Transgenesis

In situ transgenesis methods such as viruses and electroporation can rapidly create somatic transgenic mice but lack control over copy number, zygosity, and locus specificity. Here we establish mosaic analysis by dual recombinase-mediated cassette exchange (MADR), which permits stable labeling of mutant cells expressing transgenic elements from precisely defined chromosomal loci. We provide a toolkit of MADR elements for combination labeling, inducible and reversible transgene manipulation, VCre recombinase expression, and transgenesis of human cells. Further, we demonstrate the versatility of MADR by creating glioma models with mixed reporter-identified zygosity or with “personalized” driver mutations from pediatric glioma. MADR is extensible to thousands of existing mouse lines, providing a flexible platform to democratize the generation of somatic mosaic mice [1)].

1)

Kim GB, Rincon Fernandez Pacheco D, Saxon D, Yang A, Sabet S, Dutra-Clarke M, Levy R, Watkins A, Park H, Abbasi Akhtar A, Linesch PW, Kobritz N, Chandra SS, Grausam K, Ayala-Sarmiento A, Molina J, Sedivakova K, Hoang K, Tsyporin J, Gareau DS, Filbin MG, Bannykh S, Santiskulvong C, Wang Y, Tang J, Suva ML, Chen B, Danielpour M, Breunig JJ. Rapid Generation of Somatic Mouse Mosaics with Locus-Specific, Stably Integrated Transgenic Elements. Cell. 2019 Sep 19;179(1):251-267.e24. doi: 10.1016/j.cell.2019.08.013. PubMed PMID: 31539496.