Orthotopic AML tumor model – MV4-11

- **Orthotopic tumor models, Bone Marrow Engraftment (BME) models**
  In contrast to subcutaneously engrafted cells, cells proliferating inside the organ of their origin (‘orthotopically’) spread to metastatic sites in other organs, with specificities comparable to the human situation. Besides allowing the cells to spread, the organotypical stromal interactions that are allowed to occur in such orthotopic models have also been shown to affect the growth, differentiation, and drug sensitivity of tumor cells.

- **MV4-11-LN cells**
  MV4-11 cells (DSMZ-No: ACC 102) were isolated from the peripheral blood of a patient with AML (acute myeloid leukemia). These cells express an internal tandem duplication (ITD) mutation of the FLT3 gene. In order to detect orthotopic growth of implanted cells, a luciferase expressing cell line was generated via transduction of a luciferase-neomycin construct, and subsequent neomycin selection (MV4-11-LN).

  ![Figure 1: Luciferase assay. Serial dilutions of a cell lysate were tested for luciferase activity.](image1)

- **In vivo bioluminescence measurement**
  After intravenous implantation the growth of the cells will be monitored via *in vivo* bioluminescence imaging (BLI). Using BLI, the animals are randomized into treatment groups according to apparent tumor sizes. Moreover, once treatment is initiated, effects on the total *in vivo* bioluminescence signal, and thus potential metastatic loci may be monitored.

  ![Figure 2: In vivo BLI. Mice with orthotopically growing MV4-11-LN cells were measured 22 days (left panel) or 36 days (right panel) after implantation.](image2)

- **Metastasation**
  After measuring tumor sizes, potentially metastatic organs are homogenized, and the luciferase activity is assayed as a proxy for spread tumor cells. The pattern of metastatic spread is cell type specific. For preferences of MV4-11-LN see Fig. 3.

  ![Figure 3: Ex vivo BLI. Metastatic spread of intravenously implanted MV4-11-LN cells as measured via luciferase activity. PCF: Peritoneal carcinomatosis in the fatty tissue; LN: lymph nodes, ing.: inguinal, ax: axillary, br: brachial.](image3)

- **Study example**
  Sutent, a small-molecule multi kinase inhibitor, totally abolished tumor growth of orthotopically growing cells.

  ![Figure 4: Treatment. Tumor growth was monitored using *in vivo* BLI.](image4)