TACONIC

LPTA ANIMAL MODELS

LPTA Animal Model EL1-*Luc*/EL1-*TAg*
(Light Producing Transgenic Animal Model of Tag-Driven Pancreatic Cancer)

Information

Mouse Strain: FVB/N-EL1-*Luc*/EL1-*TAg*

Common Name: EL1-*Luc*/EL1-*TAg*

Genotype: Hemizygous

Background Strain: FVB/N

Coat Color: Albino

Key Applications

- Noninvasive monitoring of spontaneous tumorogenesis in the pancreas and response to therapeutic agents.

Description of the Model

Figure 1 illustrates the strategy used to generate the above model of spontaneous pancreatic adenocarcinoma with bioluminescence as a read-out for the tumor burden. Two transgenes were made using a tissue-specific rat Elastase I promoter fragment of 220 base pairs to direct the expression of both, SV40 large T-antigen and modified firefly luciferase (Promega pGL3), in pancreatic exocrine cells. The transgenes were co-injected into the pronucleus of FVB zygotes, which resulted in cosegregation of luciferase and the oncogene in subsequent generations of mice. Characterization of transgenic mice indicates that the penetrance of bioluminescent tumor development in the pancreas is close to 100% and onset ranges from 60 to 100 days of age. Histopathological evaluation of the pancreas of these mice showed that the developing lesions are predominantly of acinar cell origin.

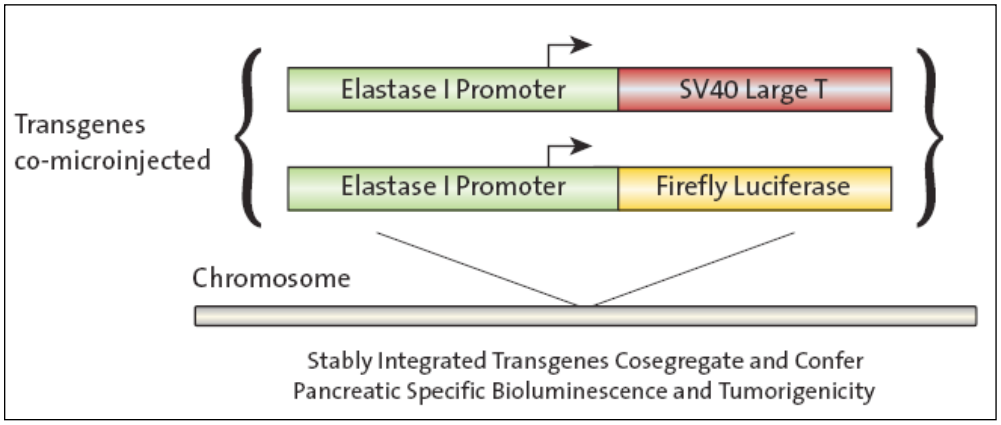


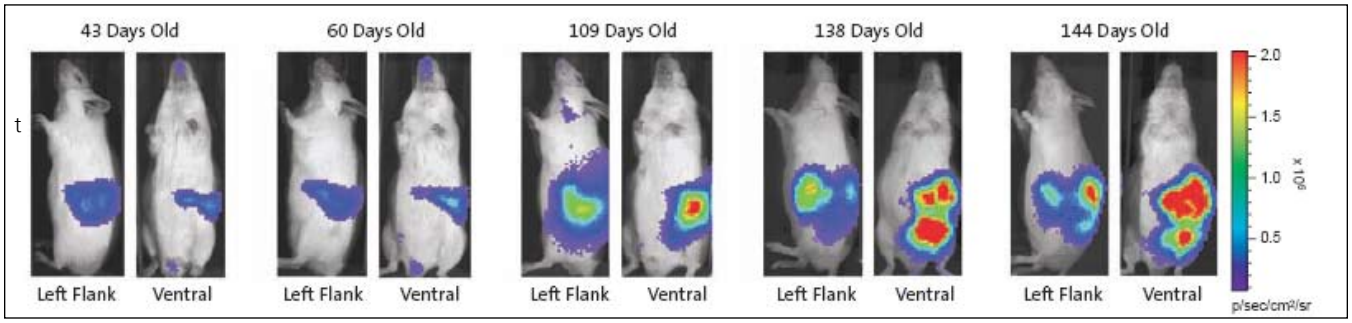
Figure 1. Pancreatic Adenocarcinoma Model - EL1-*Luc*/EL1-*TAg* Mouse

The background strain is FVB/N. This transgenic founder lines were generated by the micro-injection of the transgenes into the pronucleus of FVB zygotes.

The transgenic mice develop fast growing and aggressive pancreatic adenocarcinoma that can be monitored through noninvasive bioluminescence imaging. This model can be used for non-invasive monitoring of spontaneous tumorogenesis in the pancreas, and for efficacy studies of therapeutic agents against pancreatic cancer.

Figure 2 shows a representative example of longitudinal bioluminescence imaging analysis of EL1-*Luc*/EL1-*TAg* mouse. This provides an example of how pancreatic tumor progression can be followed non-invasively within the same subject over time using bioluminescence imaging approach.

Technical Note: We have found that the position of the pancreas within the abdominal cavity can shift significantly between imaging sessions. Bioluminescence signal intensity is negatively affected by the depth of luciferase expressing tissues. To compensate for the variability, we imaged the mice in 3 positions (ventral, and left and right flanks) at each imaging session. The average light emission from these measurements was used as an indicator of pancreatic cellularity and tumor progression.



Efficacy Studies with Anti-Cancer Agents Against Pancreatic Cancer

This mouse model is useful to study efficacy of anti-cancer drug candidates against pancreatic cancer. Rapamycin and gemcitabine showed activity consistent with the clinical performance of these compounds. Additionally, efficacy studies in this model may require rolling enrollment, and the use of different statistical methods for evaluation than those normally used for standard xenograft studies.

Example Phenotype

The coat color of this animal model is albino. EL1-*Luc*/EL1-*TAg* mice have been observed to have litters of 8 – 12 pups.
At 6 weeks of age, adult mice weights were appropriate: 20g – 30g.

Genotype

The transgenic line is hemizygous. The presence of the EL1-*Luc* transgene was determined using PCR. The 1 kb PCR product from the sequence internal to the luciferase gene was amplified using forward primer:

PCR conditions:

97 °C 5:00 min; 94.5 °C 0:40 min; 58 °C 1:30 min; 72 °C 1:30 min for 35 cycles; 72 °C 10:00 min; hold at 4 °C until analysis.

TACONIC

Disclaimer

This product is provided under license from Promega Corporation and The Regents of the University of California.

Under the terms of Promega license, the use of this product and derivatives thereof is strictly limited to *in vivo* research use. Researchers may use this product in their research and they may transfer derivatives to others for research use provided at the time of transfer a copy of this label license is given to the recipients and the recipients agree to be bound by the terms and conditions of this label license. In addition, researchers performing *in vivo* bioluminescent imaging must do one of the following: (1) use luminescent assay reagents purchased from Promega or Caliper Life Sciences for all determinations of luminescent activity resulting from the research use of this product and its derivatives; or (2) contact Promega to obtain a license for the use of the product and its derivatives in conjunction with luminescent assay reagents not purchased from Promega or Caliper Life Sciences. No reach-through payments shall be owed to Promega relating to an organization's commercialization of products that are discoveries resulting from the research use of this product or its derivatives, provided that such products of the organization do not fall within the valid claims of any issued patents assigned to or licensed by Promega, or that such commercialization would not be a violation of the terms of this label license. No right to use this product for any diagnostic, therapeutic, or commercial application is hereby conveyed to the purchaser of this product. Commercial application is defined as any and all uses of this product and derivatives by a party for monetary or other consideration and may include but is not limited to use in: (1) product manufacture; or (2) to provide a service, information or data; and/or (3) resale of the product or its derivatives, whether or not such product or its derivatives are sold for use in research. If the purchaser is not willing to accept the conditions of this limited label license, Caliper Life Sciences is willing to accept the return of the unopened product and provide the purchaser with a full refund. However, in the event the product is opened, then the purchaser agrees to be bound by the conditions of this limited label license.

Buyer acknowledges that the wild-type and mutant recombinant Coleoptera luciferase nucleic acid and protein ("UC Patented Material") is the subject of U.S. Patent Nos. 5,583,024, 5,674,713 and 5,700,673, assigned to The Regents of The University of California.

The UC Patented Material, or any material that contains or incorporates the UC Patented Material, may not be transferred or licensed to any other party, or be used for commercial purposes by any other party, without a commercial license or the express written consent of The Regents of The University of California.

The Materials may be used solely for internal research, and no right to use the Materials for any human *in vivo*, diagnostic, therapeutic, or commercial application is hereby conveyed to Buyer.

Additionally, the Buyer may not:

(1) use the Materials in the course of providing a service or data to third parties;

(2) transfer the Materials to any third party or to any place other than Buyer's premises;

(3) attempt to alter, modify or re-engineer the Materials in any way, or extract or transfer any genetic material from the product to another organism; or

(4) sublicense the rights granted herein.

- Buyer is not prohibited from using the Materials to discover or develop products that it intends to sell for consideration as long as those products do not contain any Materials.
- If Buyer has purchased breeding rights to an animal model, Buyer may have the animal model bred by a third party, provided that such third party

  (i) does not use the animal model for any purpose other than breeding for the benefit of Buyer,

  (ii) destroys or returns the animals upon conclusion of the breeding services, and

  (iii) is otherwise legally bound by the terms of this label license.