

Introduction Malignant pleural effusion (MPE) is primarily an immune-mediated manifestation of pleural-metastasized cancers, particularly adenocarcinomas that harbour *KRAS* mutations. We have previously determined that NF- κ B activation in pleural tumor cells drives MPE formation, but the NF- κ B pathways involved are obscure.

Aims and objectives To investigate the relationship between mutant *KRAS* presence and NF- κ B activation in pleural tumor cells that leads to MPE development.

Methods We profiled baseline and host-microenvironment-induced NF- κ B activity of tumor cells, and examined its relationship with *KRAS* status. We further silenced NF- κ B activating kinases in tumor cells aiming to eliminate NF- κ B activity and thus MPE competence.

Results We found that mutant *KRAS* tumor cells were MPE competent and displayed IL-1b-induced IKK α nuclear translocation that was lost when *KRAS* was silenced. In contrast, wt *KRAS* cells did not form MPE and did not respond to IL-1b with nuclear IKK α shuttling. IKK α , but not IKK β , silencing of mutant *KRAS* tumors hampered their ability for MPE formation, suggesting a mutant *KRAS*-IKK α addiction in the pleural tumor cell during MPE development. Furthermore, IL-1b, but not TNF α , originated from host immune cells was required to sustain the MPE-competent phenotype of IKK α -addicted *KRAS*-mutant tumor cells. Microarray data showed that these cells secrete CXCL5 and CCL2 in response to IL-1b.

Conclusions We demonstrate that *KRAS*-mutant tumor cells require host IL-1b signaling for MPE precipitation. This phenotype is mediated by IKK α .

Acknowledgements These studies were supported by a European Research Council Starting Independent Investigator Grant (#260524).