How proteins find their way on chromosomes

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A research team at Uppsala University has managed to clarify how proteins that regulate the activity of genes quickly find their way on chromosomes among millions of possible binding sites. The study also confirms a more than 30-year-old theory about the process. The findings are being published today in the scientific journal *Science*.

Protein synthesis is one of life's absolutely most central processes, and its correct functioning is of great importance for whether we are healthy or ill.

The production of a certain protein in cells starts with the corresponding gene on the chromosome. This production is to a great extent regulated by other proteins, so-called transcription factors, that stimulate or block production by binding to the DNA, close to the relevant gene.

These thermostat-like regulatory systems enable the cell to shut down the production of certain proteins if they are not needed at a given time. Production can also be quickly turned on when changes in the cell's environment call for new functions. For this regulation to have a rapid response time, it's necessary for bound transcription factors to be able to be released from the DNA at a given signal, but also for them to be able find their way back quickly. In the bacterium Escherichia coli this involves locating a unique DNA sequence among nearly five million incorrect sites on the chromosome.

- We have studied how transcription factors find their specific sites on the chromosome and how quickly they do so. It turns out they scan some

40 DNA base pairs at a time by sliding along the DNA filament and then testing a new chromosomal region, says Royal Academy Research Fellow Johan Elf, whose team has been addressing this question for several years.

A theory of how the right genes are found was proposed by Uppsala researcher Otto Berg more than thirty years ago. Now Johan Elf's group shows that the theoretical predictions are correct by using newly developed microscopy that is so sensitive that it's possible to see individual protein molecules in living cells.

- The findings show that problems that previously could only be studied using biochemistry in test tubes can now also be investigated in living cells. The study also stresses the usefulness of combining advanced new measurement technology with detailed physiochemical models to break new ground in molecular biology, says Petter Hammar, a doctoral candidate at the Department of Cell and Molecular Biology.

Provided by Uppsala University