Use of the Gene Trap Resource for Cancer-related lncRNAs to Study the Role of Malat1 in Pancreatic Cancer.

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Abstract: Texas A&M Institute for Genomic Medicine (TIGM) houses the world's largest library of knockout C57BL/6N ES cells and provides transgenic mice for researchers worldwide. Among multitude of genetic targets inactivated in these cells, there is a significant group of long non-coding RNAs (lncRNA), the non-protein coding transcripts longer than 200 nucleotides implicated in a variety of disease states and demonstrated their involvement in oncogenesis. Our screening of more than 18,000 clones has identified over 1,000 inactivated ncRNAs including a number of lncRNAs. One such clone, IST14461G11, was used to establish a colony of homozygous mutant Metastasis-Associated-Lung-Adenocarcinoma-TranScript-1 (Malat1) mice in pure C57BL/6N genetic background. Malat1 is an lncRNA that is overexpressed in multiple cancer cell lines and tumors. The highly conserved mouse homologue of Malat1 was found to be highly expressed in hepatocellular carcinoma and now we have demonstrated that Malat1 is also pro-oncogenic in pancreatic cancer cells. Homozygous mutants are viable and don't display any gross phenotype; therefore, in order to investigate the role of Malat1 in pancreatic cancer, these mutant mice are now being crossed with a transgenic mouse model expressing $KRAS^{G12D}$ and carrying the p53 mutation that effectively develops pancreatic tumors. The effects of loss of Malat1 expression on pancreatic tumor formation will be determined.