

Mouse lung adenocarcinoma cell lines reveal *Prl2c2* as a novel lung tumor promoter

Background

Carcinogen-inflicted human cancers, including lung tumors harbor thousands of mutations per genome, most of which are unknown (Garraway, L.A. et al, *Cell* 2013;153:17-37).

Aim

To develop a faithful mouse model of human tobacco carcinogen-induced lung adenocarcinoma suitable for the identification of novel oncogenic genes and pathways.

Methods

We repeatedly managed to obtain several murine lung adenocarcinoma cell lines (MLA) by chronically exposing various mouse strains to different tobacco carcinogens. MLA were characterized for cancer stemness and oncogenes, as well as global gene expression.

Results

To date, 12 MLA cell lines have been derived from *Wt* and transgenic mice on the *FVB*, *Balb/c*, and *C57BL/6* strains by means of urethane or diethylnitrosamine exposure. All MLA were immortal, phenotypically stable, and indefinitely passaged *in vitro* over a period of over 18 months and/or 60 passages. In addition, all cell lines were oncogenic, transplantable, metastatic, and uniformly lethal *in vivo*. Interestingly, MLA displayed *Kras* mutations in codon 61, mono- or bi-allelic *Trp53* loss, and expression of lung cancer stemness factors *Itgb3* and *Lgr6*, in amazing similarity to human lung cancers. Microarray revealed that all MLA cell lines heavily overexpressed *Prl2c2*, encoding proliferin, in comparison to the native lungs. *Prl2c2* silencing diminished MLA proliferation and stemness, to a degree comparable with *Itgb3* interference.

Conclusions

MLA are faithful models of human lung adenocarcinoma that led to the discovery of *Prl2c2* as a candidate lung tumor promoter.

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