in prognostic stratification. Interrogation on the serum proteome and site-specific secretome may provide an accurate mapping of the circulating and secreted proteins, respectively. Thus, we aim to identify potential protein markers present in human serum, faecal extracts and CRC cells, and to determine its role in CRC.

Material and methods Quantitative proteomics was performed using SWATH-MS analysis on human serum and faecal extracts representing 4 stages of CRC and healthy control. Immuno Blot was conducted to confirm the expression of target proteins in the cell line model for cell manipulation study. Transduction of lentiviral fully sequenced human open reading frames (ORFs) construct into HT29 was carried out with 25 µg/ml Blasticidin S selection for exogenous gene overexpression. Cell-based assays were performed to evaluate the functional activities and RqPCR for determining the signalling pathway activity.

Results and discussions We have identified significant upregulation of LRG1 in the sera of CRC patients, particularly in the advanced stage of cancer. The endogenous expression of LRG1 in the CRC cells increased with the advancing stage. Overexpression of LRG1 in HT29 increased cell proliferation by activation of Ki67 mRNA (p<0.01) and cell migration via ZEB1 (p<0.05). The level of TGF-β mRNA was also increased with overexpression of LRG1 (p<0.05).

Conclusion In conclusion, LRG1 is a promising marker for CRC and its overexpression may pose higher risk of metastasis via collective proliferation, migration and invasion possibly through the regulation of TGF-β pathway.