locally advanced/operable pts undergoing neoadjuvant T+D, pCR occurred more frequently in pts with a baseline HSP90 score of 3+, as compared to 2+ and 1+ (50.0% vs. 14.3% vs. none, p=0.05). These results suggest the possibility to classify HER2-positive pts into HSP90 defined subgroups and elaborate specific therapeutic strategies.

**Conclusion** Preclinical data indicate that constitutive HER2 activation induces HSP90 expression and HSP90 modulation influences the functional response to combined treatment. Baseline HSP90 expression may potentially represent a prerequisite of pharmacological response in HER2-addicted BC.

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**PO-503**

THE COHESIN STROMAL ANTIGEN 1 (SA-1) MODULATES COLONIC AND COLORECTAL CANCER (CRC) STEM CELLS: MECHANISM FOR RACIAL DISPARITIES

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**Introduction** CRC disproportionately impacts African-Americans (incidence and mortality increased by ~25% and ~50%, respectively). While mechanisms remain unclear, Vogelstein posited that the number of stem cell divisions determine CRC risk *Science* 2015. CRC stem cells may impact mortality via chemoresistance. LGR5, aldehyde dehydrogenase (ALDH1a3) and DCAMKL1 are markers of both intestinal and CRC stem cells. We have noted loss of SA-1 (a chromatin remodeler) occurred during colonic field carcinogenesis was markedly accentuated in Blacks (*Cancer Prev Res* 2016) via specific SNPs (*Neoplasia* 2018). SA-1 loss was also associated with poorer CRC prognosis. We hypothesised that SA-1 loss leads to stem cell induction and hence CRC disparities.

**Material and methods** Rectal biopsies were obtained from endoscopically normal mucosa from ~200 patients undergoing screening colonoscopy with an IRB approved protocol. SA-1 was assessed by RT-PCR normalised to β-actin. We modulated SA-1 in human CRC cell line HT29 and tested efficacy of chemotherapy 5 fluorouracil (5-FU) and oxaliplatin via annexin V apoptosis assay.

**Results and discussions** Adenoma-harbouring subjects had ~50% increase in LGR5, ALD1a3 and DCAMKL1 (p<0.05) with concomitant suppression of SA-1. Causality was indicated by demonstrating that SiRNA SA-1 knockdowns (KD) in HT29 cells caused stem cell marker induction (LGR5=380%, ALD1a3=30% and DCAMKL1=85%, p<0.05). SA-1 overexpression resulted in reciprocal effects downregulation of all 3 stem cell markers. Functionally, SA-1 KD suppressed 5-FU and oxaliplatin induced apoptosis by 56% and 72% respectively versus scramble vector (p<0.0001).

**Conclusion** This novel finding that the proneoplastic effects of SA-1 loss may be transduced through intestinal/colonic stem cell (CRC incidence) and also augmenting CRC stem cells resulting in chemotherapy resistance (CRC mortality). Future studies may mitigate CRC disparities in Blacks through development of effective biomarkers and therapeutic.

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**PO-504**

EXPEL: A NOVEL NON-DESTRUCTIVE METHOD FOR MINING SOLUBLE TUMOUR BIOMARKERS

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**Introduction** The search for biomarkers able to detect and evaluate disease such as cancer at an early stage, or to predict resistance and response to therapies, has been and remains a major challenge. Despite very important progresses in all fields of omics technologies, the success of discovery of clinically valuable biomarkers is surprisingly disappointing. Difficult mining of secreted proteins in biological fluids poses the first major hurdle, mainly because the concentration of interesting proteins in serum or urine is generally very low. The second key limitation in the field is the inaccessibility of tissue specimens from early lesions. Those are routinely required in their integrity for the complete histological evaluation in the clinical routine, leaving no residual material for research.

**Material and methods** We have developed a simple and original proximal tissue fluid mining method we named EXPEL. It enables efficient extraction of soluble biomarkers while conserving the tissue intact for subsequent pathological analysis. Importantly, the EXPEL method will not only allow the researchers to access human tissues that are very difficult to obtain, but for the first time, scientists and clinicians can share the same material for both experimental research and routine clinical analysis.

**Results and discussions** We hypothesised that subjecting tissue biopsies to cycles of low-pressure pulses under mild hypertonic conditions would allow a rapid extrusion of interstitial fluid containing the biomarkers of interest, while preserving the morphology and antigenicity of the sample for subsequent pathological investigation.

To test the value of the EXPEL method we have applied our procedure to a series of primary colorectal tumours (CRC) and liver metastasis samples (CRC-LM). This proof-of-principle study demonstrates the validity of EXPEL-extruded fluid as unique starting material for the most advanced OMICs methodologies such as proteomic, genomic, metabolic, while showing no disadvantage for routine clinical and pathological investigations.

**Conclusion** Our method enables, for the first time, both clinicians and scientists to explore identical clinical material regardless of its origin and size, which has a major positive impact on translation to the clinic.

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**PO-505**

PROGNOSTIC IMPACT OF KRAS SPlicing IN microsatellite stable colorectal cancer

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**Introduction** Mutations in the KRAS oncogene represent one of the most common genetic alterations in colorectal cancer