New way to grow embryonic stem cells holds promise of dramatic reduction in animal use

January 27 2010

A new method of priming early embryos to form embryonic stem (ES) cells has allowed ES cells to be derived from mice used in diabetes research for the first time.

This could dramatically reduce the number of animals used to study the genetic basis of type 1 diabetes and has the potential to do the same for mouse models of other diseases too.

Understanding the genetic basis of type 1 diabetes is an important area of research. Researchers often use a strain of mouse, known as the non-obese diabetic (NOD) mouse, which spontaneously develops type 1 diabetes. Previously, it was impossible to generate ES cells from NOD mice, so the only way to study a gene of interest was to breed the NOD mouse with a strain of mouse that could be genetically modified. This involved extensive breeding programmes, involving many hundreds of animals, and taking up to two years.

The research has been awarded this year's annual NC3Rs 3Rs Prize. The prize, sponsored by GlaxoSmithKline, was awarded to Dr Jennifer Nichols, University of Cambridge, and her co-authors who used a precise cocktail of molecules to control the growth of the cells to generate ES cells from the NOD mouse. The resulting ES cells can be directly manipulated to disable or repair a specific gene of interest and then injected into early mouse embryos to breed a NOD mouse with the desired genetic makeup, reducing the overall number of mice required.

Because ES cells can be transformed into all other cell types in the body many more experiments can be conducted in vitro than before, potentially leading to further reduction of animal use. Dr Nichols said: "We are already looking to turn these embryonic stem cells into beta cells found in the pancreas which are known to be involved in the onset of type 1 diabetes. Because these mice spontaneously develop type 1 diabetes we will be able to do experiments in vitro that were previously impossible."

Dr Vicky Robinson, chief executive of the NC3Rs, said: "This is an exciting and impressive piece of research. The potential for reducing animal use and advancing the field of diabetes research is huge. Importantly, the new method has implications for other areas of research involving mice."

Dr Gianni a dal-Negro, Director of Animal Research Responsibility at GlaxoSmithKline said: "As sponsor of this award, GSK are delighted to see such an innovative application of science to the 3Rs. This project demonstrates an originality in applying emerging stem cell science with genetics and immunology in a complicated disease. It will no doubt contribute to new understandings in diseases processes and drug discovery and improved animal welfare."

Dr Nichols and her collaborator Professor Anne Cooke have already made the NOD ES cells freely available to the research community, potentially reducing the number of mice used in type 1 diabetes research worldwide. They plan to use the £10k prize winners' grant to host researchers from other groups so they can learn the culture technique and it can be quickly and widely disseminated.

Dr Nichols said: "The technique for extracting the embryonic stem cells is very visual and therefore difficult to learn from written instructions. Getting researchers to visit us will help encourage quicker uptake of this

new approach."

About 1 in 250 of the UK population develops Type 1 diabetes at some stage, usually as children or young adults. In Type 1 diabetes the body stops making insulin because the pancreatic beta cells are selectively destroyed, leading to a very high blood glucose level. Treatment to control the blood glucose level is with insulin injections and a healthy diet. Although the cause of type 1 diabetes is still not fully understood it is believed to be of immunological origin, but the development is thought to be governed by both genetic and environmental factors.

Provided by National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3Rs)

Citation: New way to grow embryonic stem cells holds promise of dramatic reduction in animal use (2010, January 27) retrieved 17 July 2024 from https://phys.org/news/2010-01-embryonic-stem-cells-reduction-animal.html

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