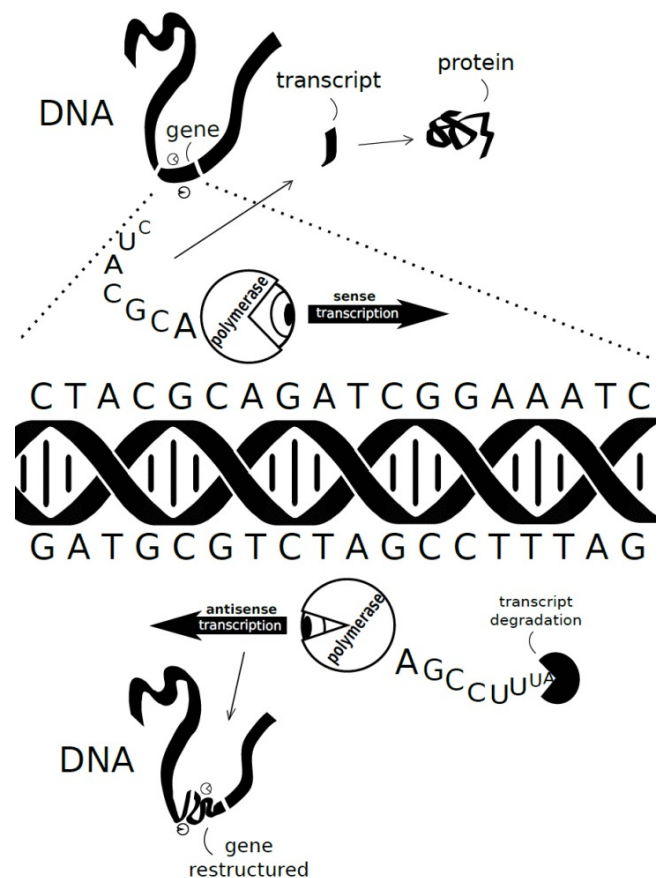


## Genes are read backwards to restructure our DNA

In English, we read in one direction – from left to right across the page. We need to read words in a certain order, so that the information makes sense to us.

In the cells of our bodies, our DNA contains a complicated code. This code contains our genes - genetic 'blueprints' for creating proteins, such as insulin, or the enzymes that break down alcohol in our livers. As with written languages, genes must also be 'read' in one direction, in order for their code to make sense. Just as reading a sentence backwards would produce nonsense, reading a gene backwards also produces nonsense.



The actual 'reading' in our cells is performed by polymerases, enzymes that attach to the start of our genes, scan along to the end, reading the code and producing an identical string of code as they go. It's like someone transcribing a single sentence of a large book to a smaller piece of paper. In fact, this process is called transcription, and is the way in which the information in our genes is passed on to the machinery that makes our proteins, translating the language of DNA into the language of proteins.

However, in recent years it has become clear that genes are in fact read backwards. Growing evidence shows that polymerases jump on to genes at their ends – like starting a sentence at a full stop – and move backwards along the gene, transcribing the information and producing a transcript. This transcript is nonsense, however, and the protein machinery is unable to make sense of it. This process of backwards reading is called antisense transcription, and its presence has been the source of much confusion.

On the face of it, it seems pointless to be reading genes backwards. No protein can be made from it, and the transcript itself is usually quickly destroyed. However, recent work in our lab demonstrates that it may in fact play a very important role within our cells, and that it is the action of the polymerases reading backwards that is critical to this.

Our cells contain a lot of DNA. If you were take the DNA from a single cell in your body, and lay it out end to end, it would stretch to 2 metres. All the DNA in your body would stretch to the sun and back more than fifty times. DNA must therefore be very tightly wound in order to fit inside a cell. To achieve this, DNA is wrapped around proteins called histones. The DNA in our cells is not a long linear string, but is in fact a complex, ordered three-dimensional structure. This structure effects how genes are read – depending on how our DNA is wrapped, some genes are more readily accessible to the polymerases than others. It also changes between cells – the DNA in our liver cells is wound up very differently to the DNA in our neurons.

Our recent work has found that these backwards-reading polymerases dramatically change how a gene is packaged, in ways that make its structure more dynamic. This could be essential in reforming the structure of our DNA response to external changes – for example, to allow different genes to be activated after a meal. Others have found that antisense transcription is present during embryonic development, and our work sheds light on why this may be necessary. The backwards reading of genes could make the structure of our DNA more fluid, allowing it to change as our cells proliferate and our bodies develop. Our work could have important ramifications for our understanding of developmental disorders and proliferative diseases like cancer.

## **Publication**

[Sense and antisense transcription are associated with distinct chromatin architectures across genes.](#)

Murray SC, Haenni S, Howe FS, Fischl H, Chocian K, Nair A, Mellor J.  
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