Researchers map all the fragile sites of the yeast Saccharomyces cerevisiae's genome

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The research group of Dr. François Robert, a researcher at the Institut de recherches cliniques de Montréal (IRCM), in collaboration with the team of Dr. Daniel Durocher (Samuel Lunenfeld Research Institute and University of Toronto) accomplished a technical breakthrough: they mapped all the fragile sites of a living organism, the budding yeast *Saccharomyces cerevisiae*. The method used by the researchers can be applied to humans. This study has been published online today in the scientific journal *Nature Structural and Molecular Biology*.

S. cerevisiae is a model organism commonly used in molecular biology to study basic cellular phenomena such as the regulation of gene expression, DNA replication or, as in the present case, DNA repair. DNA, which forms the genetic material of our cells, is continuously under stress challenging its integrity. On average, the DNA contained in each one of our cells suffers, on a daily basis, about 1 million damages. If not repaired, those genetic damages can lead to cancers. Hopefully, each cell has mechanisms that detect and then repair these injuries. It has long been known that some areas of the genome were more susceptible to be damaged than others. However, a complete list of those fragile areas had not been drafted until now.

The researchers made an unexpected discovery as they analyzed the newly identified fragile sites. They found that many of those fragile sites were located in regions of the genome that contained inactive genes. "This observation was quite surprising, commented Dr. Robert, because previous studies suggested, on the contrary, that the most active genes

were more at risk." Pushing their investigation further, the scientists found that the way in which inactive genes were "wrapped" was what made them most fragile. "Inactive genes are wrapped more tightly than active genes, and our results suggest that this wrapping makes them more vulnerable. This comes as a surprise. Intuitively, one would have thought that this tight wrapping would have provided a greater protection."

DNA damages tend to occur at these fragile sites and they play a key role in cancers. Since the methods that were used for this study can easily be adapted to human cells, this key phenomenon in cancer development could be better understood.

"The research that Drs. Durocher and Robert and their teams have undertaken improves our ability to identify changes in DNA, and increases our understanding of how these changes influence the likelihood of developing cancer," said Dr. Morag Park, Scientific Director of the Institute of Cancer Research, part of the Canadian Institutes of Health Research (CIHR), the Government of Canada's health research agency. "CIHR is proud to support the work of Canadian researchers who are illuminating the mechanisms that lead to formation of cancerous cells, which can lead to preventative therapies as well as more effective treatments for those already afflicted with cancer."

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More information:
http://www.nature.com/nsmb/journal/vaop/ncurrent/index.html

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