

Genetics question



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Genetics/question

The chimeric mouse gene is what we are targeting for the agouti coat colour gene. The human protein/domain is expressed while the mouse protein/domain is suppressed in all cells and tissues. The design of the humanized model requires thorough analysis and accurate risk assessment to preserve physiological expression and regulation of the human gene inserted into the mouse genome. In order to determine the optimal expression and functionality of the human protein in a mouse environment, both mouse and human genes and proteins are analysed for accuracy and structure.

The gene structure will be as follows.

Stage 1 Targeting vector construction after coming up with a model design.

The plasmid structure is shown as section FR resulting in the gene structure above. This gene will be targeted by homologous recombination (stage 2) and Fip recombination (stage 3) below resulting in condition Knock-in.

Stage 2 Homologous recombination by (ES cells genotyping) electroporation resulting in targeted ES

Stage 3 Fip recombination.

The targeted ES cells are injected into blastocyst which is the implanted into the foster mother. The embryo formed will have cells/tissue derived from targeted cells or wild type cells.

It should be noted that 1/3 of the genes are essential so deletion or replacement of more than a third of the gene may lead in embryonic or early post natal lethality. These insertions and manipulations yield custom mouse models possessing specialized alterations in gene function tailored to the

research goals.

References:

LeDoux, M. (2005). *Animal models of movement disorders*. Burlington, MA: Elsevier Academic Press.

Ruvinsky, A., & Graves, J. A. M. (2005). *Mammalian genomics*. Wallingford, Oxfordshire, UK: CABI Pub.