

The impact of genomics

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Working with worms may not be your average person's idea of a good time, but for University of Toronto researcher Dr. Andrew Fraser, they are fascinating.

"I think <u>worms</u> are totally cool, like humans only simpler and easier," writes Dr. Fraser on his website.

In fact, working with the invertebrates is what will bring Dr. Fraser to the upcoming AAAS conference in San Diego, California where he will present some of his research findings in a symposium called "The Impact of Genomics."

What the NSERC-funded researcher actually studies is not just worms, it's genetics. The benefit to working with the simple creatures is that half the 20,000 genes in a worm are similar to humans, and the way those genes work together also share some similarities with us, says Dr. Fraser. But researchers are able to carry out experiments in worms that they would never be able to attempt in people, he says.

Using a process called <u>RNA interference</u> (RNAi) Dr. Fraser is able to turn off one gene at a time in a worm, in order to identify what that gene does.

The real challenge here is not mapping the genome, but predicting how genes work to create the actual characteristics we see in an organism, such as its shape, behaviour or the onset of inherited genetic disease in the organism. Finding the link between the genotype and that final



outward expression, known scientifically as the phenotype, can be far from trivial.

The presentation will focus on how genetic background affects disease risk, because even though two individuals may inherit the same gene for a particular disease, their risk of actually getting the disease varies based on their genome and genetic background. The goal of the research, says Dr. Fraser, is to predict the effects of inherited mutations and to understand how multiple mutations combine to be expressed phenotypically.

The point of this is to identify how inherited mutations can affect human health. But the problem, says Dr. Fraser is that humans don't exist in the same controlled environment as worms in a lab. In fact, there are approximately three million differences between any human genomes.

"Modeling this extent of difference between genomes by looking at one gene at a time is hard," says Dr. Fraser.

To account for this, Dr. Fraser is looking at natural isolates of the worms to see how mutations will affect the population, which has a level of genetic variability similar to humans. This gives the researchers the ability to look at how genetic mutations affect phenotypes within a species. It also lets them see how predictable phenotypic expression is based on genetic variation. This is the first time a study like this has been undertaken, and will have implications for humans in the areas of genetic disease and disease predictability.

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