Scientists discover genes are controlled by 'nano footballs'

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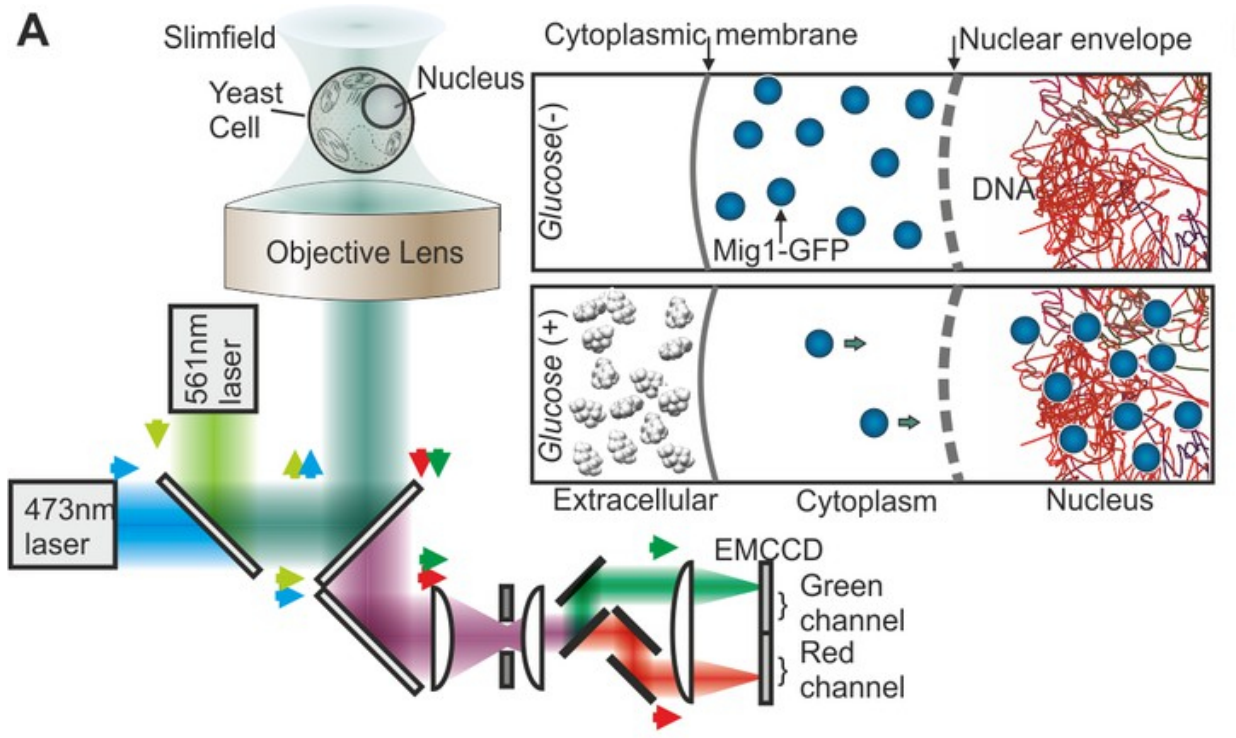

Dual-color fluorescence microscopy assay. Credit: *eLife*, doi.org/10.7554/eLife.27451.001

Research at the University of York has revealed that genes are controlled by 'nano footballs' - structures that look like footballs but 10 million times smaller than the average ball.

By placing tiny glowing probes on transcription factors - special chemicals inside cells which control whether a gene is switched 'on' or 'off' - researchers gained a remarkable new insight into the way in which genes are controlled.

Crucially, they discovered that transcription factors operate not as single molecules as was previously thought, but as a spherical football-like cluster of around seven to ten molecules of roughly 30 nanometres in diameter.

The discovery of these nano footballs will not only help researchers understand more about the basic ways in which genes operate, but may also provide important insights into human health problems associated with a range of different genetic disorders, including cancer.

The research, supported by the Biotechnology and Biological Sciences Research Council (BBSRC) and published in *eLife* was carried out by scientists from the University of York, and the University of Gothenburg and Chalmers University of Technology, Sweden. The researchers employed advanced super-resolution microscopy to look at the nano footballs in real time, using the same type of yeast cells utilised in baking and brewing beer.

Professor Mark Leake, Chair of Biological Physics at the University of York who led the work, said: "Our ability to see inside living cells, one molecule at a time, is simply breathtaking.

"We had no idea that we would discover that transcription factors operated in this clustered way. The textbooks all suggested that single molecules were used to switch genes on and off, not these crazy nano footballs that we observed."

The team believe the clustering process is due to an ingenious strategy of

the cell to allow transcription factors to reach their target genes as quickly as possible.

Professor Leake said: "We found out that the size of these nano footballs is a remarkably close match to the gaps between DNA when it is scrunched up inside a cell. As the DNA inside a nucleus is really squeezed in, you get little gaps between separate strands of DNA which are like the mesh in a fishing net. The size of this mesh is really close to the size of the nano footballs we see.

"This means that nano footballs can roll along segments of DNA but then hop to another nearby segment. This allows the nano football to find the specific gene it controls much more quickly than if no nano hopping was possible. In other words, cells can respond as quickly as possible to signals from the outside, which is an enormous advantage in the fight for survival."

Genes are made from DNA, the so-called molecule of life. Since the discovery that DNA has a double helix shape, made in the 1950s by pioneering biophysics researchers, much has been learned about transcription factors which can control whether a gene is switched on or off. If a gene is switched on, specialised molecular machinery in the cell reads off its genetic code and converts it into a single protein molecule. Thousands of different types of protein molecules can then be made, and when they interact that can drive the building of all of the remarkable structures found inside living cells.

The process of controlling which genes are switched on or off at any particular point in time is fundamental to all life. When it goes wrong, this can lead to serious health problems. In particular, dysfunctional switching of genes can result in cells which grow and divide uncontrollably, which can ultimately lead to cancer.

This new research may help provide insights into human health problems associated with a range of different genetic disorders. The next stages will be to extend this research into more complicated types of cells than yeast - and ultimately into human cells.

More information: Transcription factor clusters regulate genes in eukaryotic cells, *eLife*, doi.org/10.7554/eLife.27451 , elifesciences.org/articles/27451

Provided by University of York