EMBRYO ELECTROPORATION – 'SHOCKING' ADVANCES IN THE GENERATION OF MOUSE MODELS OF HUMAN DISEASE

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The generation of high quality, accurate genetically altered mice are essential for advancing our understanding of human disease and gene function. The recent application of the CRISPR/Cas system to the genetic manipulation of mouse embryos has enabled scientists to introduce highly specific mutations into the mouse genome with high efficiency. Prior to CRISPR the production of precise, true mouse mutants was; limited, financially costly, time inefficient and required the use of many animals.

The Electroporation of mouse zygotes offers an attractive alternative to the traditional microinjection technique for gene editing, for example the delivery of CRISPR/Cas9 reagents into one-cell zygotes via pronuclear injection. Electroporation can target a larger number of zygotes within the same time window and with greater simplicity, due to its user friendly procedure. The procedure requires skills that are more widespread within the scientific community; basic microscopy and embryo handling skills.

Electroporation data collated from the Gene Delivery Team show a reduction in physical damage and zygote lysis post CRISPR/Cas9 delivery, with greater viability and consequently a reduction in number of animals used for model generation. Mouse zygote electroporation offers versatility as the technique does not require the visibility of pronuclei and therefore non-accessible zygotes can be targeted; removing this developmental constraint also supports its application with IVF embryos. The high throughput technique delivers consistency by removing user variation, whilst also ensuring that all embryos electroporated within the same session are targeted at the same time; limiting the effects of several associated confounding variables.

Electroporation has been successful with both deletions and more complex point mutations, producing accurate on target founders at MRC Harwell. Advancing to embryo electroporation supports the 3R's ethos; reducing animal usage, improving the efficiency in which zygotes are used and transgenic zygotes are created for the generation new mouse models.

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