A bioluminescent mouse model of pancreatic {beta}-cell carcinogenesis

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The Rip1Tag2 transgenic mouse model of pancreatic beta-cell carcinogenesis has been instrumental in identifying several hallmarks of cancer, including tumor cell evasion from apoptosis, tumor angiogenesis and tumor invasion. Moreover, Rip1Tag2 mice have been helpful in the development and testing of innovative cancer therapies and tumor imaging protocols. However, based on tumor localization in the mouse, primary tumor growth and metastatic dissemination cannot be easily monitored in a longitudinal axis by non-invasive and low-technology approaches. Here, we report the generation of a new transgenic mouse line as a versatile tool to study beta-cell carcinogenesis. Transgenic expression of a bicistronic messenger RNA encoding simian virus large T antigen and firefly luciferase in pancreatic beta-cells recapitulates insulinoma development in a reproducible multistage process. In the mouse line called RipTag-IRES-Luciferase line (RTL) 1, the beta-cell-specific expression of luciferase allows the non-invasive monitoring of primary tumor growth over time in vivo and the detection and quantification of disseminated tumor cells and micrometastases in distant organs ex vivo. When crossed to mouse lines in which the expression of cancer 'modifier' genes has been manipulated, tumor initiation and tumor progression are similarly affected as previously reported for Rip1Tag2 mice, indicating a robust tumor progression pathway shared between the two different transgenic mouse lines. Together, the data indicate that the RTL1 mouse line will be of great value to study anti-tumoral therapeutic approaches as well as to define the functional roles of cancer- and metastasis-related genes when crossed to appropriate transgenic or gene-targeted mouse lines.
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