HT29 Human colon cancer cell orthotopic xenograft

A MODEL FOR HUMAN COLORECTAL CANCER ASSOCIATED WITH METASTASIS

Model

We developed an orthotopic xenograft preclinical model of colorectal cancer based on the widely used HT29 cells (human colon cancer cell line).
In collaboration with Flash Therapeutics*, HT29 cells were initially transduced with luciferase and a reporter fluorescent protein. This approach allows *in vivo* imaging of tumor growth and metastasis by luminescence (BLI) and fluorescence (FLI). We could also offer inducible genetic approaches to over-express or silence any target gene.

Specie

SCID Beige mouse

Interest

- Xenogeneic models combine the advantage of working with human cancers with the relevance of an *in vivo* host.
- HT29 cells are inoculated in the proper tumor microenvironment enabling metastases development.
- BLI enables real-time, non-invasive monitoring of tumor growth and test item response over time.
- FLI allows metastasis visualization and quantification.
- This model is validated with the clinically relevant compound Fluorouracil (5-FU).
- Test compound treatment or gene activation/silencing can be initiated in a desired schedule (before or after tumor establishment).

Model Description

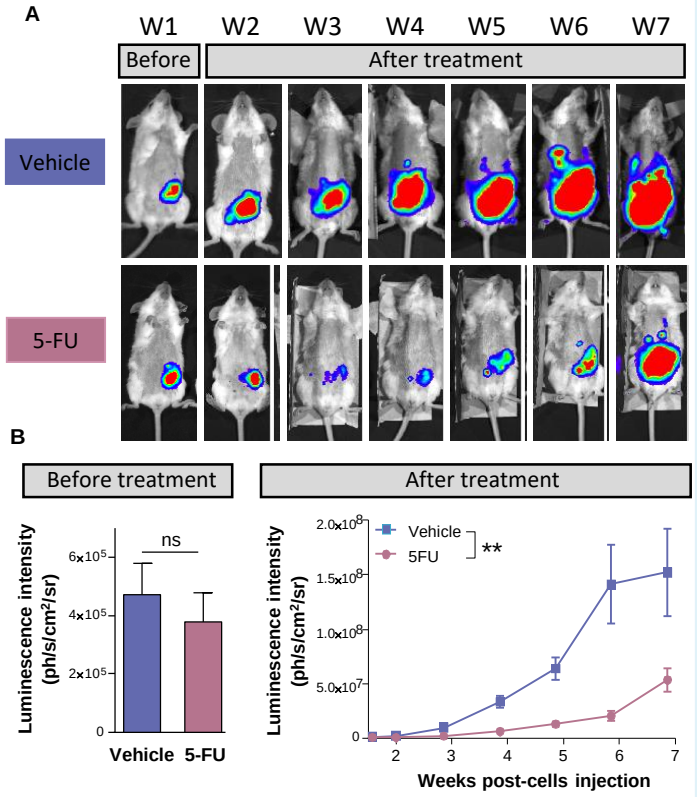
- Cancer cells are injected directly into the caecal wall.
- Mice are imaged by luminescence once or twice weekly.
- Endpoint fluorescence are performed at week 7.
- Test compounds can be administered *via* various routes (i.v., i.p., s.c., p.o.) in preventive or curative treatment.

Parameters evaluated

- Tumor growth: bioluminescence intensity
- Metastasis: localisation, incidence (%), scoring and fluorescence intensity
- Test item efficacy: tumor growth / metastasis delay or inhibition
- Tumor can be resected for histological, molecular or biomarkers analysis

* Flash Therapeutics (formerly Vectalys) is a new gene therapy company developing gene and cell-based therapies by leveraging its proprietary lentiviral platform and bioproduction technologies.

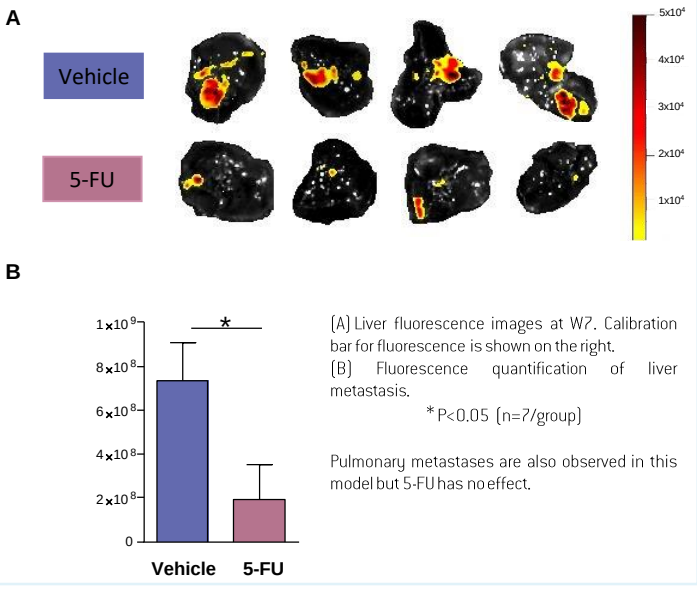
5-FU delays tumor growth on mice-bearing HT29 colorectal cancer



(A) Bioluminescence time-course images of orthotopic HT29 tumor. Mice with established tumor were i.p. injected with 5FU (75 mg/kg) or vehicle at W1 (after imaging), W2 and W3.
(B) Tumor growth determined by bioluminescence. Luminescence intensity is represented by radiance (ph/sec/cm²/sr), which refers to the number of photons per second that are leaving a square centimeter of tissue and radiating into a solid angle of one steradian (sr).

ns P>0.05, ** P<0.01 (n=7/group)

5FU decreases metastatic spread to the liver



(A) Liver fluorescence images at W7. Calibration bar for fluorescence is shown on the right.
(B) Fluorescence quantification of liver metastasis.

* P<0.05 (n=7/group)

Pulmonary metastases are also observed in this model but 5-FU has no effect.