Background Our laboratory has a unique cohort of patients with pre-invasive lung squamous cell carcinoma (SqCC) lesions, within which there is a clear discrepancy between the prevalence of pre-invasive lesions and the incidence of lung cancer, suggesting that not all pre-invasive lesions progress to cancer. Using gene expression microarrays we identified 1846 genes significantly differentially expressed between progressive and regressive pre-invasive SqCC lesions.

The macrophage metalloelastase MMP12 gene was found to be highly expressed in progressive lesions, and we hypothesised that it plays a role in epithelial-to-mesenchymal transition (EMT). Conversely, the actin binding protein LIM-domain only 7 (LMO7) gene was highly expressed in regressive lesions, and we postulated that it may be protective against EMT due to its role in the maintenance of epithelial architecture.

Results We observed that MMP12-knockdown decreases tumorigenicity in an immuno-compromised mouse model. Both A431 and H357 MMP12-knockdown cells produced significantly smaller tumours compared with non-silencing shRNA cells. We found that MMP12-knockdown decreases cell adhesion, which is currently being further investigated along with effects on integrin signalling pathways. Levels of EMT markers were assessed in MMP12-knockdown and LMO7 overexpressing cells using western blotting, qPCR and immunostaining. Results indicate that higher MMP12 expression is associated with a mesenchymal phenotype, whereas higher LMO7 expression is associated with an epithelial phenotype.

Conclusions Our results suggest that MMP12 is a key driver of migration and invasion in SqCC and its high expression may contribute to EMT, whereas LMO7 is a putative tumour suppressor with a crucial role in maintaining epithelial cell architecture. MMP12 and LMO7 may be potential early stage therapeutic markers for lung cancer.