progression in a range of solid tumours. This study investigates the role of CAFs in EAC invasion and resistance to chemotherapy.

**Methods** Functional biological analyses comparing primary fibroblasts from tumour stroma (CAF) and normal oesophagus (NOF) were carried out using organotypic culture, transwell invasion assays, collagen-1 gel contraction assays, siRNA gene silencing and colony forming assays. T-Tests (>95% CI) were carried out for all statistical analyses.

**Results** Primary oesophageal CAFs displayed an activated phenotype as demonstrated by α-SMA expression and increased collagen-1 gel contraction in comparison to NOFs (p<0.01). CAF-conditioned medium supported tumour colony formation in the presence of cisplatin and 5-Fluorouracil compared to NOF conditioned medium (p<0.05). Ex vivo analysis revealed a twofold (p<0.05) increase in EAC cell invasion in response to primary (CAF) conditioned medium in transwell invasion assays that was replicated in 3D organotypic models containing co-cultures of fibroblasts and EAC tumour cells. Down-regulation of the CAF secreted molecule Periostin (PN) resulted in a 70% reduction in tumour cell invasion in transwell assays (p<0.05), and a total loss of invasion in organotypic culture. Furthermore, collagen-1 gel contraction was abrogated by PN down-regulation. NOFs exposed to TGF-β from 72 h demonstrate features of myofibroblastic activation including, PN expression and the ability to support increased EAC tumour cell invasion (p<0.05).

**Conclusion** This study has demonstrated that oesophageal derived primary CAF protect EAC cells from chemotherapy and promote tumour cell invasion. Increased α-SMA expression and collagen-1 gel contraction indicates CAF have a myofibroblast like phenotype. PN siRNA reduced gel contraction supports a hypothesis of autocrine regulation of the myofibroblast phenotype. Therefore targeting pathways that determine fibroblast activation may offer a novel therapy for preventing oesophageal cancer invasion and metastasis.

**Competing interests** None declared.

### OC-123 OBESITY DRIVES RADIORESISTANCE AND ENHANCES GENOMIC INSTABILITY IN OESOPHAGEAL ADENOCARCINOMA

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**Introduction** Obesity is strongly associated with oesophageal adenocarcinoma (OAC). However, its role in regulating radiosensitivity and genomic instability is unknown. We developed an isogenic model of radioresistance in OAC called OE33R. We assessed levels of anaphase bridges, a functional genomic instability event, in OE33R compared to an age and passage matched control (OE33P) cells.

**Methods** OE33R and OE33P cell lines were cultured with ACM and quantified the number of bridges present over the 30-day morbidly (classified according to the Clavien-Dindo [CD] criteria). Expression of MAD2L2 and BUB1B correlated with obesity status (BMI and VFA, p<0.05). Levels of anaphase bridge formation correlated with obesity status (BMI and VFA, p<0.05). OE33R cells treated with ACM showed significantly increased expression of the SAC genes MAD2L2 and BUB1B, CDC20, CENPE, and ESPL1 was assessed using qPCR. Survival was determined in both cell lines following ACM treatment using a clonogenic assay.

**Results** OE33P and OE33P showed a significant increase in anaphase bridges in response to ACM (p<0.05, p<0.001 respectively). This increase in anaphase bridge formation was three times greater in the resistant line (p<0.05). Levels of anaphase bridge formation correlated with obesity status (BMI and VFA, p<0.05). OE33R cells treated with ACM showed significantly increased expression of the SAC genes MAD2L2 and BUB1B compared to controls (p<0.01). Expression of MAD2L2 and BUB1B correlated with obesity status (p<0.05). OE33P cells treated with ACM showed increased radiosensitivity (p<0.05). In contrast, the resistant OE33R cell line, ACM treatment reversed this radioresistance (p<0.001).

**Conclusion** Obesity drives genomic instability and alterations in SAC gene expression in radioresistant OAC and alters radiosensitivity in OAC.

**Competing interests** None declared.