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Automated Three-dimensional Phenotyping of Mouse Embryos

Status	Current
Competition	Development of New Technologies Competition
Sector	Development of New Technologies
Genome Centre	Ontario Genomics Institute
Project Leader	Mark Henkelman

Project Description

Scientists in the 21st Century face a major challenge and opportunity to define the relationship between the DNA sequence and the biological result of that sequence on the development and physiology of an individual. This is particularly important in the human population as the genetic basis of the more common human diseases is being defined. Although ultimately we want to know these relationships in the human, much of the detail will be worked out in the mouse where genetic manipulations can be performed easily. The overlap in sequence similarity between human and mouse is greater than 99%. It is, therefore, believed that an understanding of the genetic basis of disease in the mouse will direct investigations in the human.

As one approach to define the relationship of genes in the mouse to their function in the organism, there is an internationally funded program to mutate all of the genes in the mouse (approximately 25,000), one gene at a time. This will result in 25,000 different mice for which the question will need to be asked, “How do these mice differ from a normal mouse which has all of its genes intact?”

This application will develop new technology based on imaging and automated computer analysis to visualize embryos and compare them to the non-mutated embryo. The three dimensional imaging will make use of magnetic resonance imaging (MRI) which has a major role in human diagnosis because of its capability of seeing soft tissues. An alternative imaging based on optical 3D imaging will also be investigated because it potentially has better resolution and unique tissue sensitivities. For both of these imaging modalities, sophisticated computer analysis will be developed to compare images of an embryo with a single mutation to the reference embryo, and as a consequence, point out the regions of difference. This is essential technology for making use of the 25,000 individual gene-modified animals. At the end of two years, we will have determined the best way to take images of embryos such that a computer can find most of the differences. This developed technology will then be available to Genome Centres in Canada and will be made available as a service to Genome facilities in other countries. Beyond the scope of this grant, it is our intension to establish a company in Ontario that will provide image-based phenotyping to the rest of the world.