The informant: A jumping gene

March 21 2011

Scientists at the European Molecular Biology Laboratory (EMBL) in Heidelberg, Germany, have developed a new method for studying gene regulation, by employing a jumping gene as an informant. Published online today in Nature Genetics, the new method is called GROMIT. It enables researchers to systematically explore the very large part of our genome that does not code for proteins, and which likely plays a large role in making each of us unique, by controlling when, where and to what extent genes are turned on, or expressed. Thanks to GROMIT, scientists can also create mouse models for human diseases such as Down syndrome.

"Our findings change how we think about gene regulation, and about how differences between individual genomes could lead to disease," says François Spitz from EMBL, who led the study.

Until now, scientists thought that regulatory elements essentially controlled a specific gene or group of genes. With GROMIT, Spitz and colleagues discovered that the genome is not organized in such a gene-centric manner. Instead, it appears that each regulatory element can potentially control whatever is within its reach. This means that mutations that simply shuffle genetic elements around (without deleting or altering them) can have striking effects, by bringing genes into or out of specific regulators' zones of influence.

The EMBL scientists also discovered that many of these regulatory elements act in specific tissues, which suggests that the expression levels of every gene, even those that are active all over the body, are fine-tuned

at the tissue level.

Jumping genes – or transposons – are sequences of DNA that can move from place to place within a cell's genome. This can have detrimental effects, for example if this extra genetic material is inserted into an important gene, disrupting it. But Spitz and colleagues used this property to their advantage.

The scientists enlisted a jumping gene to act as an informant, revealing where genetic regulation was occurring. They engineered that jumping gene to react to the presence of regulatory elements, and devised a method to control when it jumps to a different location in a mouse's genome. Through selective breeding, Spitz and colleagues were then able to generate lines of mice with the jumping gene in many different places. In each of these lines, the jumping gene gave them information about the regulatory activity happening in the area of the genome where it was sitting.

"This new technique is easier, faster, less invasive and more efficient than previous approaches," says Spitz: "we don't have to go through the complex and time-consuming process of engineering embryonic stem cells to create a mouse from; with GROMIT, we only have to mate the mice."

GROMIT also allows researchers to easily delete or re-shuffle areas of the genome, to assess their biological role. This approach can be used to create mouse models in which to study human diseases like Williams-Beuren syndrome, which occurs when part of chromosome 7 is missing, and Down syndrome, in which part or all of chromosome 21 is repeated.

Provided by European Molecular Biology Laboratory