

Importance of different cell types underestimated

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Choosing the right cell type is particularly important in genetic studies. This is apparent from research published on 16 October in *PLoS Genetics*. Dutch researcher Alice Gerrits has shown how variations in the genome can influence the activity of genes. This effect was found to be strongly dependent on the cell type in which these genes were active.

Although all the cells in our body contain essentially the same DNA (genome), they do not all exhibit the same functions. This is usually because different sets of genes are active in different types of cells. Gerrits investigated four types of blood cells in 25 mouse strains with slightly different genomes. In each of the four cell types, she looked for differences in gene activity between the 25 mouse strains and determined which pieces of the genome caused these differences. She discovered that some pieces of the genome had the same effect on the activity of genes in all four cell types. Yet interestingly, a far larger number of pieces exerted an effect on gene activity mostly in one, two or three of the four cell types.

The 25 different mouse strains were generated many years ago by crossing two clearly different laboratory mice with each other. The two mice differed, for example, in fur colour, average life expectancy and the number of blood-forming stem cells in their <u>bone marrow</u>. By repeatedly crossing the offspring of the two mice 25 different strains of mice were eventually obtained, all of which had a unique mosaic of the genomes of the two starting mice. Molecular markers were used to indicate which pieces of the genome originated from each of the two



mice. By comparing variations in the genome of the 25 different mouse strains with variations in gene activity, Gerrits could see which pieces of the genome exerted an influence on the activity of which genes.

It is known that some variations in the genome play a role in the development of diseases such as leukaemia. Gerrits' research revealed that variations in the genome do not always have the same effect on the activity of genes, but that this effect is strongly dependent on the type of cell in which these genes are active. This means that in future genetic studies as many different <u>cell types</u> as possible must be examined. This is the only way to properly investigate how variations in the genome can lead to changes in <u>gene activity</u> or eventually even to the development of diseases.

Gerrits carried out her research together with Yang Li and Bruno Tesson. The research was largely funded by the Vici grants of Gerald de Haan and Ritsert Jansen, received from NWO's Innovational Research Incentives Scheme.

More information: On 16 October 2009 PLoS Genetics published Expression Quantitative Trait Loci are Highly Sensitive to Cellular Differentiation State by Alice Gerrits, Yang Li, Bruno M. Tesson, Leonid V. Bystrykh, Ellen Weersing, Albertina Ausema, Bert Dontje, Xusheng Wang, Rainer Breitling, Ritsert C. Jansen, Gerald de Haan. Direct link to the article: www.plosgenetics.org/article/info %3Adoi%2F10.1371%2Fjournal.pgen.1000692

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