

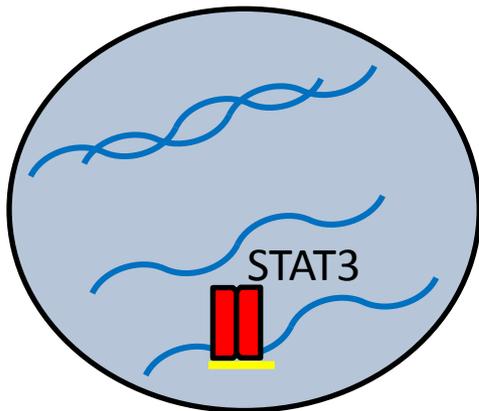
What are transcription factors?

Background:

- Protein products made from genes will have specific functions in the cell. One type of protein product is called a transcription factor. Transcription factors are proteins with a specific job: they bind the regulatory/non-coding DNA of a gene which will then cause the gene (coding DNA) to be expressed (transcribe into RNA).
- If a transcription factor is not present, then theoretically nothing will bind that DNA regulatory sequence and the gene is not expressed.
- One transcription factor that is being studied in the Loughran lab and is known to cause dysfunction in LGL cells is STAT (Signal Transducer and Activation of Transcription). There are at least 7 STAT proteins, but the lab focuses on STAT3 and STAT5b.

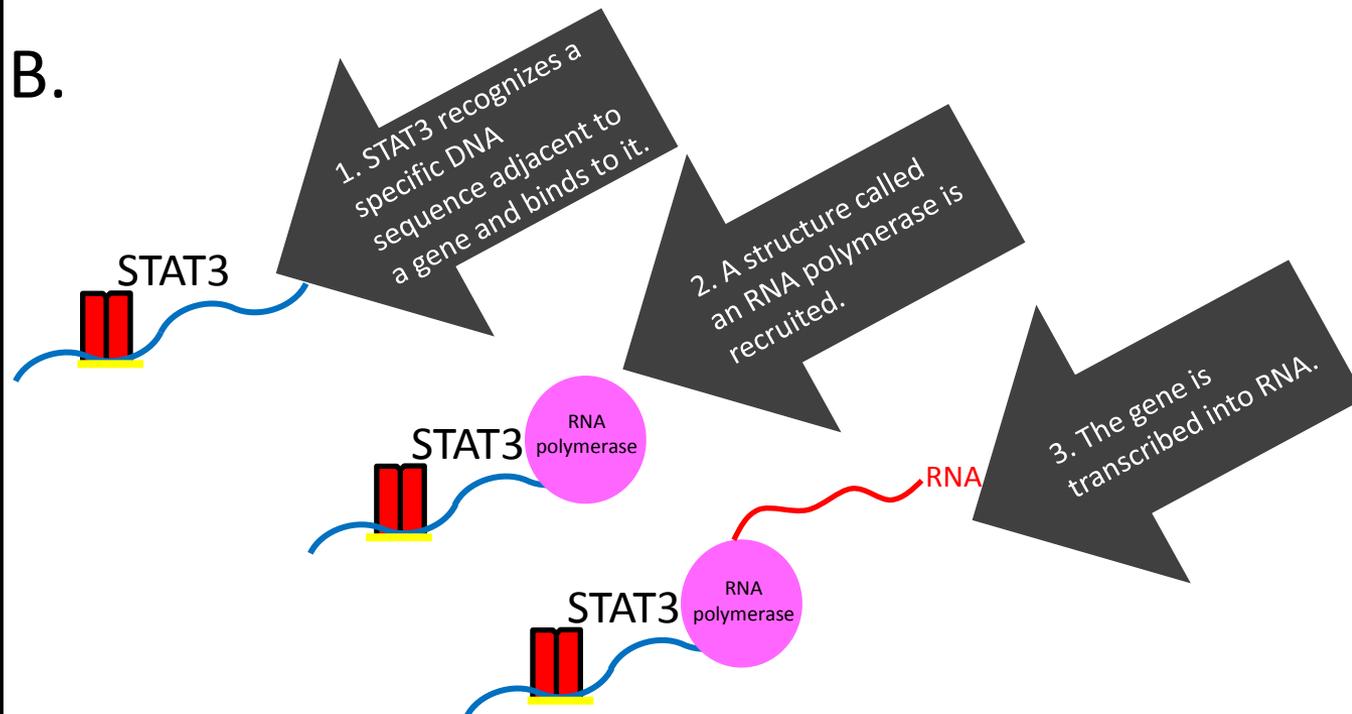
Panels A and B are described in more detail on the next page.

A.

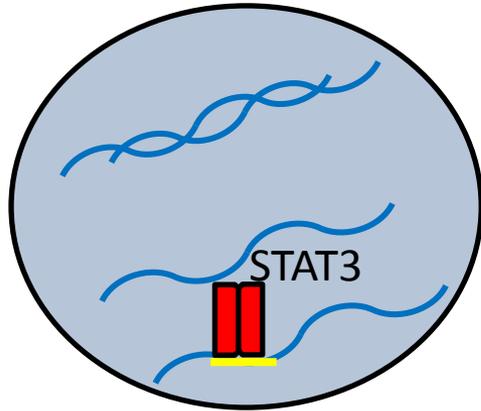


Nucleus of a cell

B.



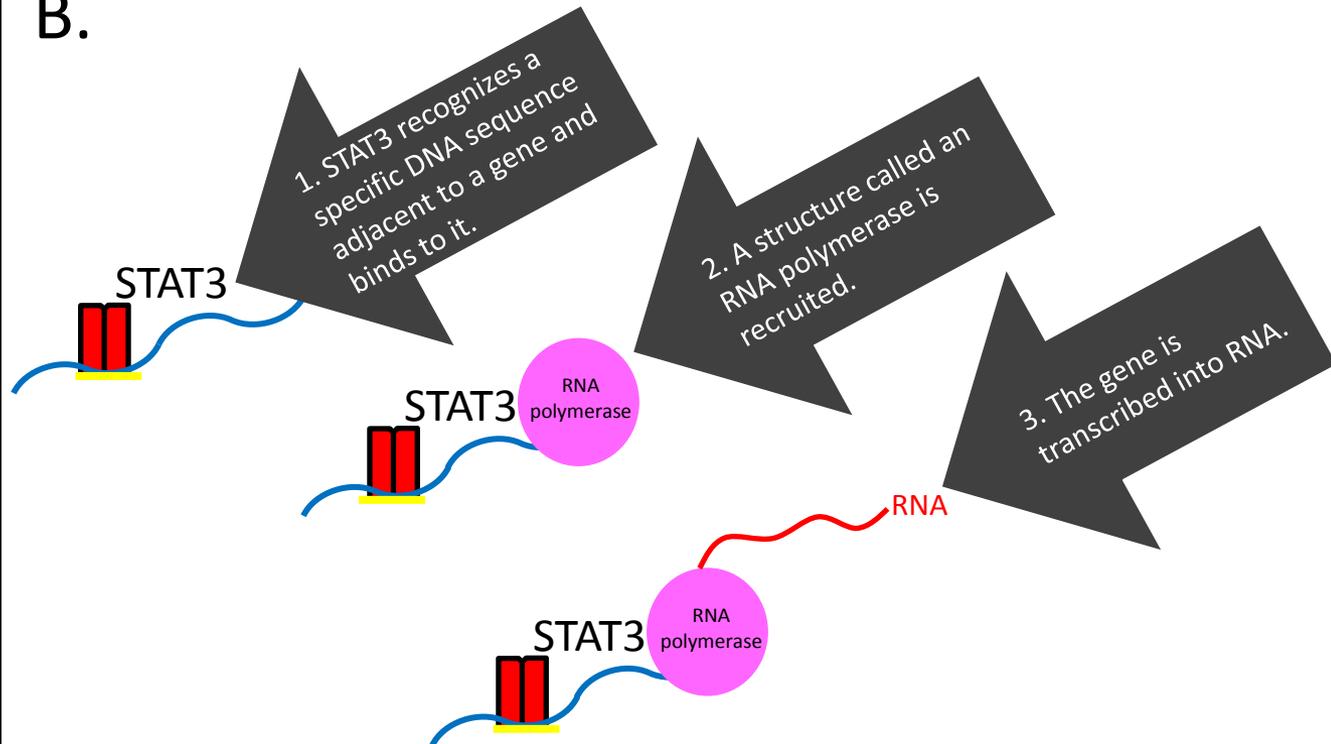
A.



Nucleus of a cell

The nucleus of a generic cell is depicted with STAT3, a transcription factor, binding to single stranded DNA.

B.



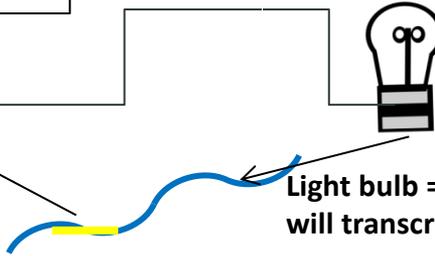
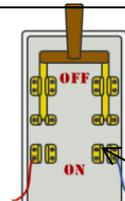
The process of STAT3, a transcription factor, binding to a regulatory/non-coding region (in yellow) of a gene is shown. This process occurs in the nucleus. In step 1, STAT3 recognizes a specific DNA sequence (the regulatory/non-coding region that only it can bind to), and binds to it. In step 2, a structure called the RNA polymerase is recruited. This is composed of many proteins bound together but shown as a circle for simplicity. In step 3, the polymerase transcribes the gene into RNA (uses the DNA sequence/building blocks to match RNA building blocks, creating a single strand of RNA). In reality, there are other factors, not described here, which assist in the process.

Analogy to describe how transcription factors turn on gene expression

- STAT is a transcription factor that must exist as a dimer (two STAT proteins bound together) in order to function. A STAT monomer (1 protein) alone does not function as a transcription factor.
- Let's say that 1 person is a STAT protein (monomer).
- A light switch is the regulatory/non-coding part of a gene (where the STAT dimer will bind)
- A light bulb is the gene that STAT will transcribe
- The light produced is the gene product (RNA).

Transcription Off

1 person =
1 STAT protein (monomer)



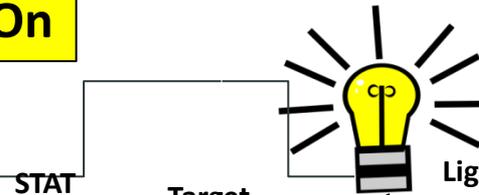
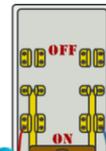
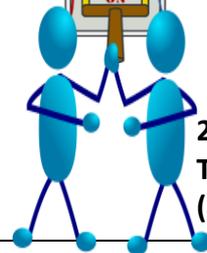
Light switch = regulatory/non-coding DNA (yellow) where the STAT dimer will bind.

Light bulb = target gene that STAT will transcribe (cause expression)

- In your house, this light switch is high up on the wall; luckily there are 2 tall people living at your house.
- It is also a difficult light switch to turn on, so 2 people need to work together to turn it on.
- In order to make light/gene product, you need the STAT to exist as a dimer (two STATs bound together). In our analogy, that means we need two people.
- This light switch is regulated because we need the strength of 2 people to turn it on, and it is high up on the wall, so only tall people can reach it. One tall person cannot turn it on because that person is not strong enough. If one person tries, then no transcription will occur (in this analogy, no light will be turned on).

Transcription On

STAT dimer



2 people holding hands = 2 STATs bound together (dimer). The dimer binds to the regulatory/non-coding region (light switch) which causes transcription of a gene.

Light produced = RNA (red wavy line)

- This is a simplistic view of transcription factors. While it is true that usually one specific factor is used, sometimes a factor with a similar property can be used. In the analogy, if 2 different tall people visited your house, then your light switch could be turned on by those people; i.e. a different transcription factor turning on a gene.