



THE VICTOR CHANG
CARDIAC RESEARCH INSTITUTE

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New technology to keep up with complex disease

Scientists are using new technologies to knock out genes at specific times and locations in the body in an effort to better understand and treat complex genetic diseases, including heart disease and a deadly form of childhood cancer.

Professor Mario Capecchi, from the University of Utah, USA, pioneered using the mouse as a model for human genetic disease and co-invented the initial technology for knocking genes out in mice.

“Many diseases, including some heart diseases and cancers, are caused by defective genes. This means that there is a defect in the blue print that controls how our bodies are built and how they function,” Prof. Capecchi said. “As our understanding of disease increases, including all of its complexities, so will our ability to generate more effective therapies.”

Using new technology, Professor Capecchi has recently created a mouse model for a rare but deadly childhood cancer, *alveolar rhabdomyosarcoma*, that claims eighty percent of sufferers within five years of diagnosis. The new technology allows scientists to knock-out a single gene with high precision and without affecting any of thousands of other genes. Such gene knock-out studies are aimed to help our understanding of complex disease in people.

“To understand such diseases, technology needs to keep abreast of its complexity so that the design of animal model systems truly reflects in detail the same disease in humans.”

In the past, scientists were limited to knocking out genes in every cell of the body. They disrupted specific genes in the developing embryo, before birth, by completely knocking it out of all cells in every tissue and organ in the body. However many genes have multiple functions in the embryo and later in the adult. If the gene disruption compromises the mouse during early development, then that would prevent study of the gene’s function in the adult.

“The new technology allows us new freedoms by specifically allowing the knock-out of genes at any time during development, or after development in specific tissue, almost down to the cellular level,” Prof. Capecchi explained.

“In *alveolar rhabdomyosarcoma*, we knew that a specific gene was generated that resulted in the initiation of the disease. In the past researchers tried to create a mouse model using the old technique, but failed. However, with the new technology we waited until after birth to generate the culprit gene in the muscles only. Doing so allowed us to develop a mouse model of the disease.”

Now that the model of *alveolar rhabdomyosarcoma* has been developed, scientists can begin the task of trying to understand how this gene product causes the disease with the ultimate hope of developing specific drug therapies that will control this devastating disease.

Prof. Capecchi is presenting his findings today at the 15th International Society of Developmental Biologists Congress in Sydney. Organised this year by senior scientists from the Victor Chang Cardiac Research Institute (VCCRI), which is a research centre for excellence in heart development and adult cardiac stem cell research.

For further information and interview opportunities with Prof. Capecchi at the Congress, please contact Samantha Lucia, Communications and Marketing Manager, Victor Chang Cardiac Research Institute.

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