UNIVERSITÉ DE GENÈVE

PRESS RELEASE

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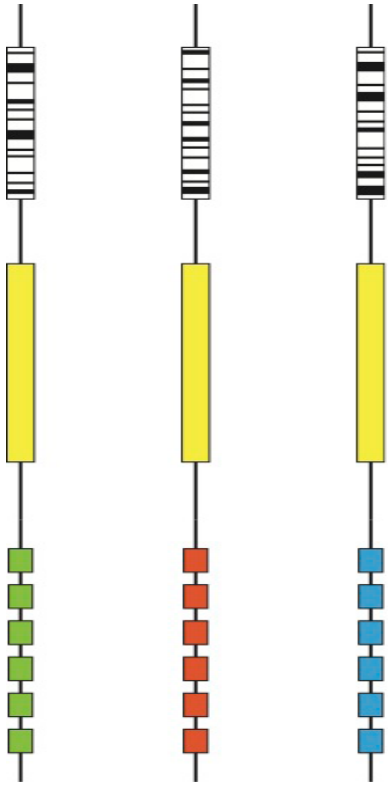
Barcodes to identify gene regulators

The same DNA is present in every cell of an organism, but only some genes are expressed in a given cell. These genes are activated by proteins called transcription factors, in response to various biological signals. Transcription factors thus regulate most of the cellular processes, both in health and disease. A group of biologists from the University of Geneva (UNIGE), Switzerland, has developed a novel technology to identify all the transcription factors involved in any process and in response to any signal. The applications of this method, published in the journal *Genes & Development*, are virtually unlimited, whether in the medical field or that of basic biology.

Each of our cells produces certain proteins following a signal, like a pancreatic cell synthesizing insulin or a white blood cell secreting antibodies to neutralize micro-organisms. Once detected by the cell, the signal activates a biochemical cascade to stimulate the expression of a given gene. The transcription factor responsible for activating this gene binds to specific DNA sequences in a region called 'promoter', located upstream of the gene.



Examples of promoters of the library, containing random repeated DNA sequences (different colors), followed by a luminescent marker (yellow) and genetic barcodes.
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Random DNA for an accurate targeting

'There are more than 1,000 human transcription factors that regulate most of the cellular processes. Simultaneously identifying all of those involved in various functions would save a lot of time in many basic and applied biology research projects', says Ueli Schibler, professor emeritus at the Department of Molecular Biology of the UNIGE Faculty of Science. To this end, the biologist and his group have developed an original technique of screening. 'We built a library consisting of more than 3,000 promoters composed of repeated random DNA sequences, followed by a luminescent marker and genetic barcodes. The repetition of random sequences greatly increases the likelihood of identifying a specific transcription factor', explains Pauline Gosselin, a researcher of the group and first co-author of the article.

All of these promoters were introduced into human cells in culture before stimulating the cells with a signal. 'The synthetic genes of the library activated by this signal are transcribed into messenger RNAs. We then trace them by identifying the barcodes with which they are associated. Finally, the repeated

random DNA sequences contained in these promoters allows to pick up the transcription factors that bind to these sequences, in an existing database', says Gianpaolo Rando, a researcher of the Geneva team and first co-author of the study.

A universal pioneering tool

This method, named *BarCoded Synthetic TAndem Repeat PROMoter* (BC-STAR-PROM) *screening*, is based on a technique developed within the group in 2013. 'We optimized it in order to monitor the activity of some 3,000 promoters simultaneously in a single experiment, rather than introducing promoters one by one into the cells. This represents a tremendous saving of time and work', says Ueli Schibler.

The BC-STAR-PROM technology can be applied to any research project aimed at exploring the cellular effect of a biological signal or of a chemical. This pioneering tool, whose applications are countless, enables for example to identify the transcription factors activated - or inhibited - by a drug, an infection, or a treatment under development. Using their method, the Geneva researchers have already identified the transcription factor stimulated by vinblastine, a drug used in chemotherapy to treat different types of tumors.

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