

Measuring gene expression using Microarrays

Peter Ellis

Overview

- Genes and gene expression
- What happens when a gene is expressed
- Measuring gene expression
- Expression profiling and Institute Science
- Expression profiling and the clinic

What is a gene? A gene can be defined as a unit of heredity that carries the information to make a functional molecule, usually a protein.

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Insulin gene

Collagen gene

Haemoglobin
gene

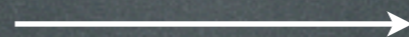
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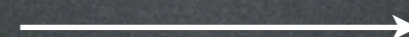
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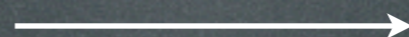
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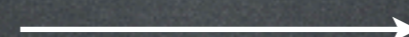
Insulin

Collagen gene



Collagen

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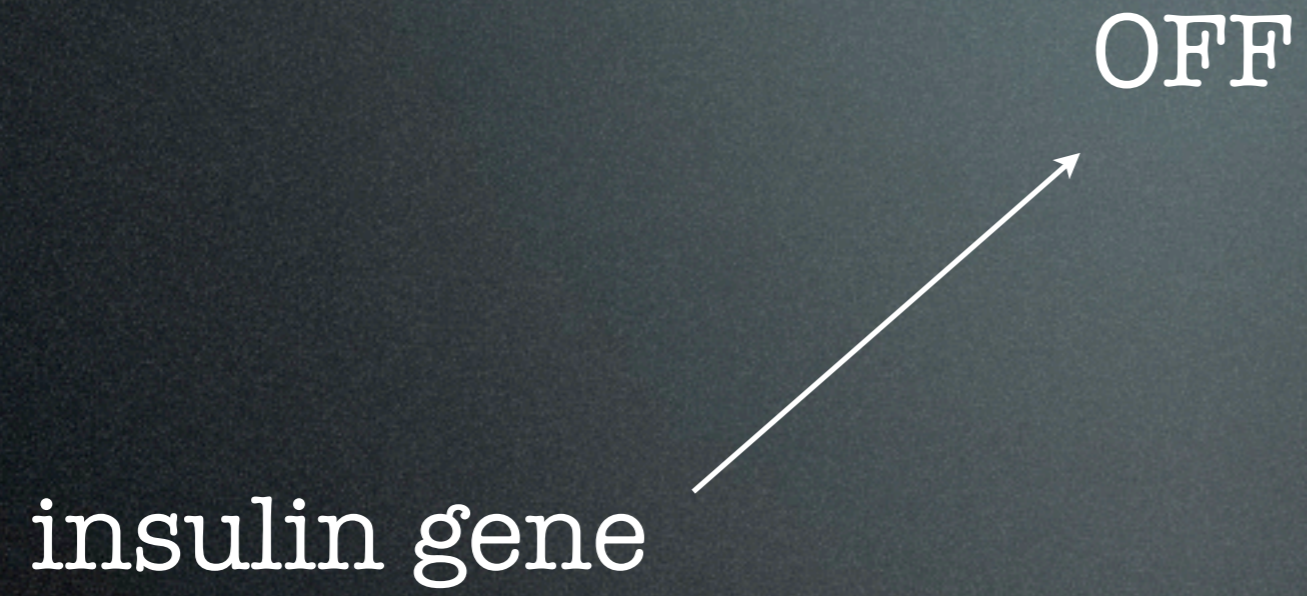
Haemoglobin

**Human genome contains
approximately 25,000 genes**

Gene expression

insulin gene

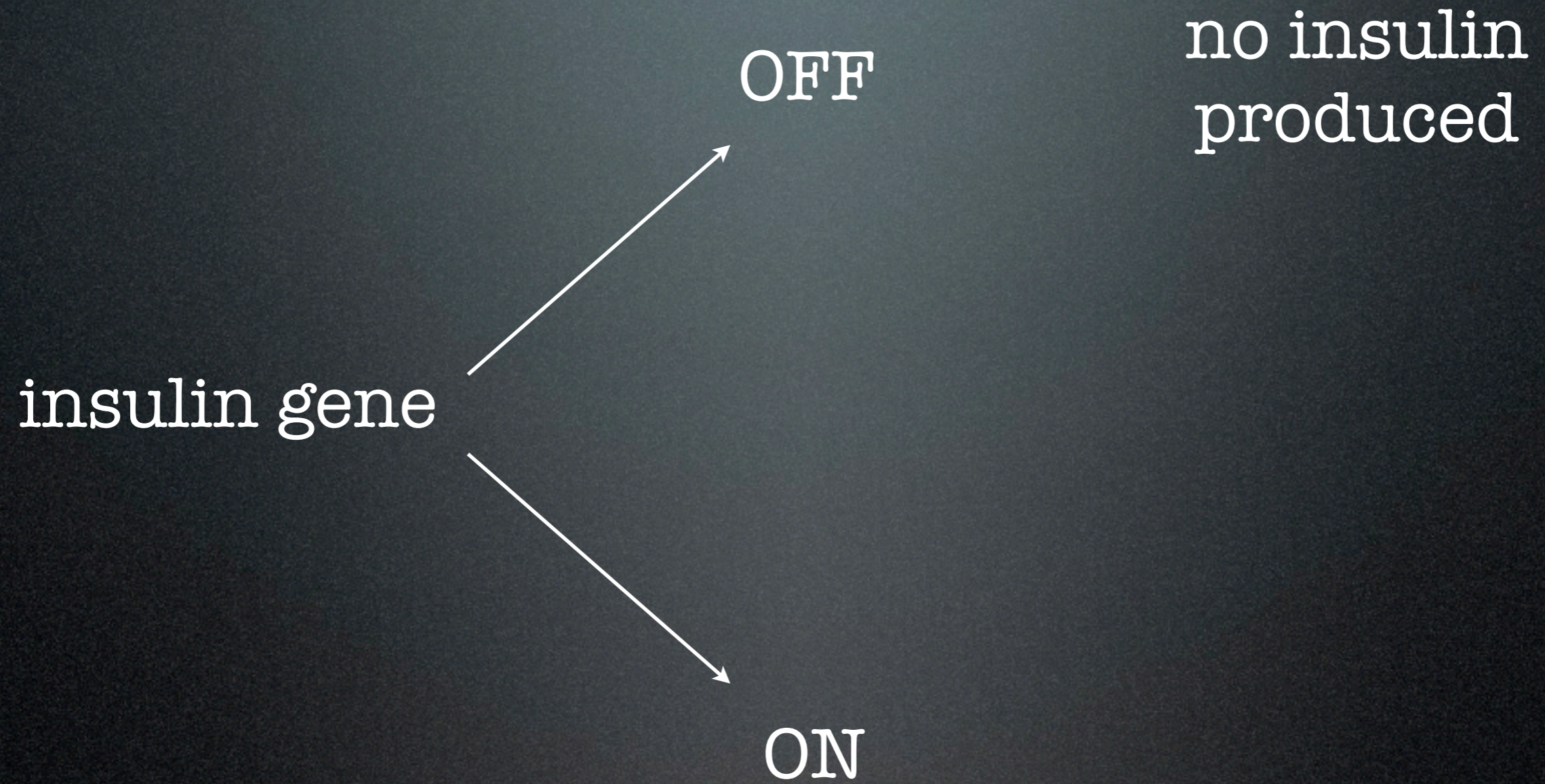
Gene expression



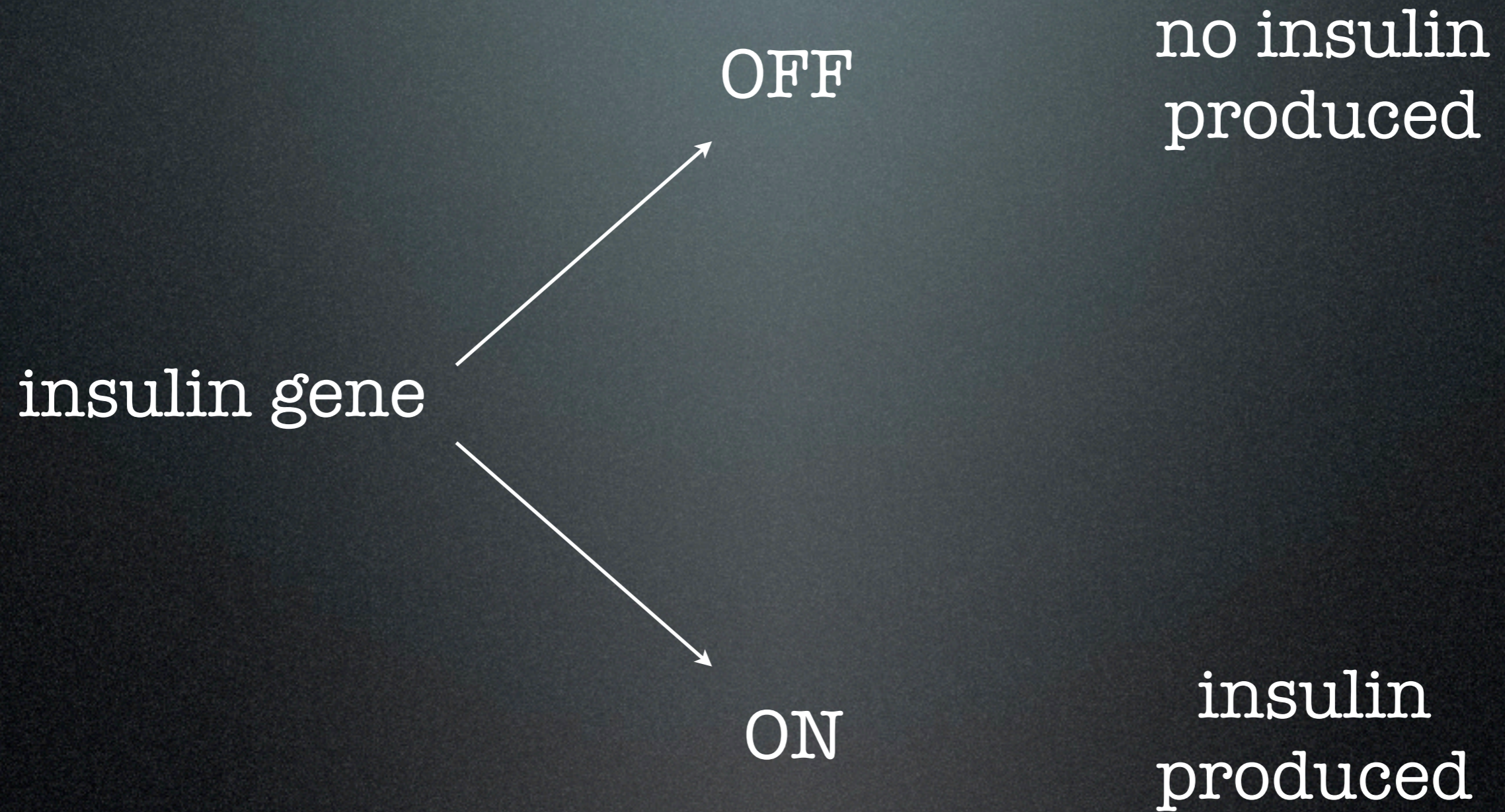
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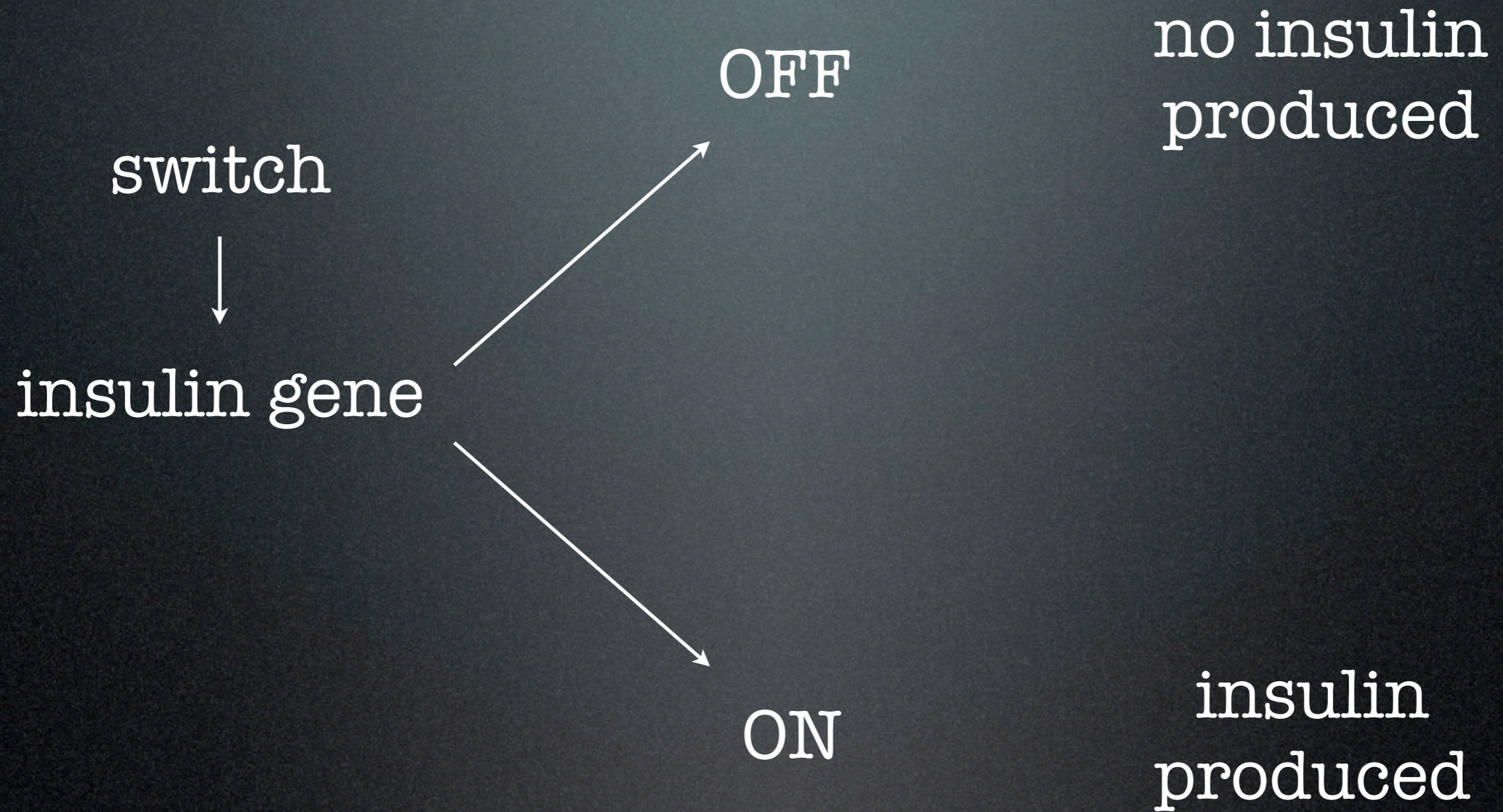
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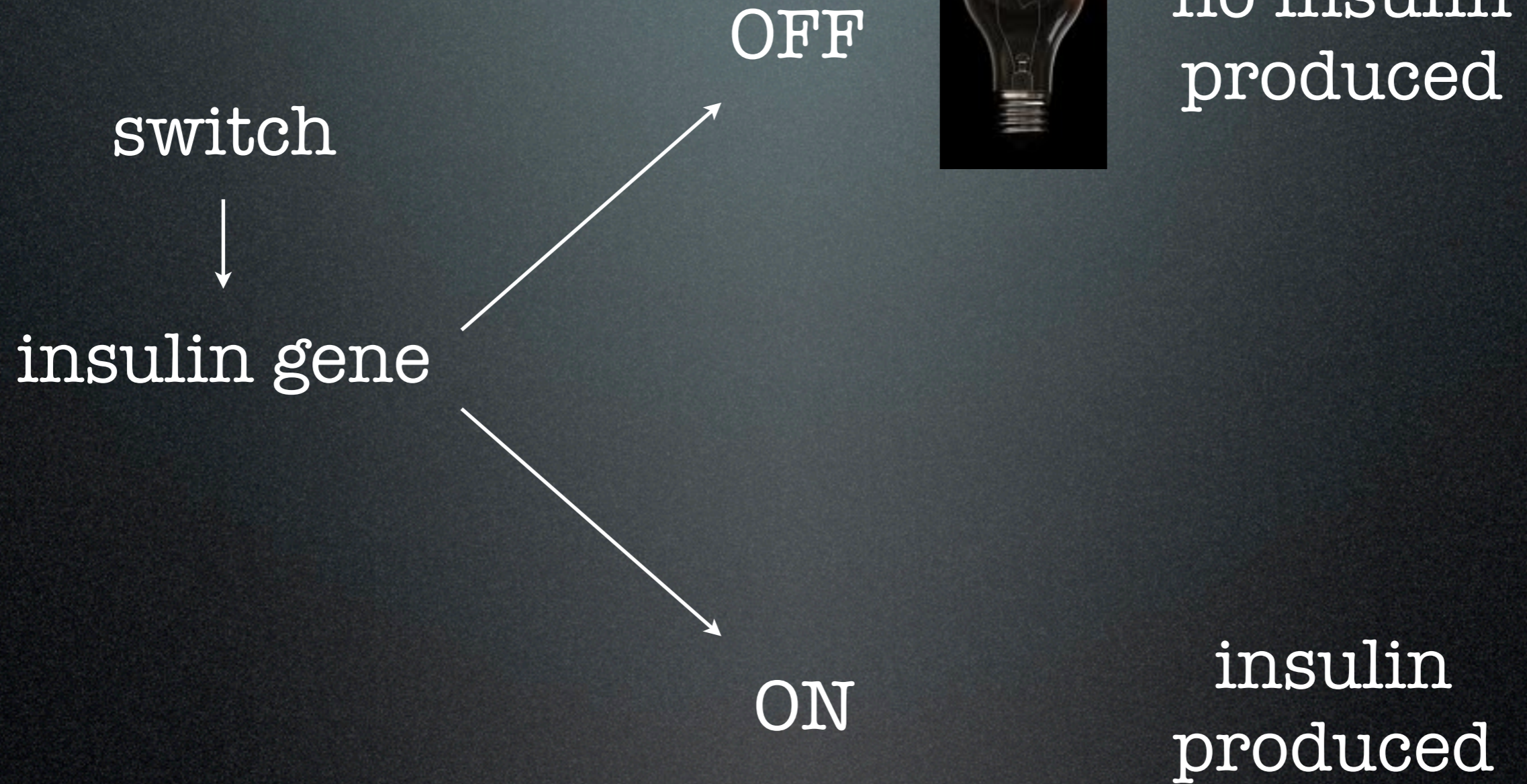
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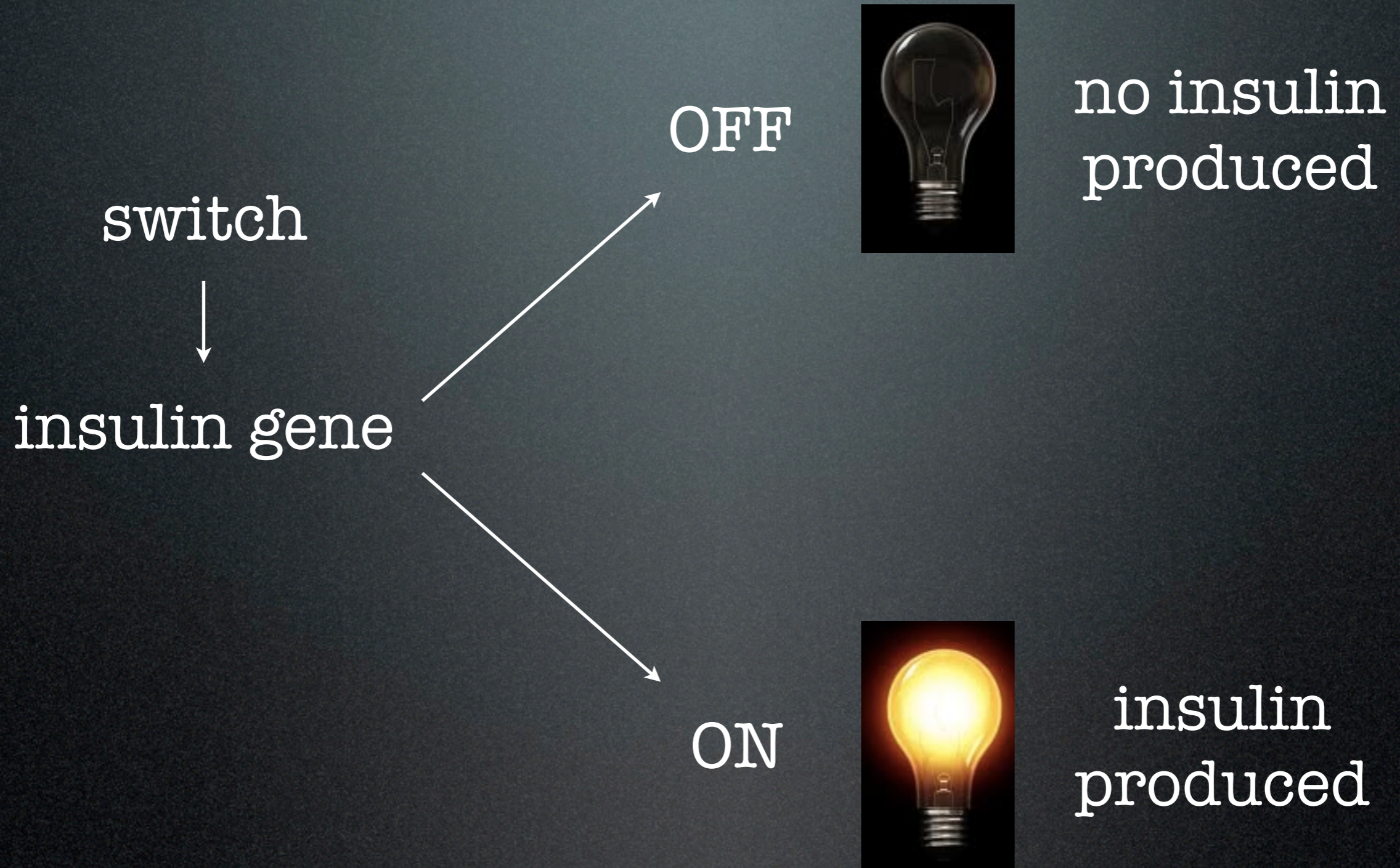
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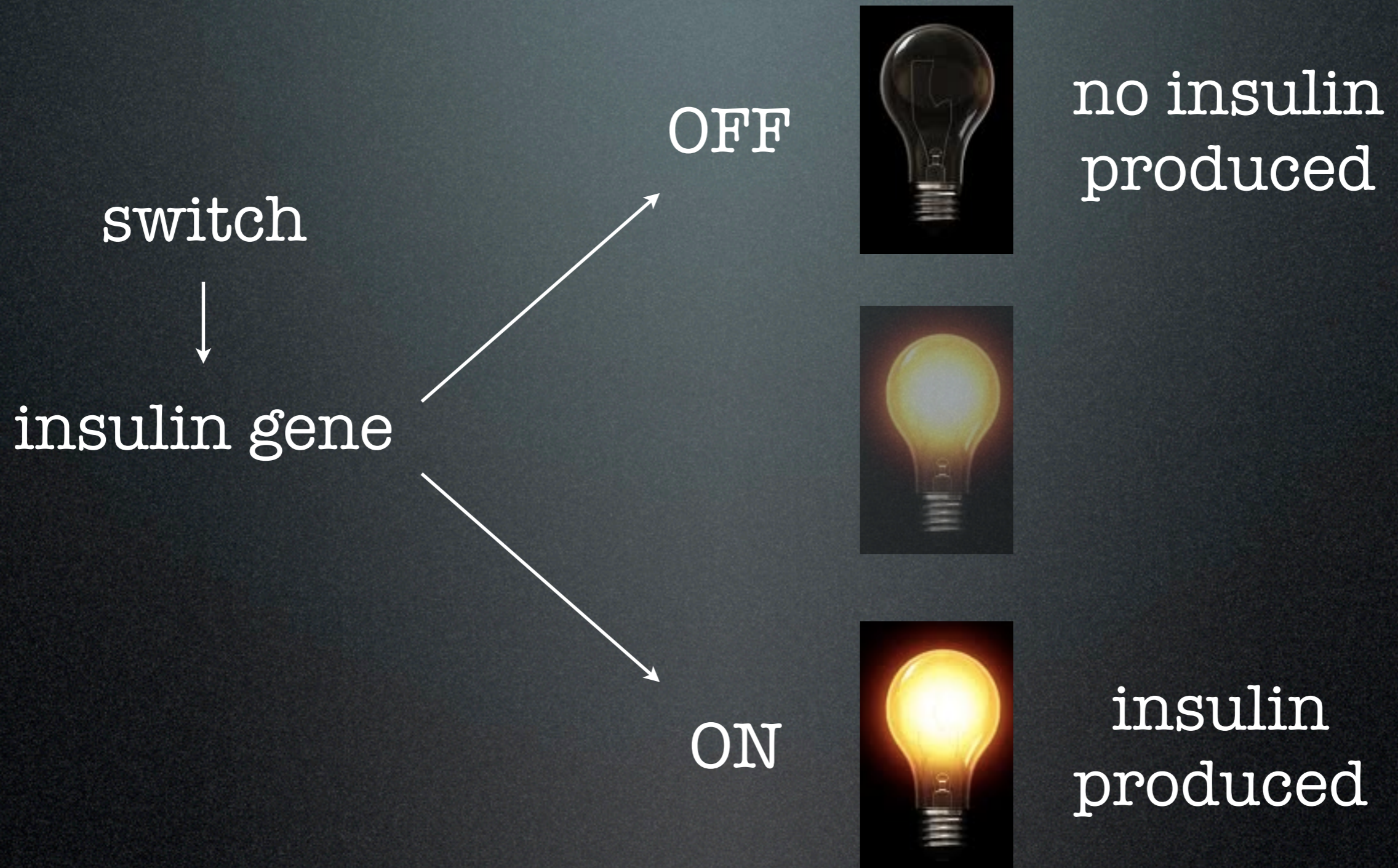
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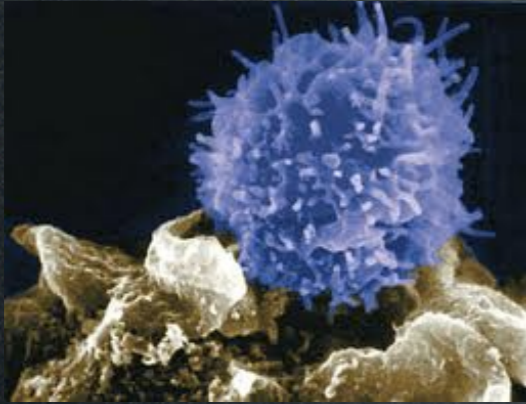
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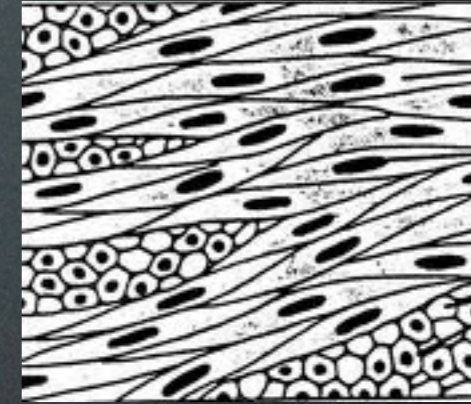
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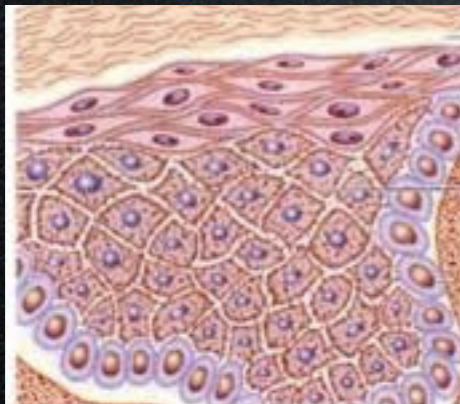
Why is understanding gene expression important?



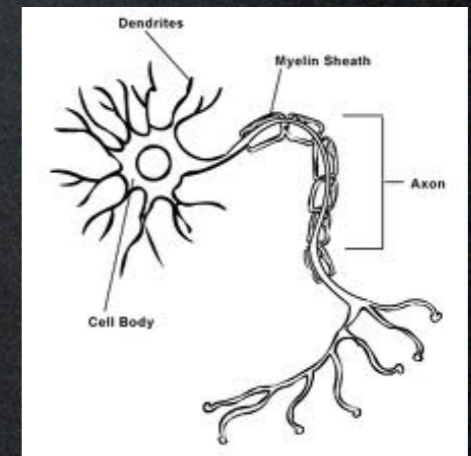
white blood cell



muscle cells

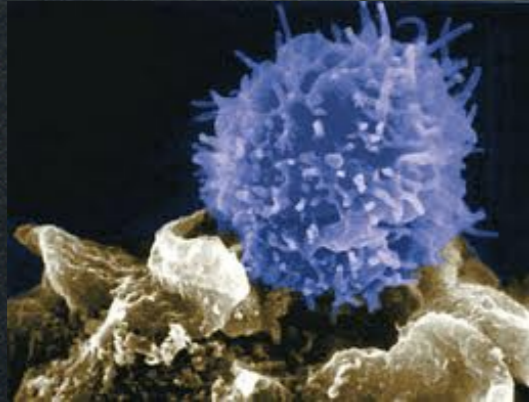


skin cells

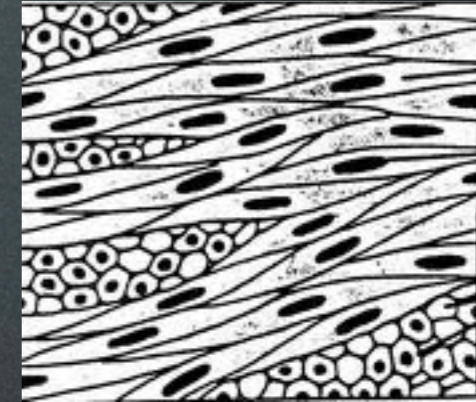


nerve cells

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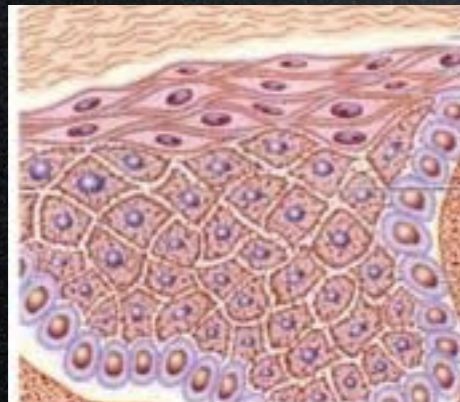


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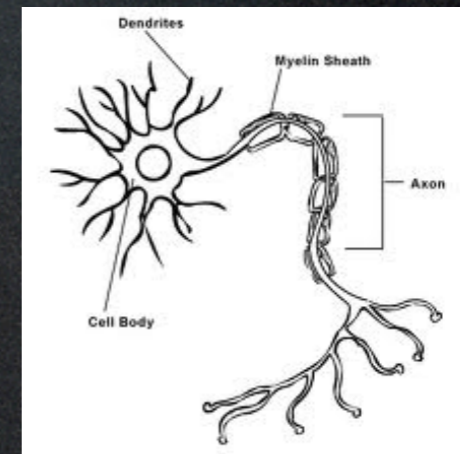


muscle cells

Same genome



skin cells



nerve cells

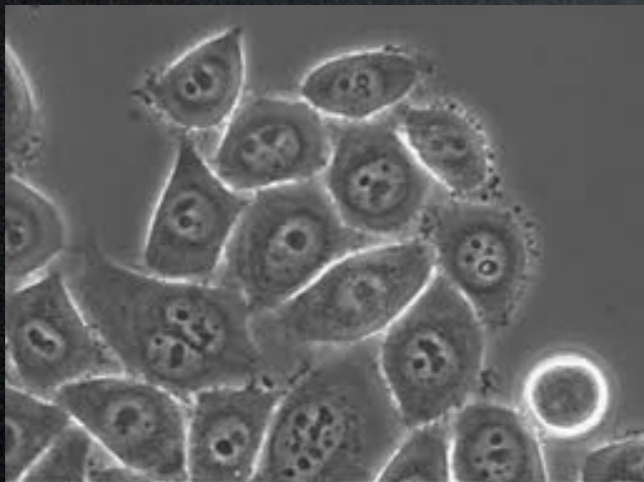
Differential gene expression in disease



healthy liver cells

What do these 2 cell populations have in common?

- Liver cells
- Morphology
- Growth



diseased liver cells

The flow of genetic information: from genes to proteins

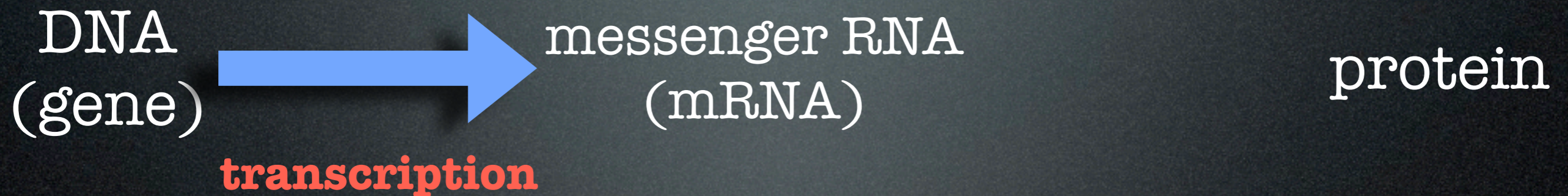
DNA
(gene)

protein

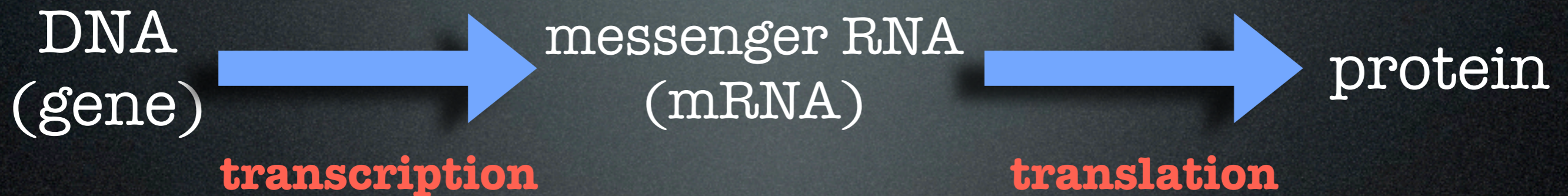
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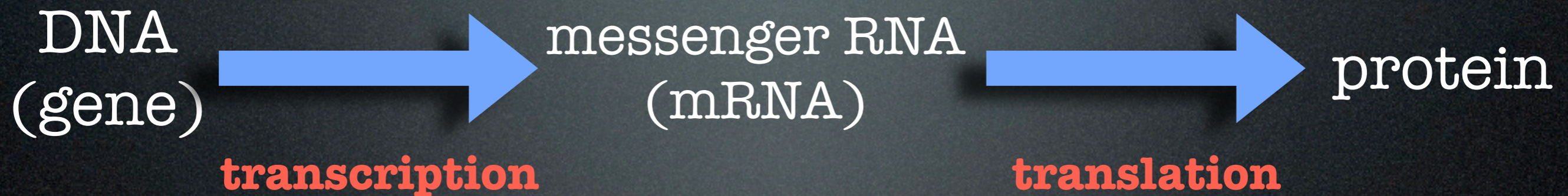
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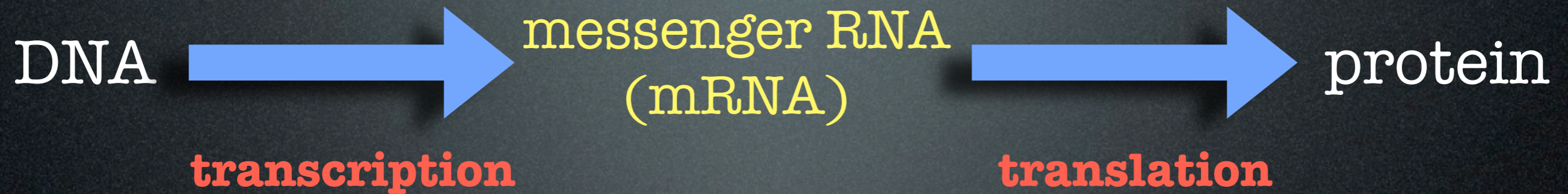


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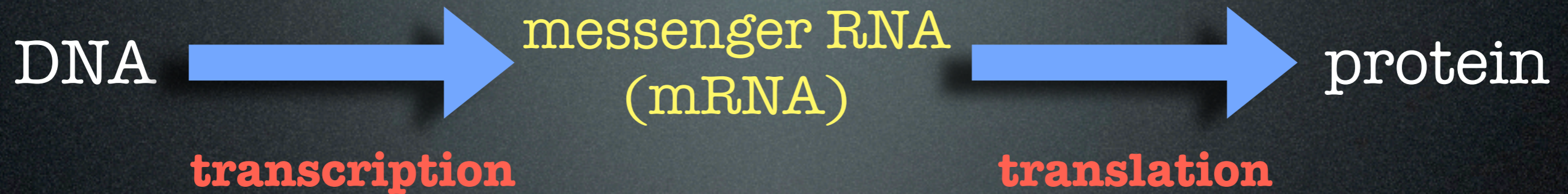


mRNA is an information-carrying intermediate

How do we measure gene expression?

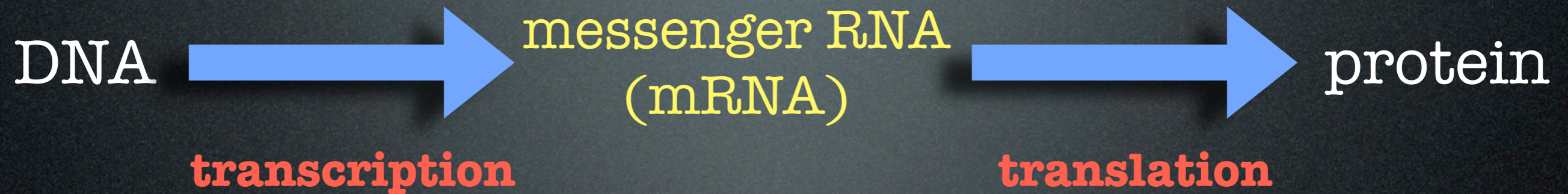


How do we measure gene expression?



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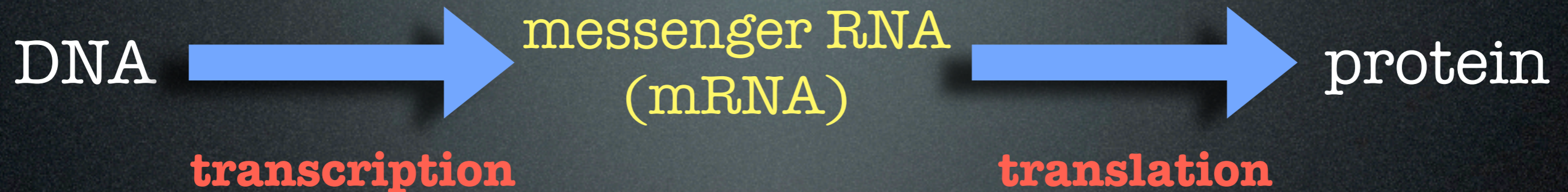
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mRNA - Yes!

Using DNA probes to measure mRNA levels

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DNA PROBE for gene B:

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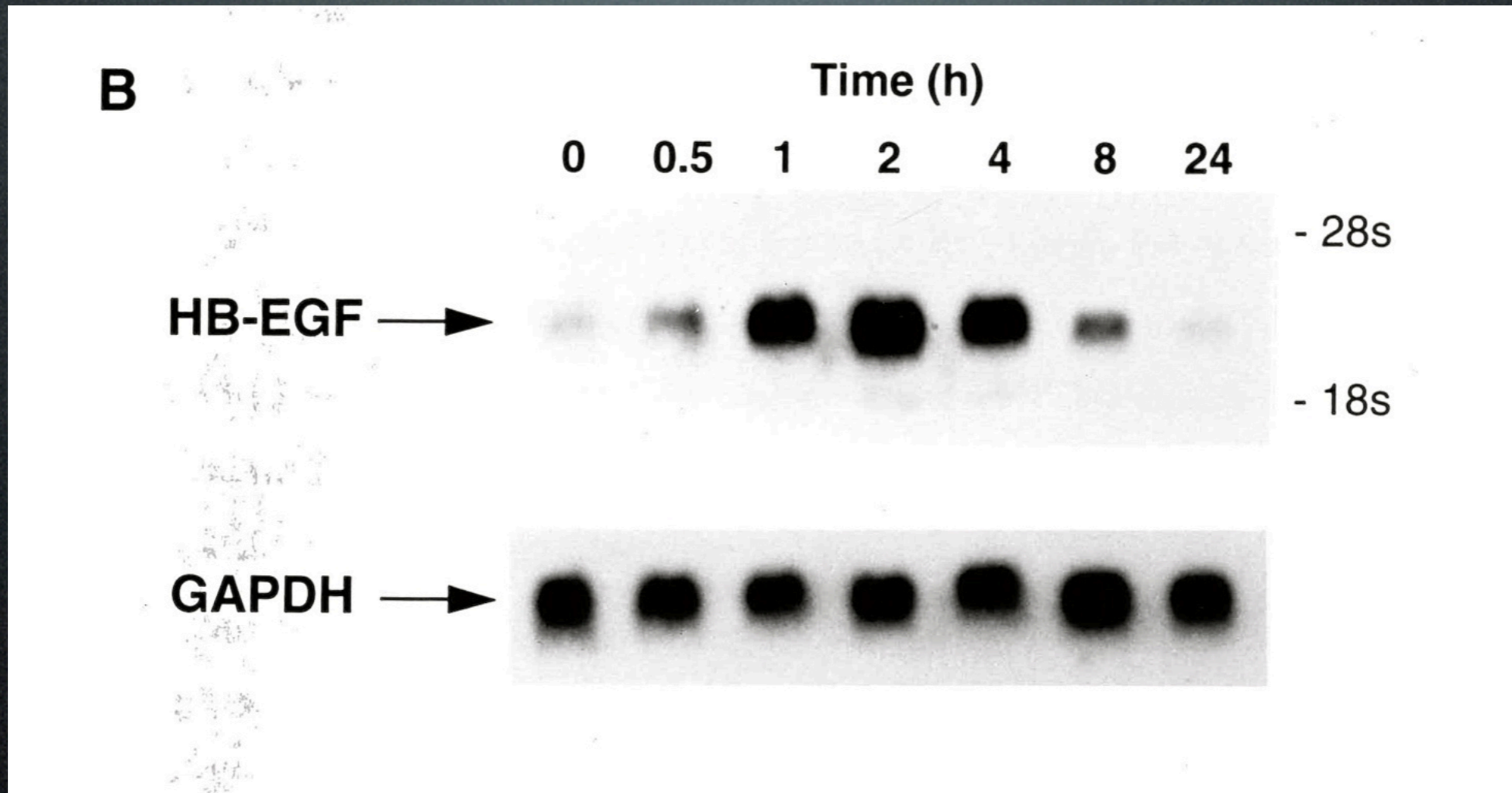


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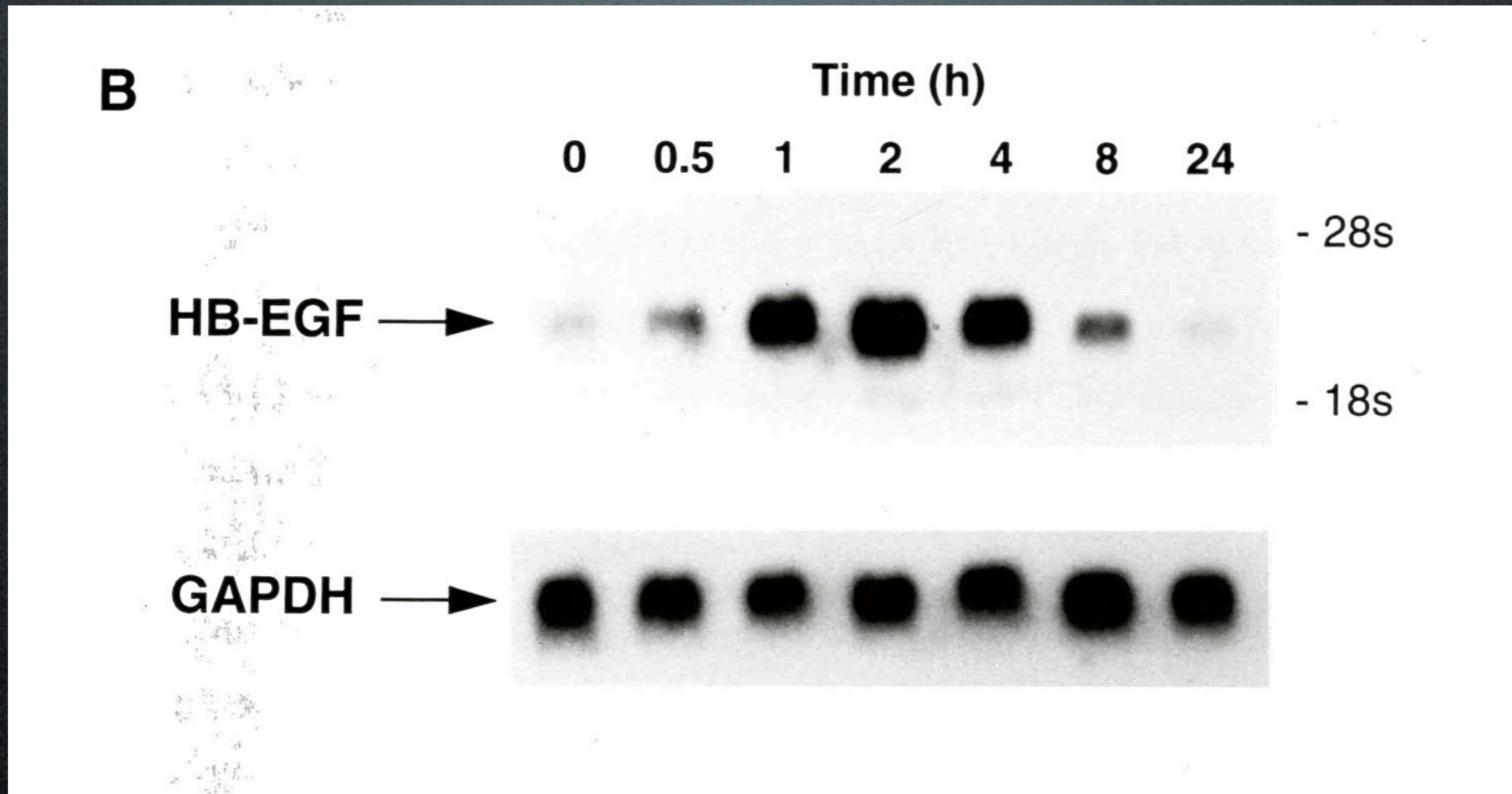
mRNA from gene D. AATGAAAAACCTATGCACTTTGTTTAGGTT

**The level of our reporter indicates the level
of mRNA from gene B in our sample**

Northern blot



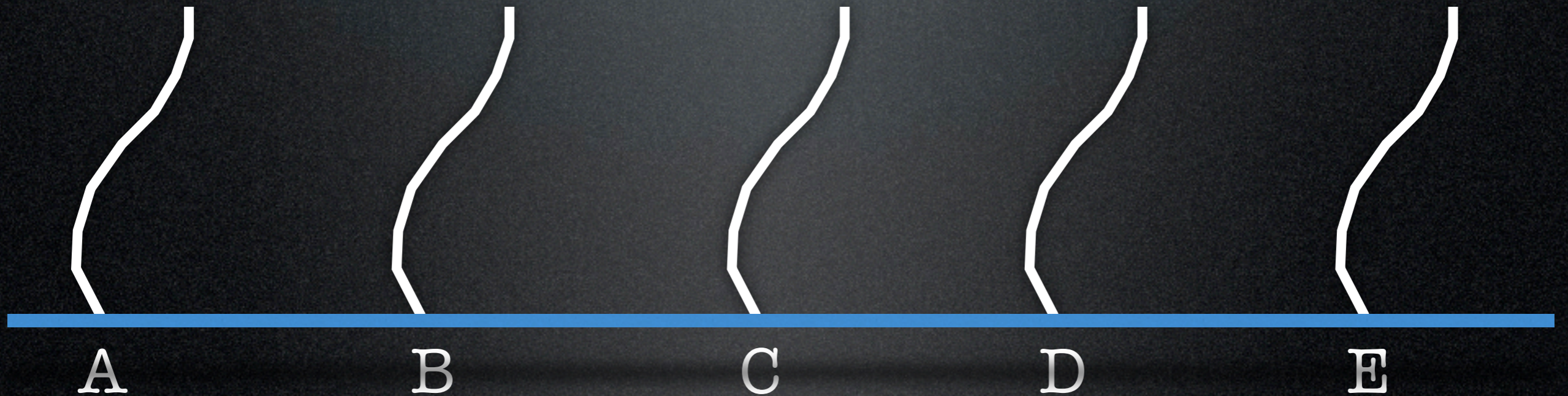
Northern blot



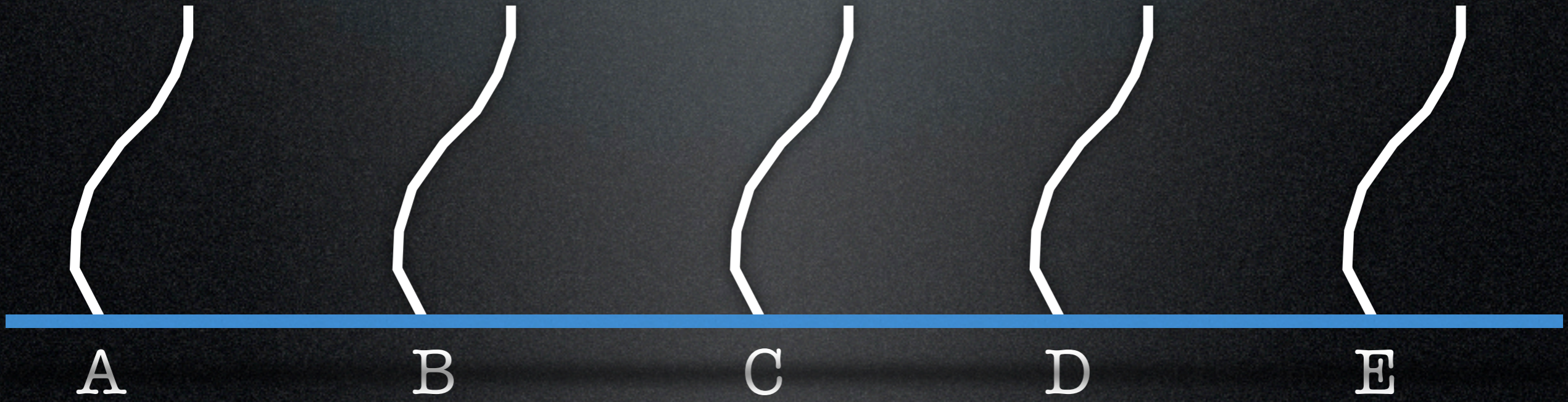
1-2 genes at a time!

What if we put several probes on a solid support and label the sample instead?

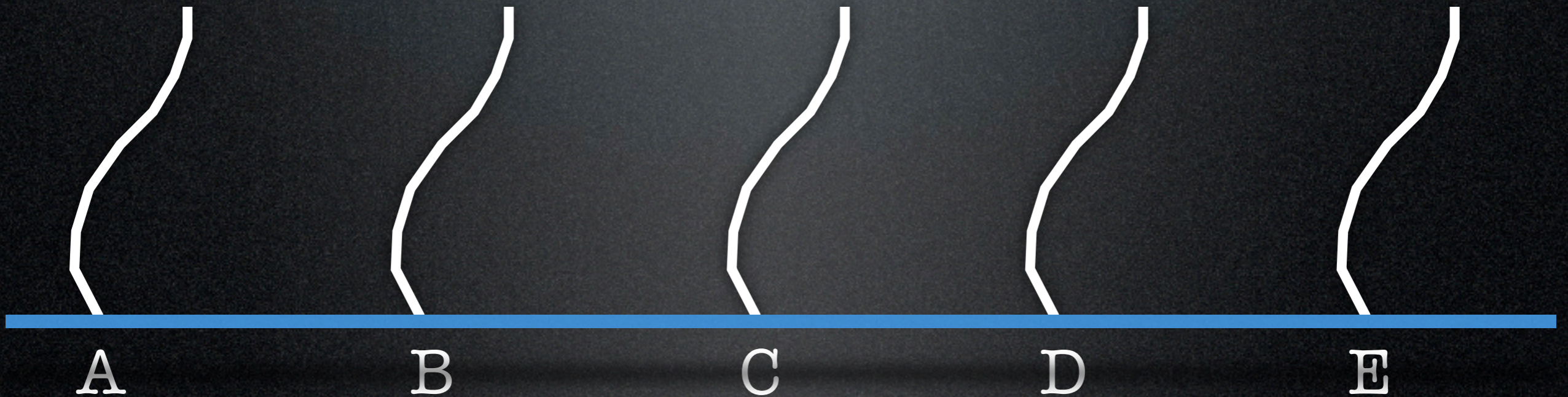
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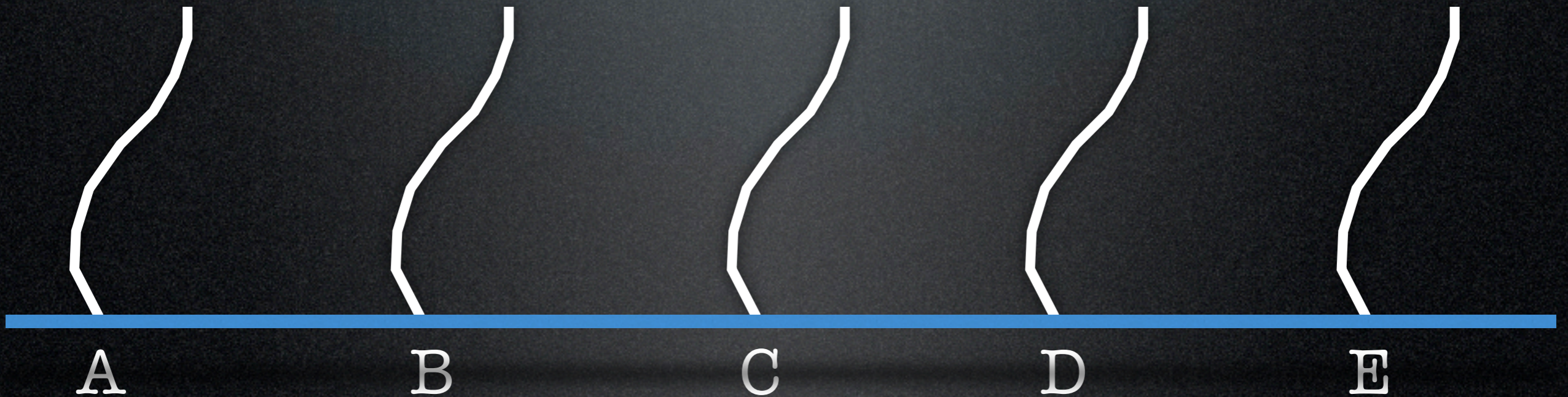
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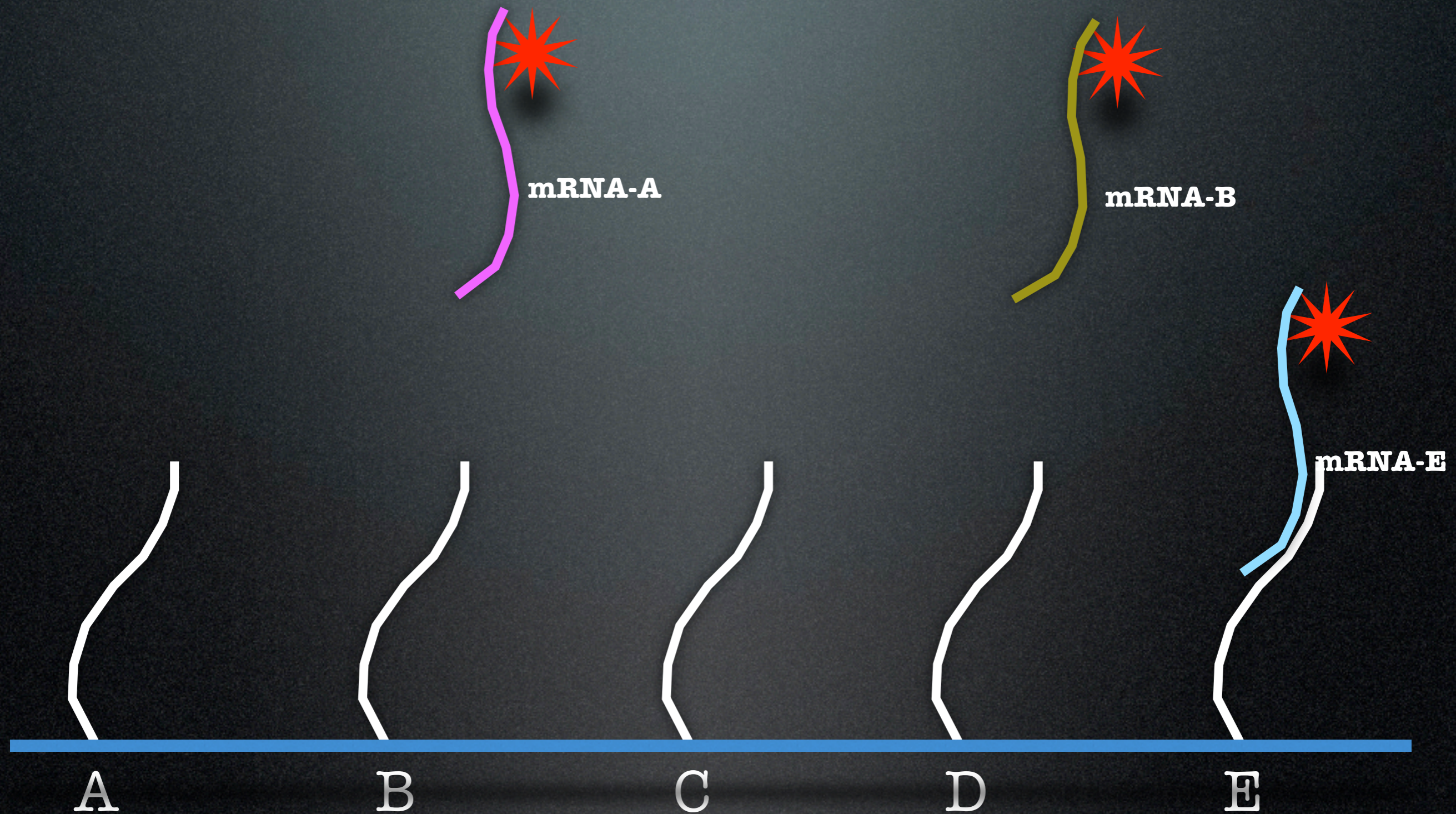
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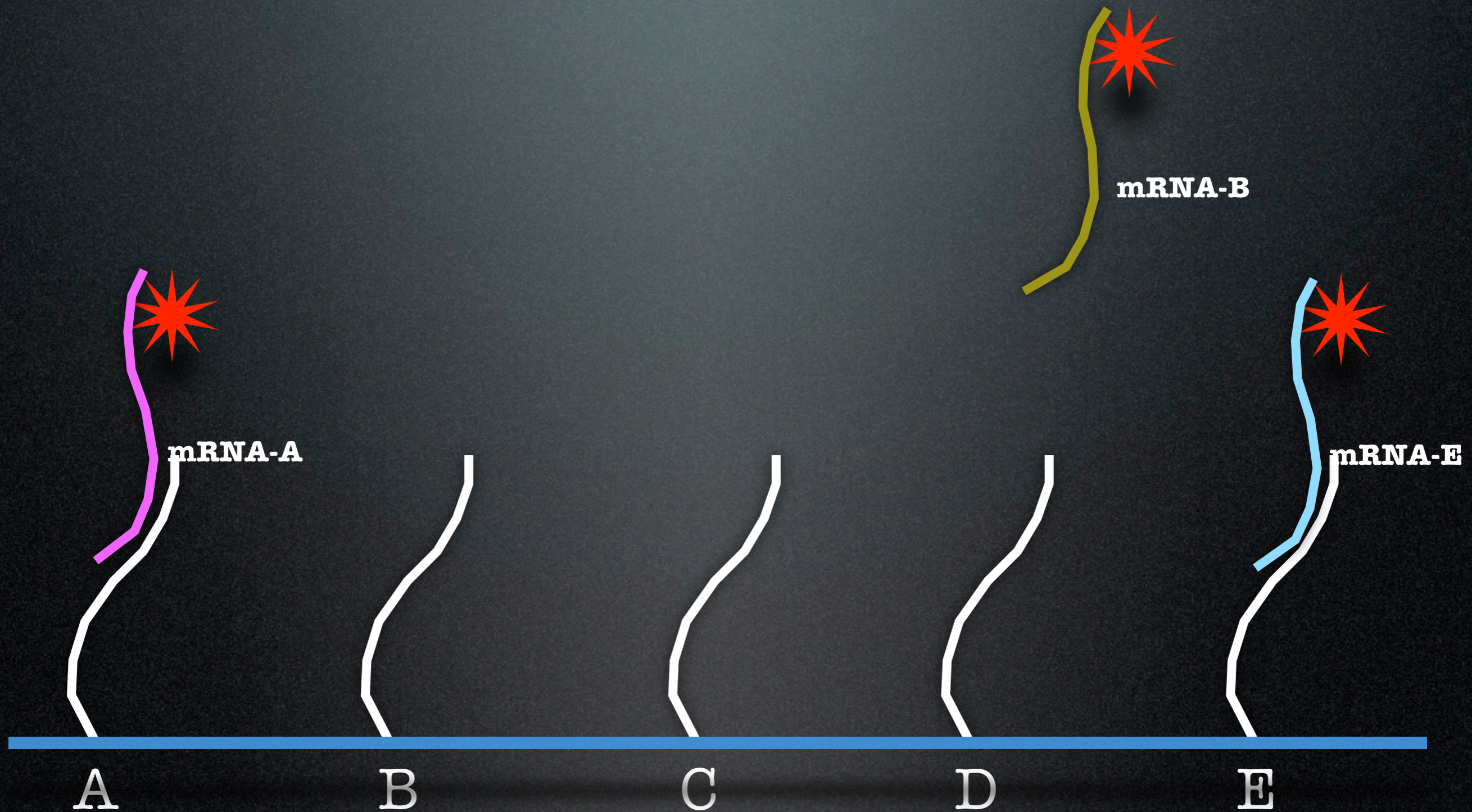
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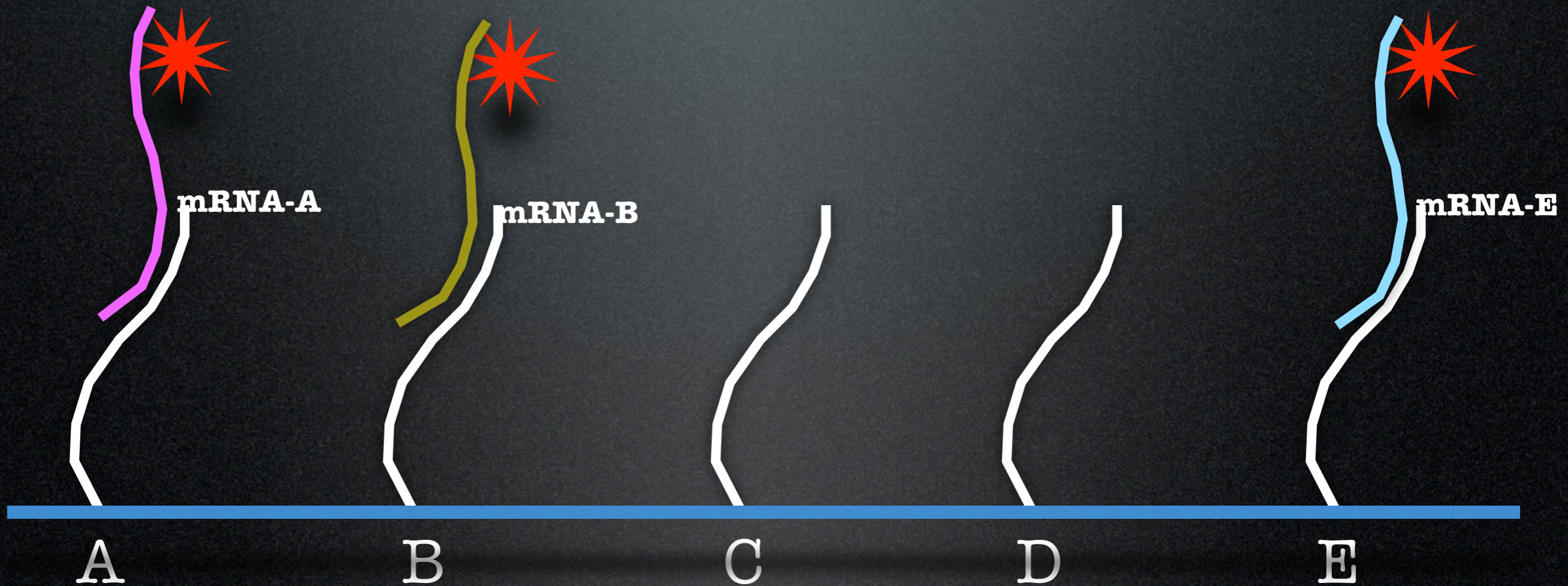
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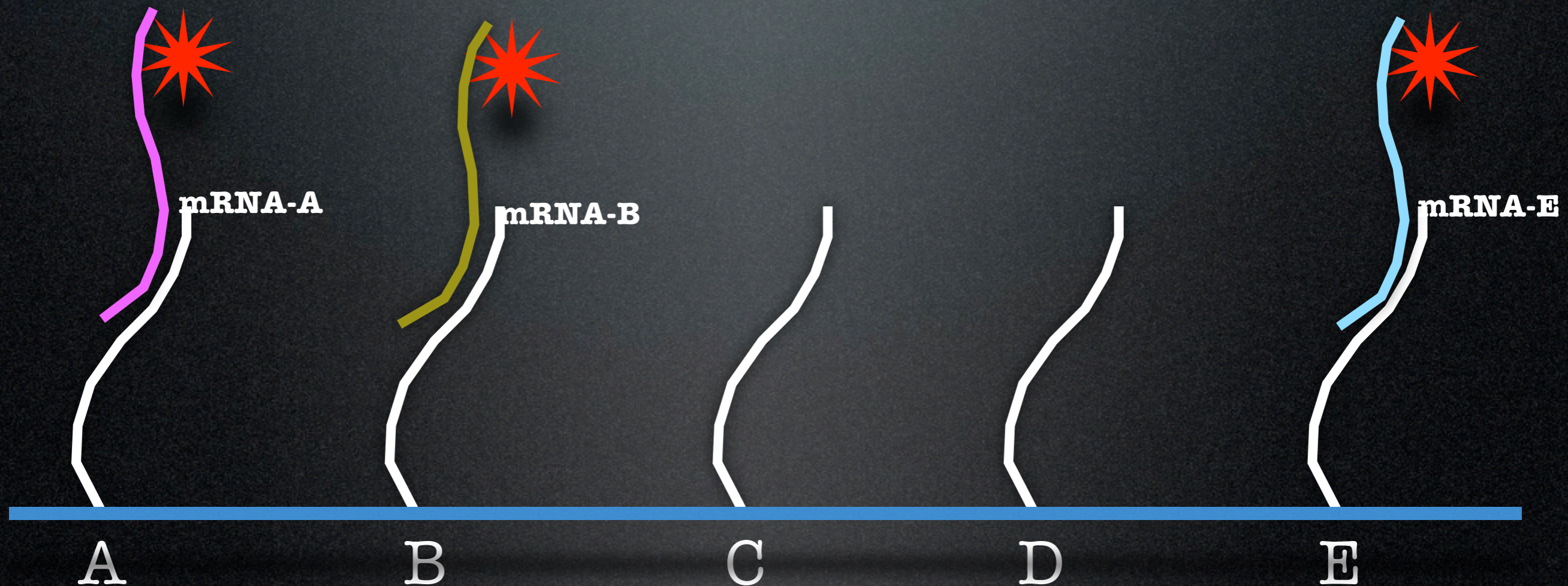


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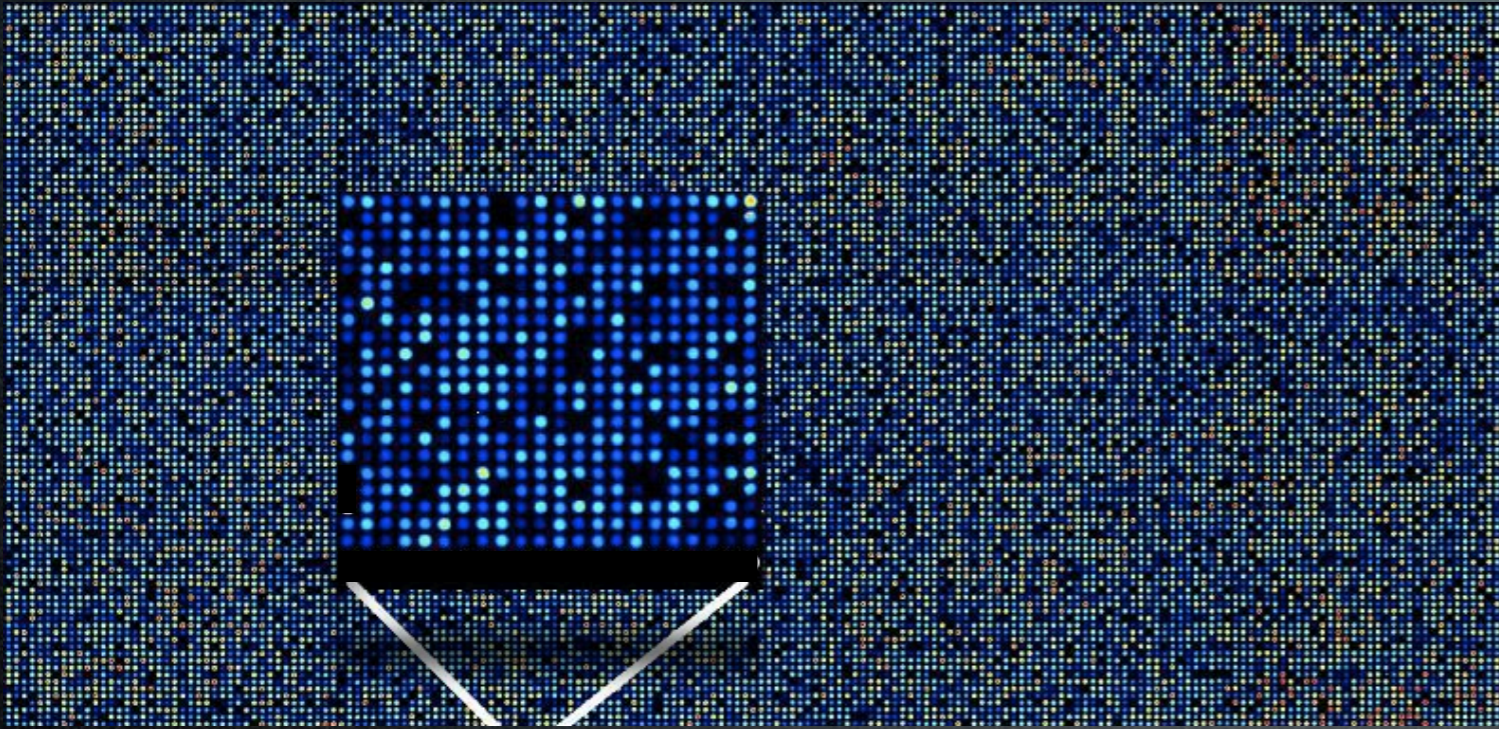


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**In our sample, gene A, B and E are active
The level of our reporter tells us how active**

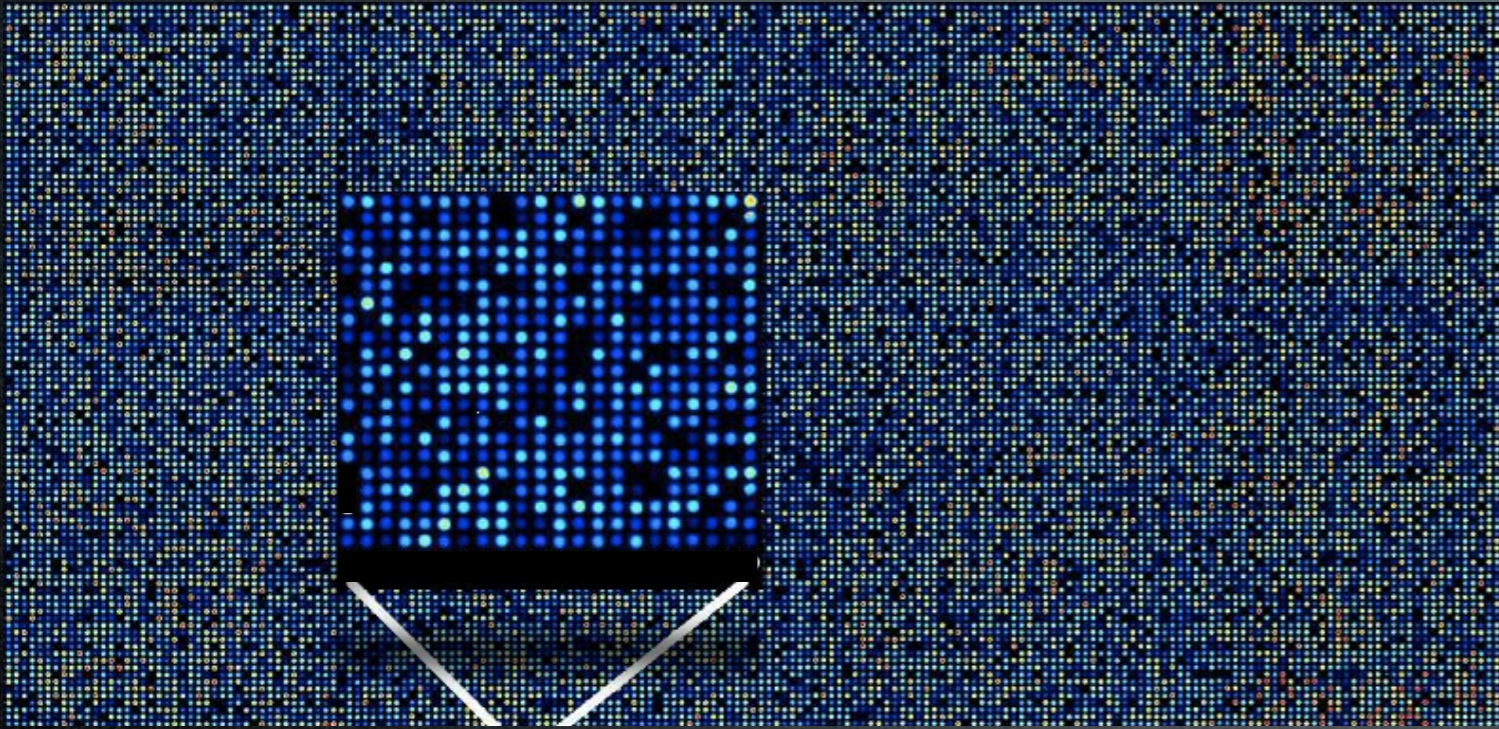


Microarrays



- Probes are distributed across the surface of a glass slide
- Each co-ordinate represents the DNA probe for a different gene
- Use fluorescent reporters

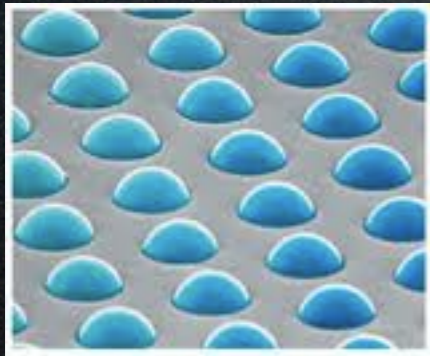
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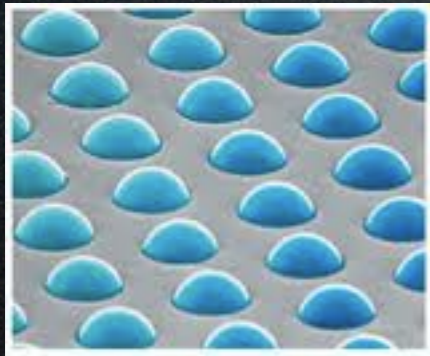
Allows the measurement of many thousands of genes at the same time - **gene expression profiling**

Modern microarrays allow us to make more than a million measurements from a single sample



3 um
beads

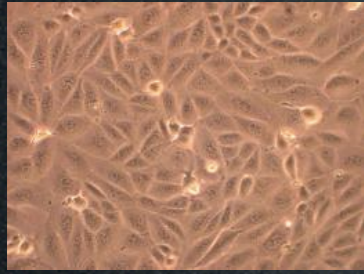
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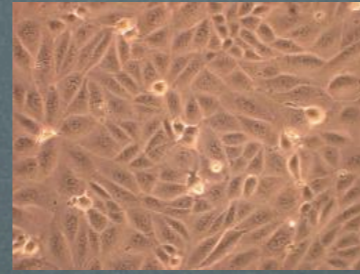
3 um
beads

The screenshot shows the Illumina BeadScan software interface. At the top, there is a navigation bar with buttons for START, SETUP, TILT, ALIGN, SCAN (highlighted), and REVIEW. The main window is divided into several sections: a vertical strip on the left showing a zoomed-in view of the bead array, a large central area displaying a dense field of green spots, and a right-hand panel with a small schematic of the bead array and a data table. The data table has columns for Sentrax ID, Section, G Sat, G P95, G P5, and R Sat. Below the table are buttons for '<< Stop' and 'Pause'. At the bottom, a status bar shows 'Scanning "5388913060 : E_2", Capturing Analytic Images' and various system metrics like TX/RX status, gain, filter, and elapsed time. The Windows taskbar at the very bottom shows the Start button and several open applications including Illumina BeadScan, GenomeStudio, and Scatter Plot.

Simple experiment: Comparing normal and diseased cells



normal cells



diseased cells e.g. cancer

Isolate RNA

↓ **1 day**

Label RNA

↓ **1 day**

Add to array

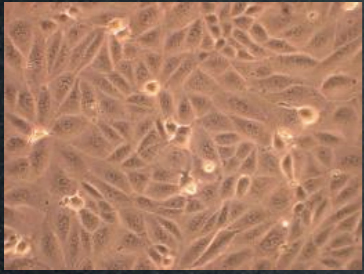
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wash and scan

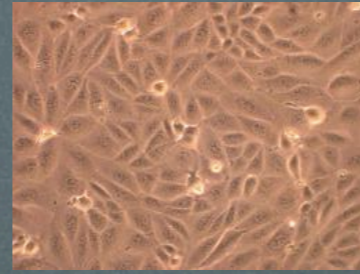
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compare profiles of gene activity

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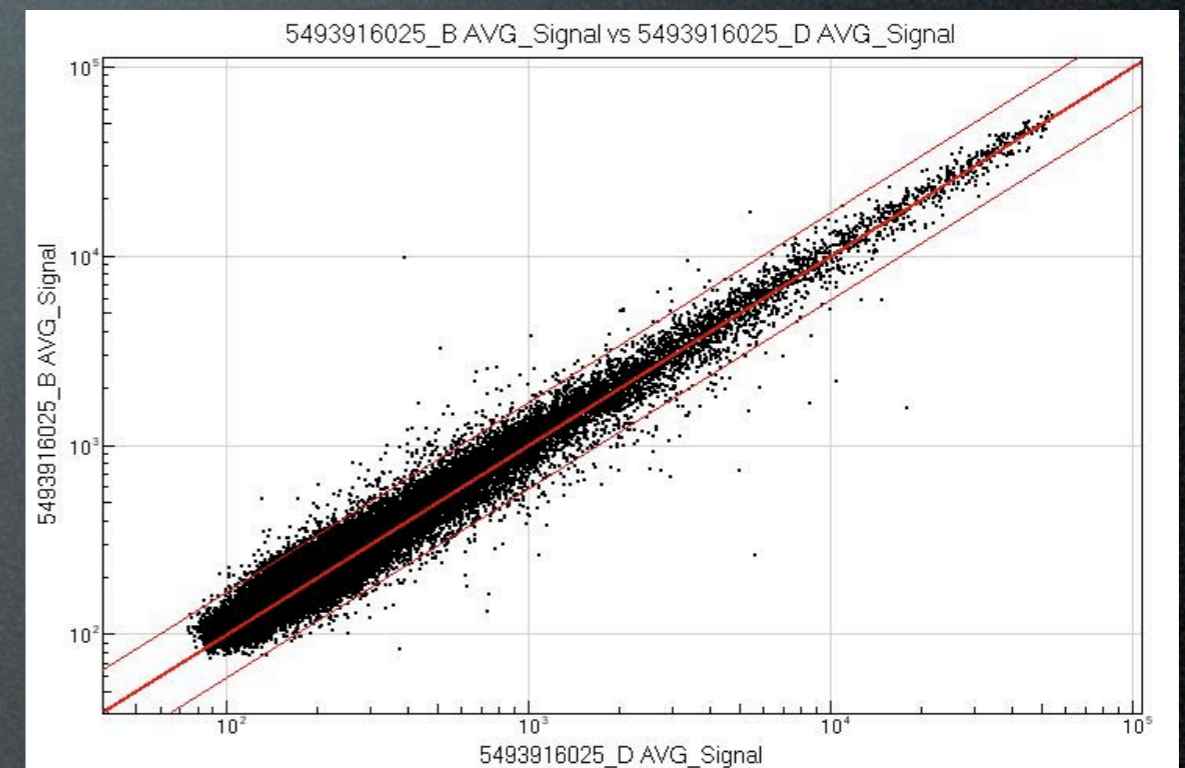
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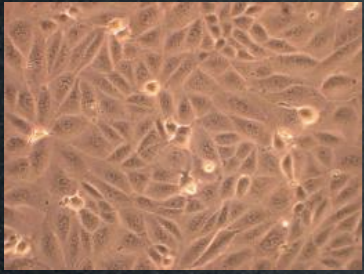
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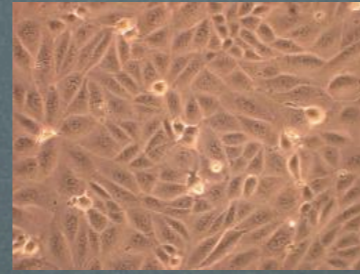
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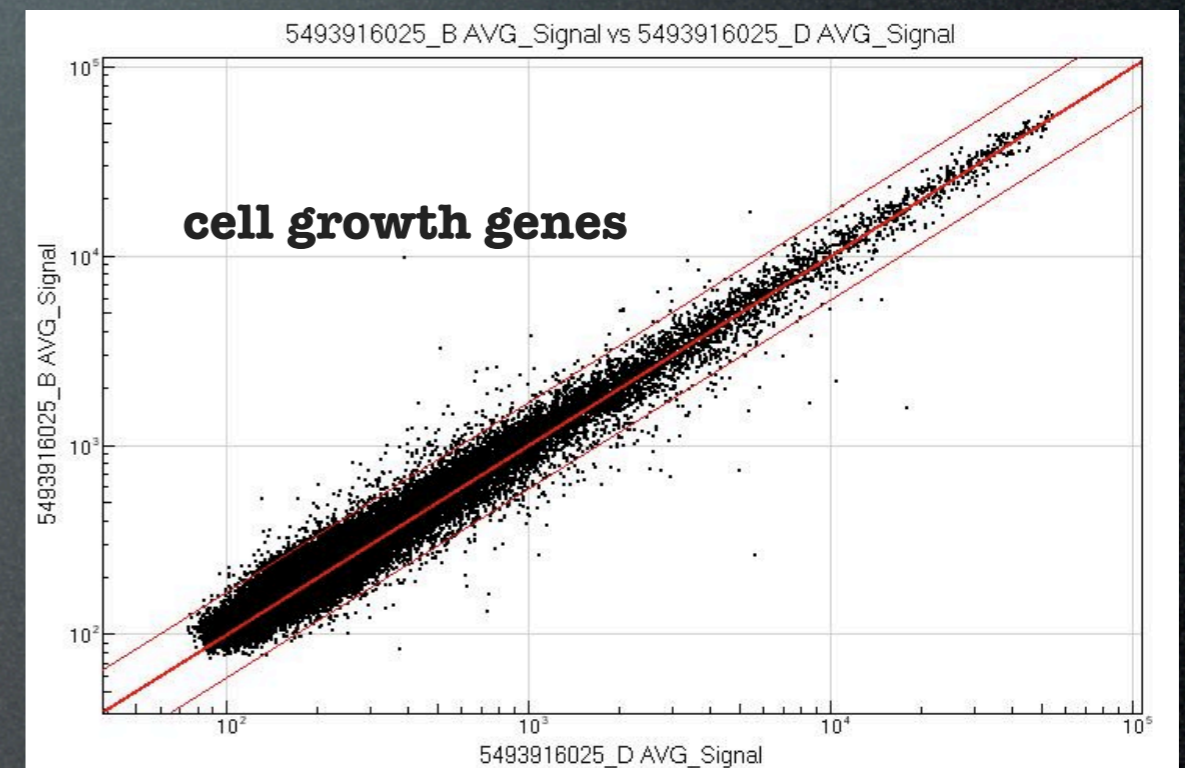
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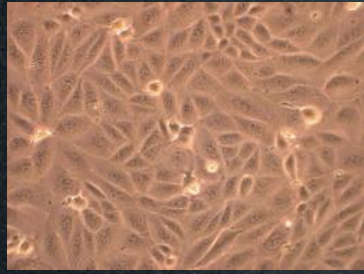
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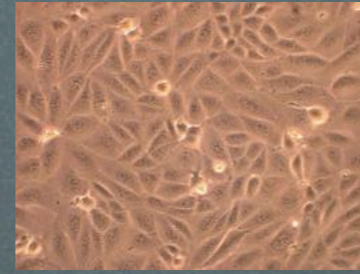
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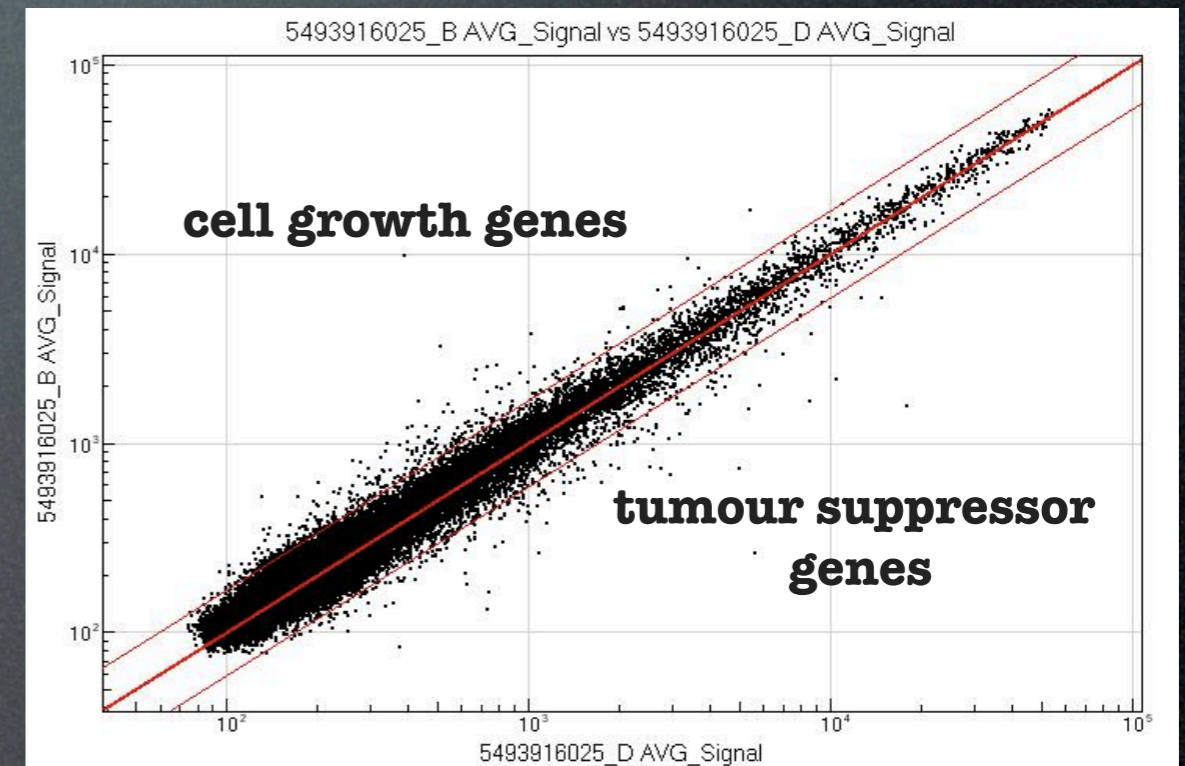
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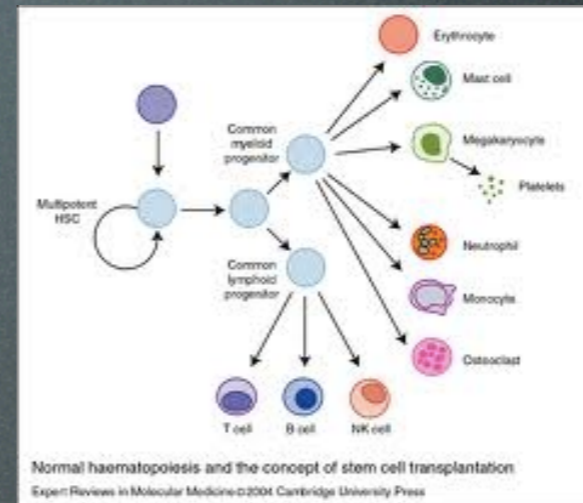
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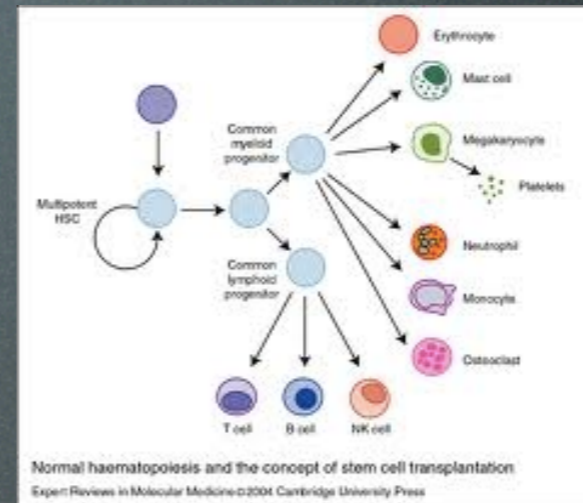
Gene expression profiling at the Sanger Institute

- Different cell types, e.g. haematlas



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- Response to drugs e.g. vaccines, cancer drugs

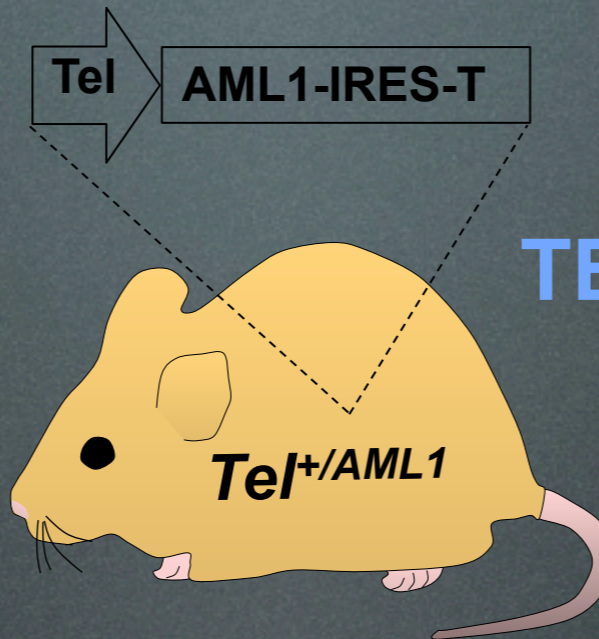


+



Gene expression profiling at the Sanger Institute

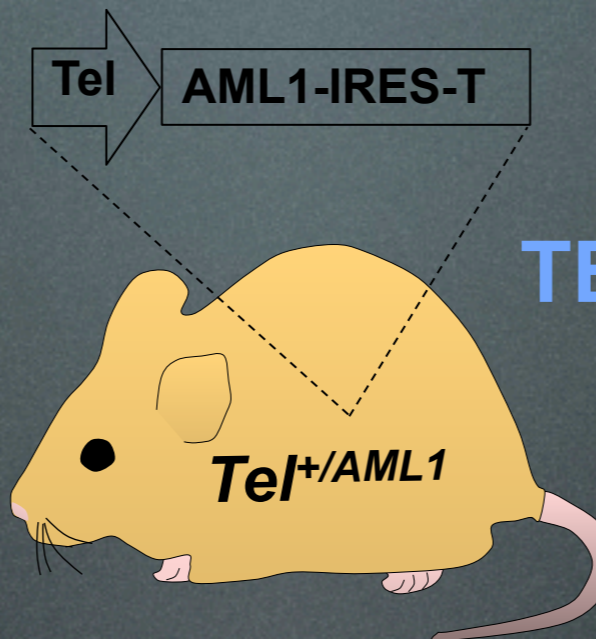
- Mouse models



TEL-AML1 mice develop leukaemia

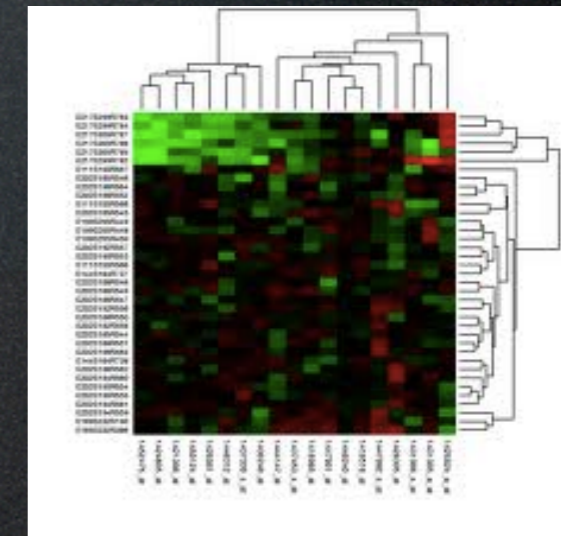
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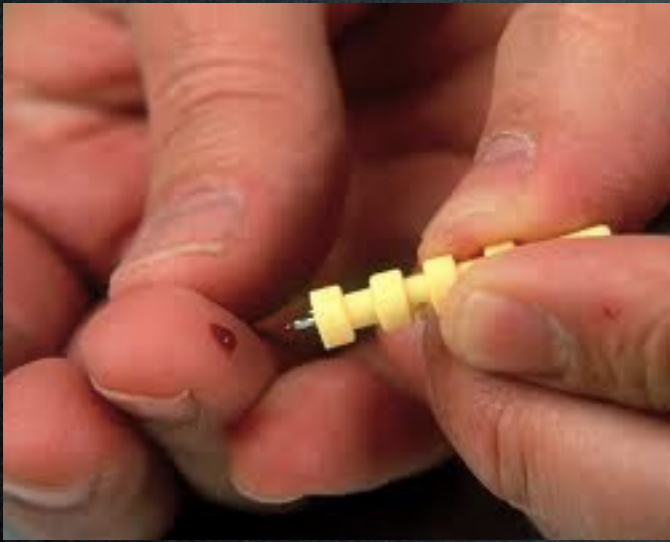


TEL-AML1 mice develop leukaemia

- Disease

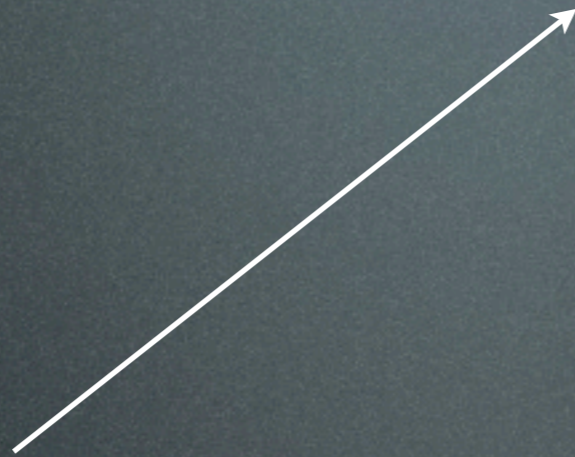
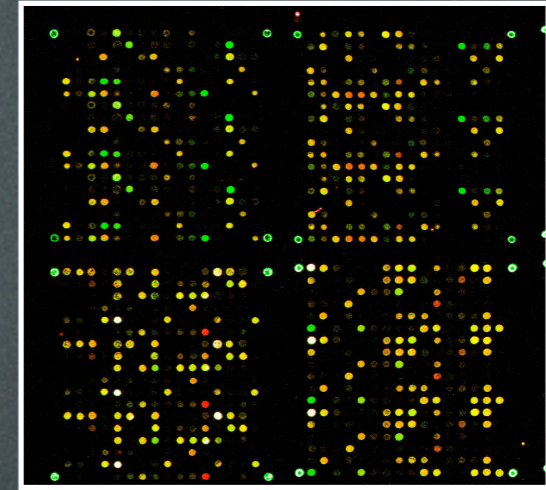


Microarrays and medicine

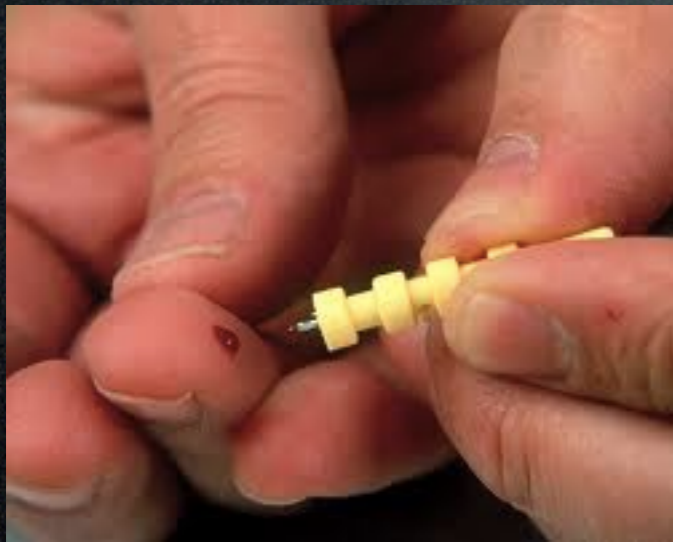


Microarrays and medicine

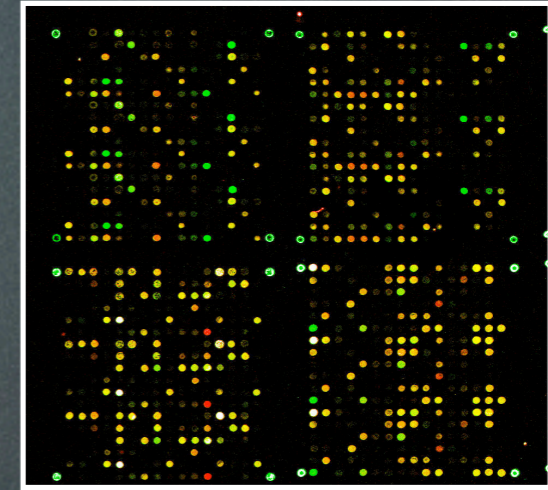
Diagnosis



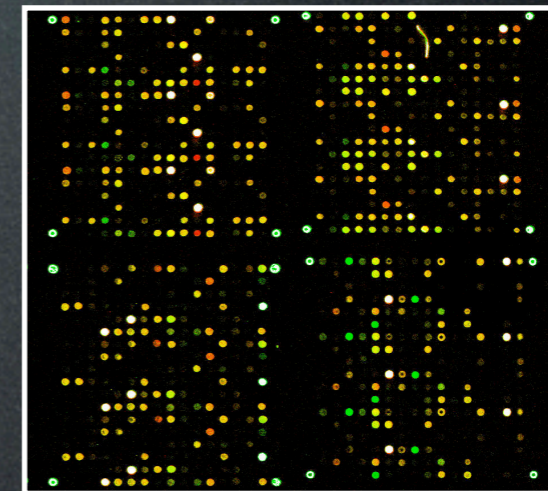
Microarrays and medicine



Diagnosis



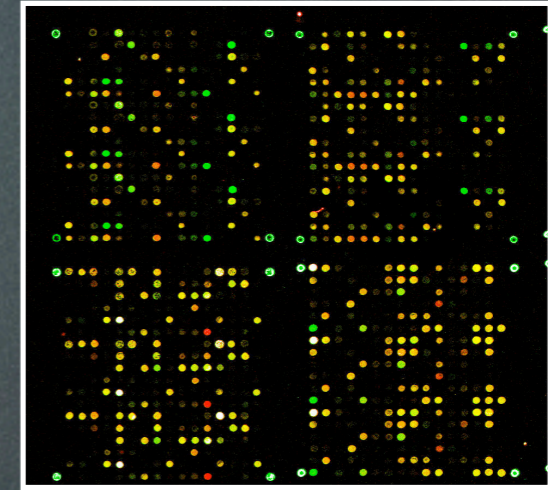
Prognosis



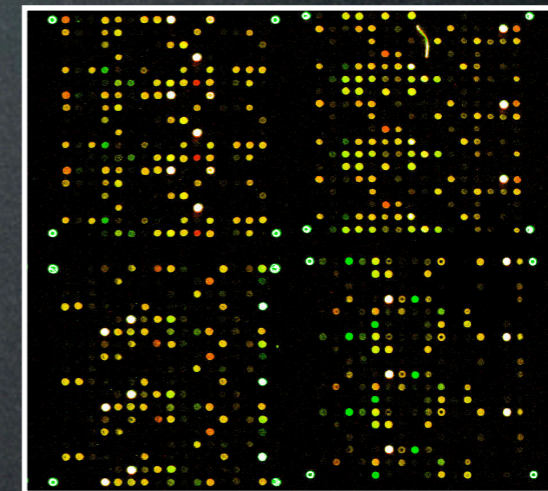
Microarrays and medicine



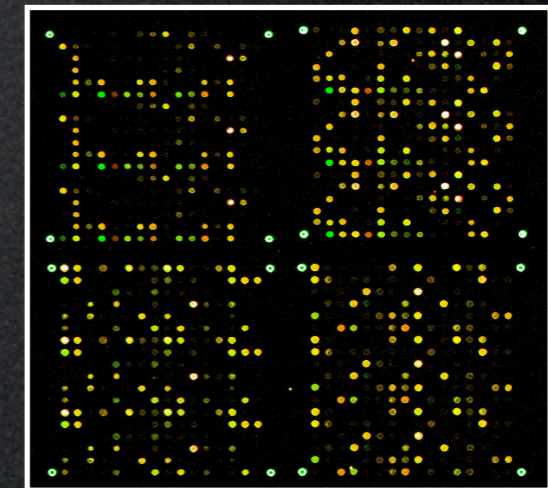
Diagnosis



Prognosis



Treatment



Microarray Facility
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