Polycystic Ovary Syndrome

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What is Polycystic Ovary Syndrome (PCOS)?

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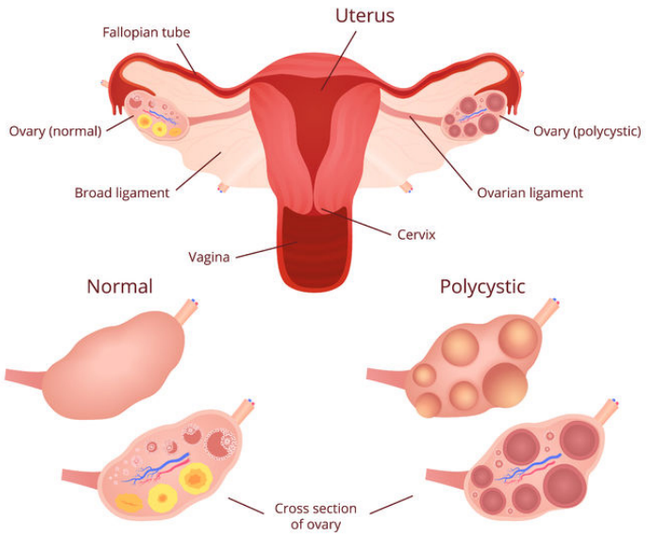
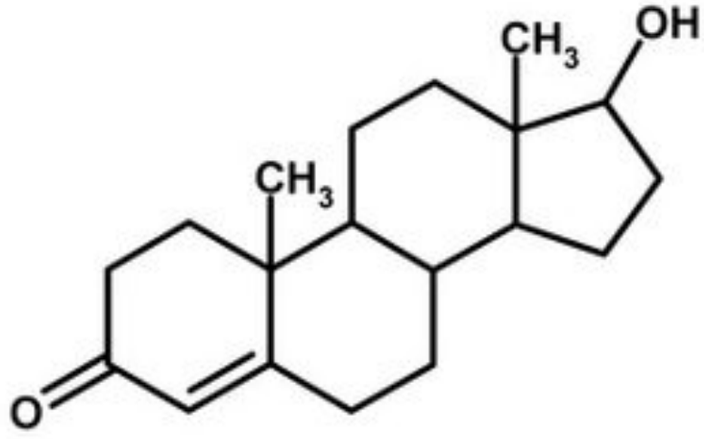
2/3 of following are required for PCOS diagnosis



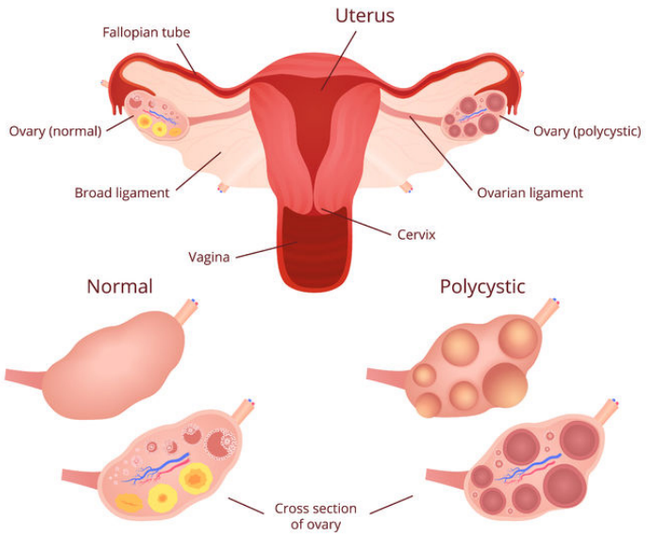
Polycystic ovaries

Irregular menstrual cycle



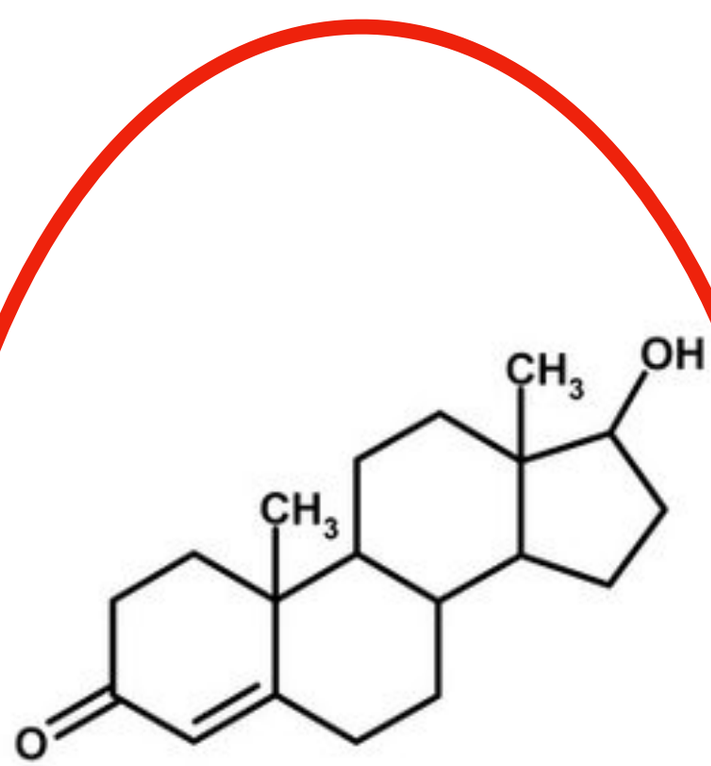
Excess testosterone

2/3 of following are required for PCOS diagnosis



Polycystic ovaries

Irregular menstrual cycle



Excess testosterone

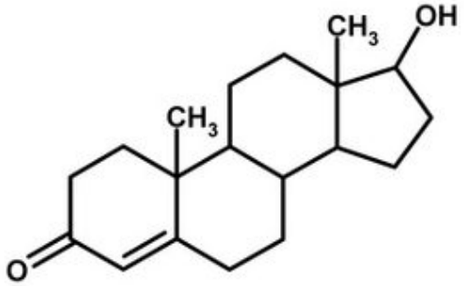
What gene is associated with PCOS?

StAR

What gene is associated with PCOS?

StAR

Biological Process

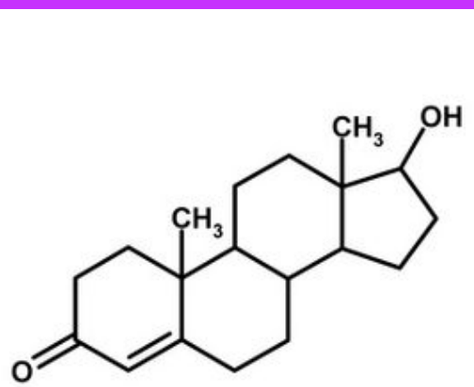


Steroid Biosynthetic Process

What gene is associated with PCOS?

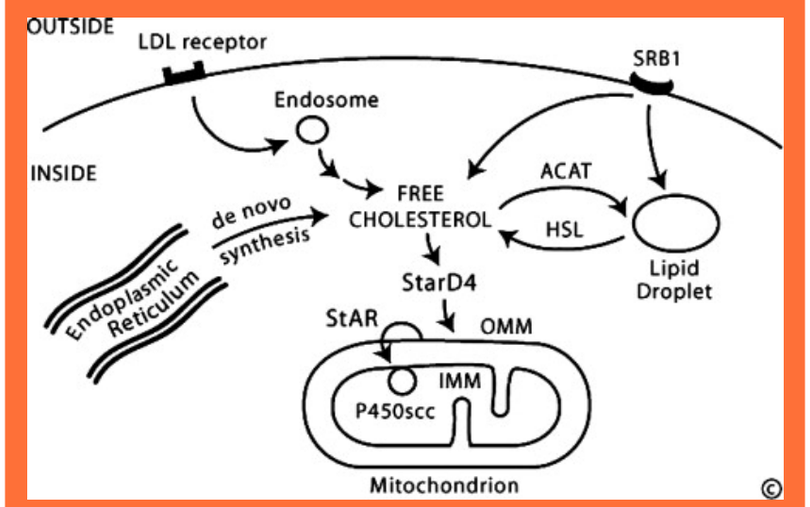
StAR

Biological Process



Steroid Biosynthetic Process

Molecular Function

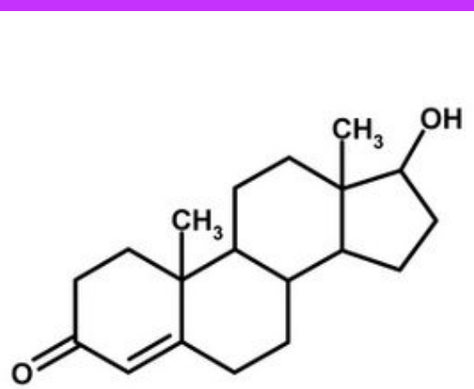


Cholesterol Transport Activity

What gene is associated with PCOS?

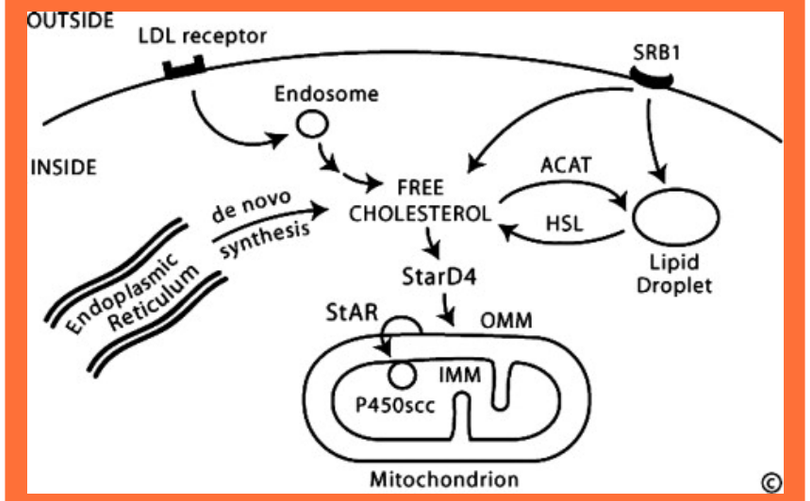
StAR

Biological Process



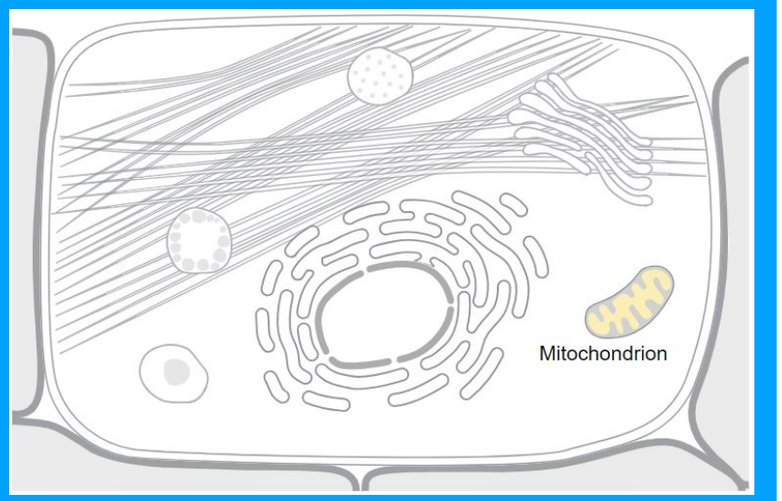
Steroid Biosynthetic Process

Molecular Function



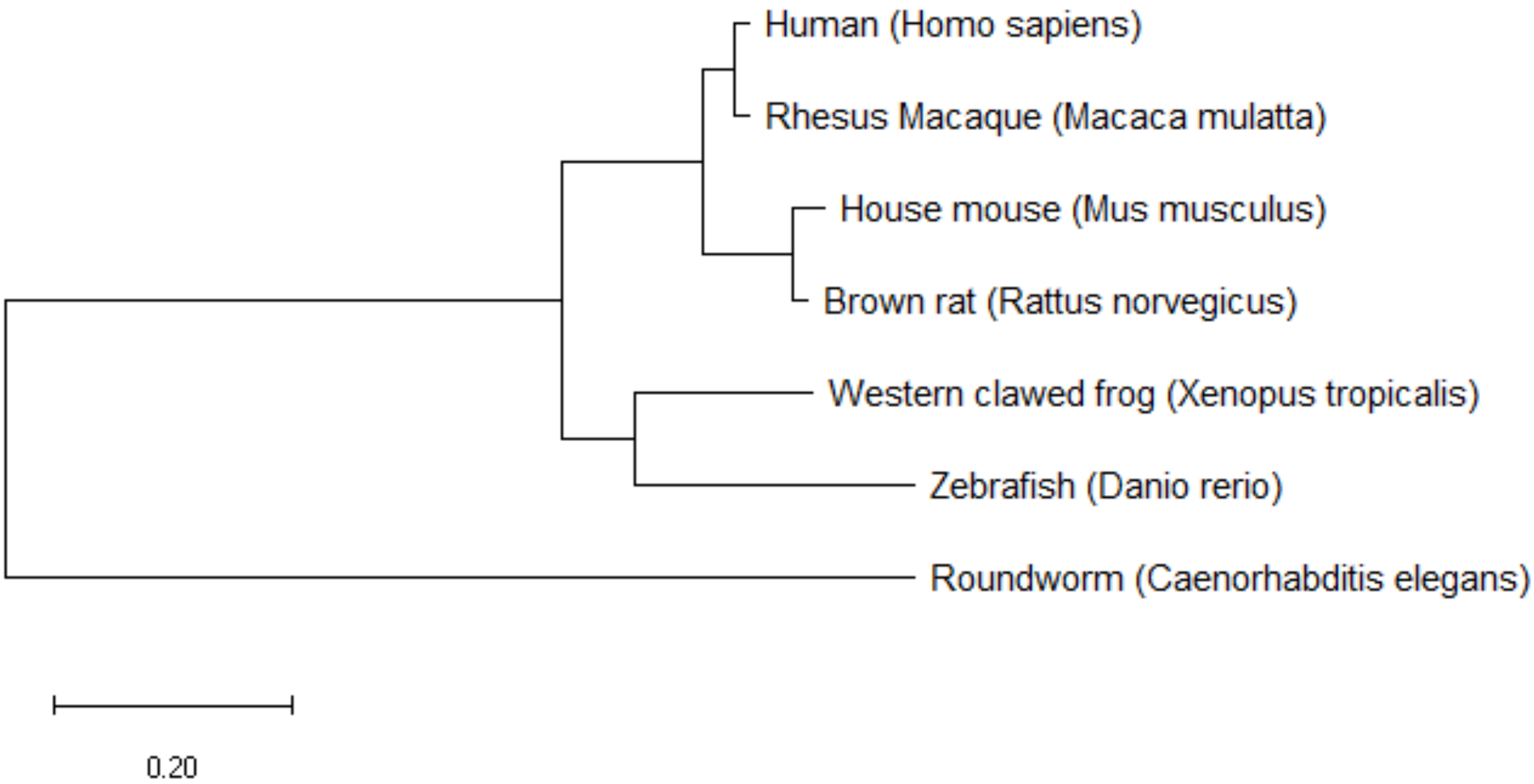
Cholesterol Transport Activity

Cellular Component

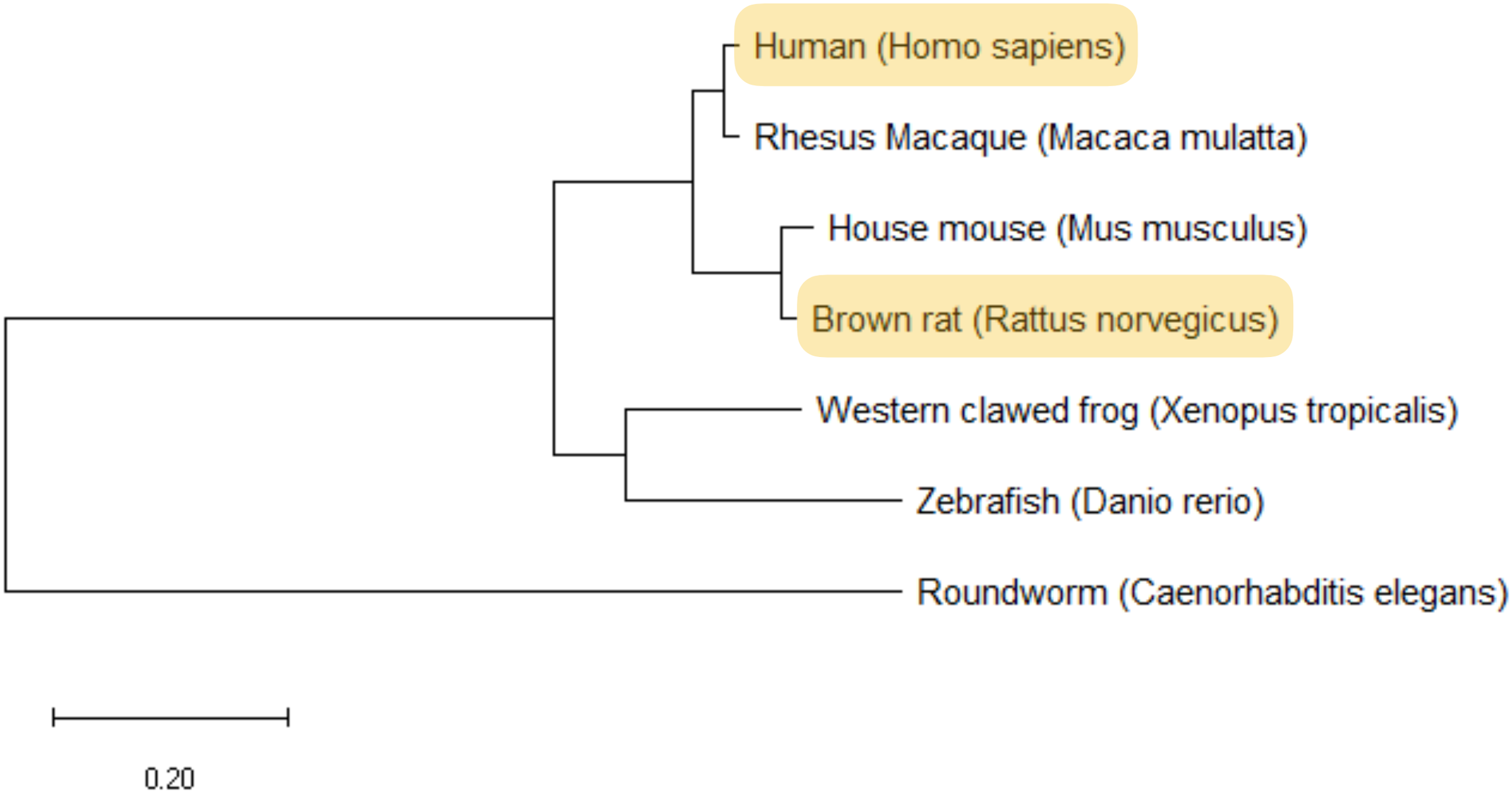


Mitochondrion

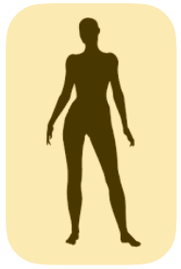
Is StAR conserved across species?



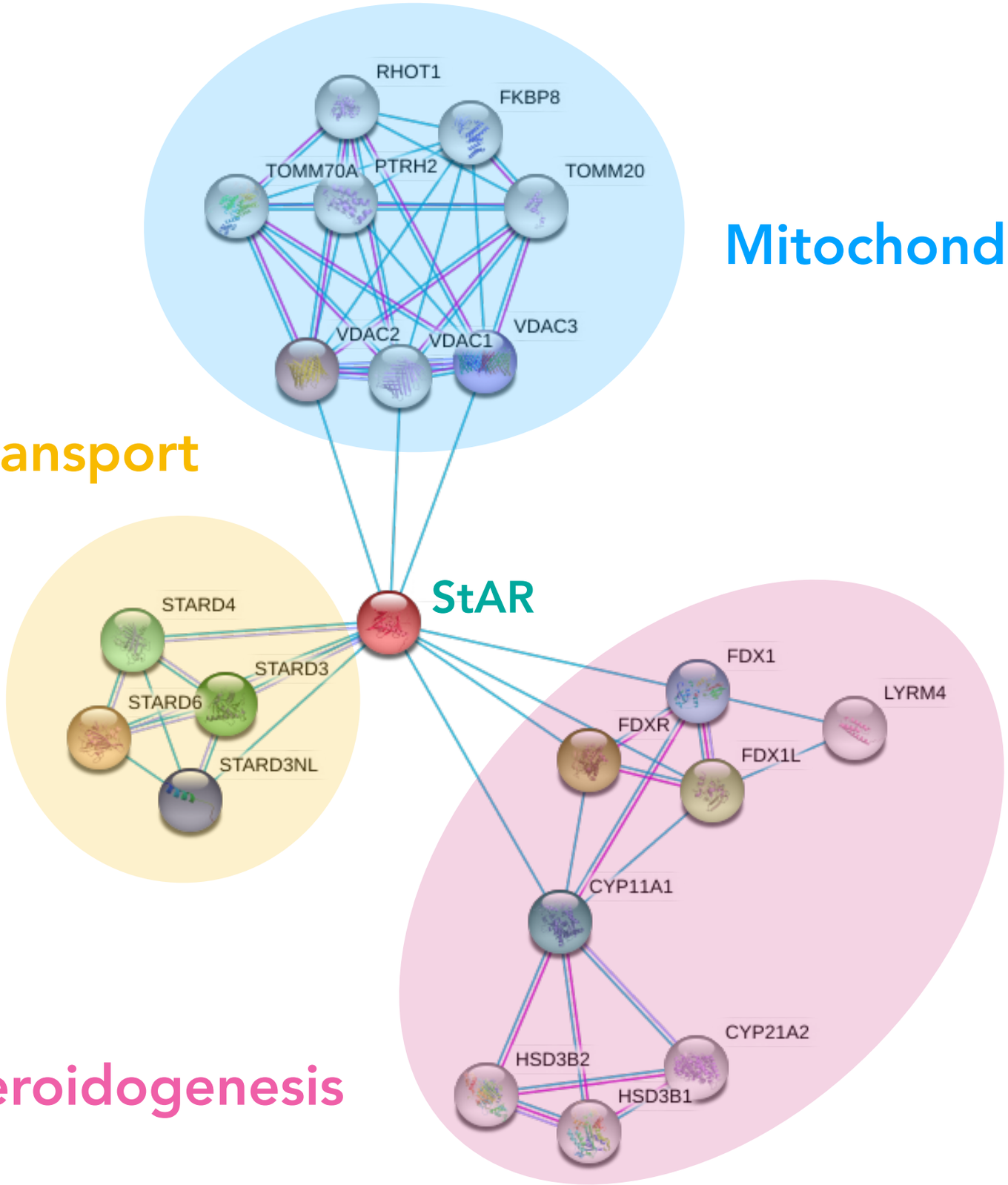
Is StAR conserved across species?



StAR domains across species



StAR protein interactions

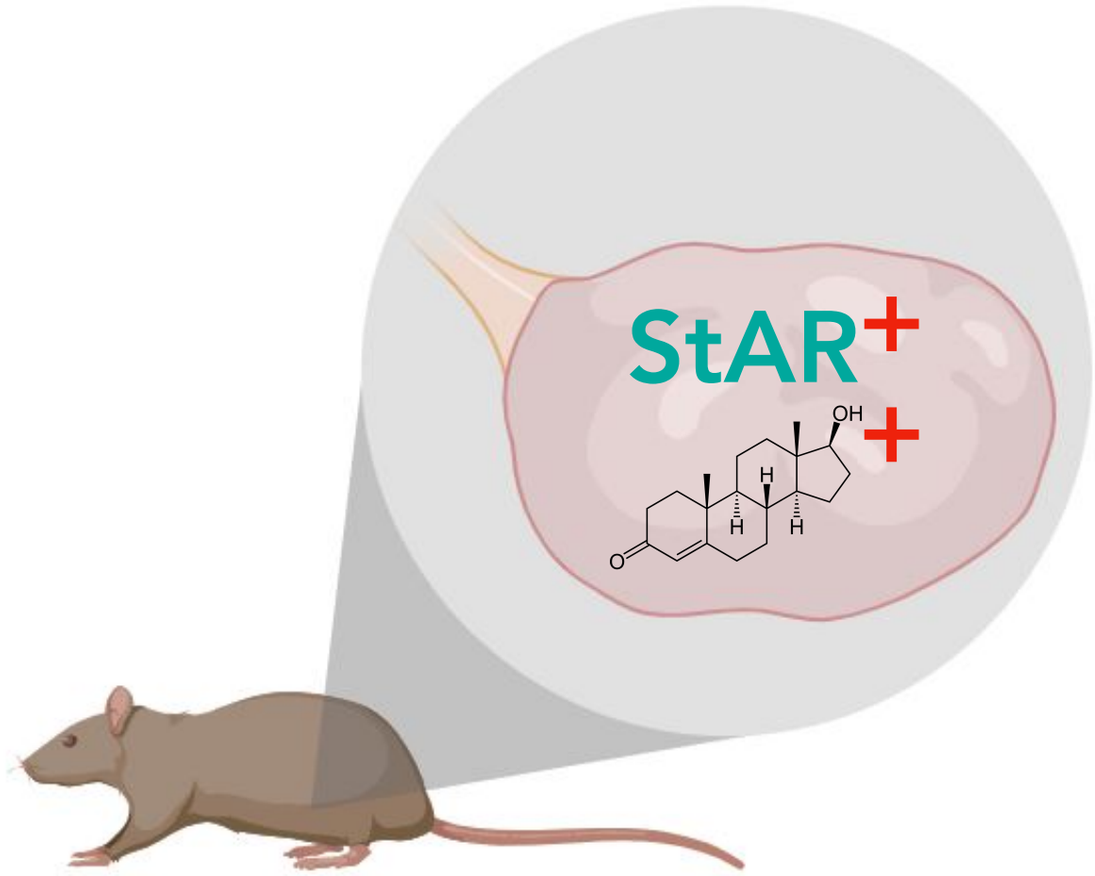


Mitochondrial Transport

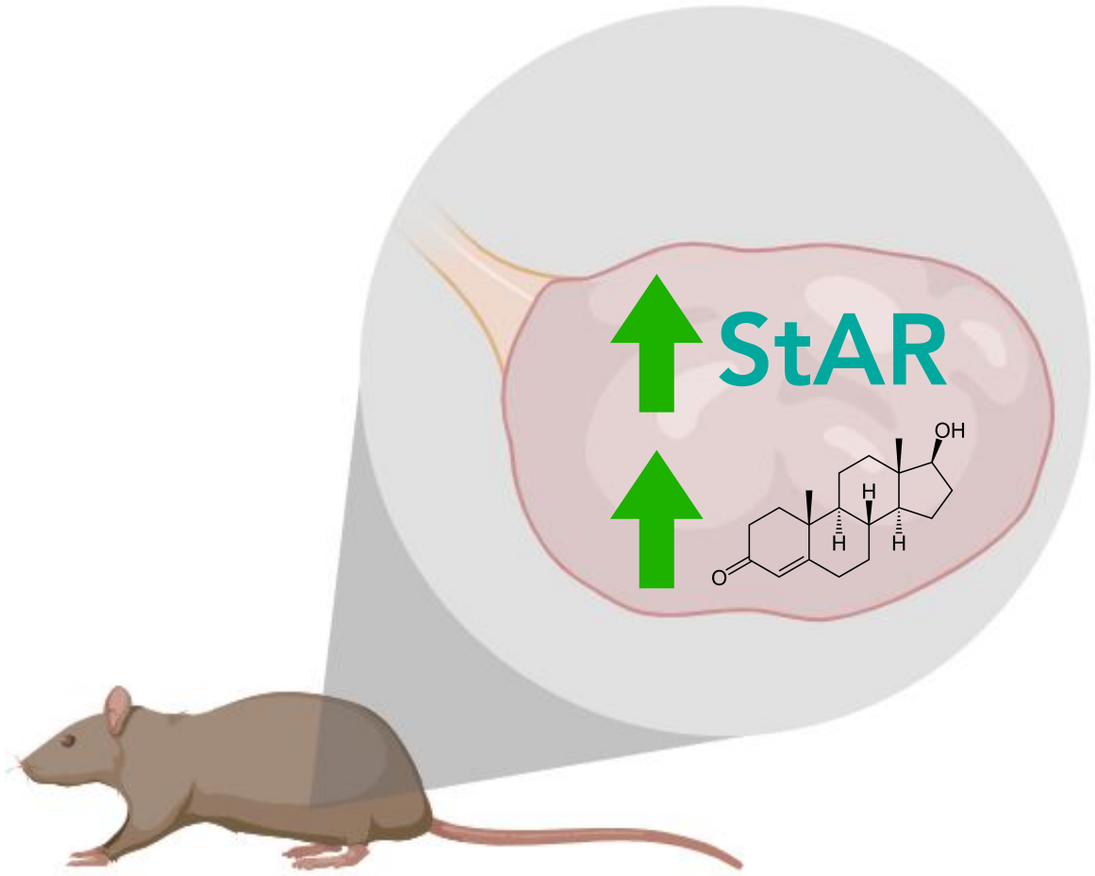
Cholesterol Transport

Steroidogenesis

Rattus norvegicus:
a great model organism for PCOS



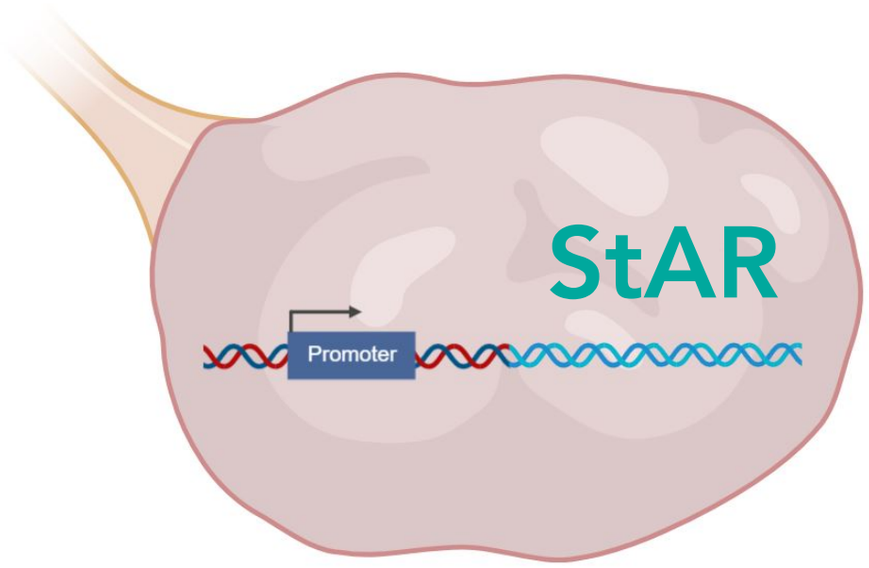
Wild type

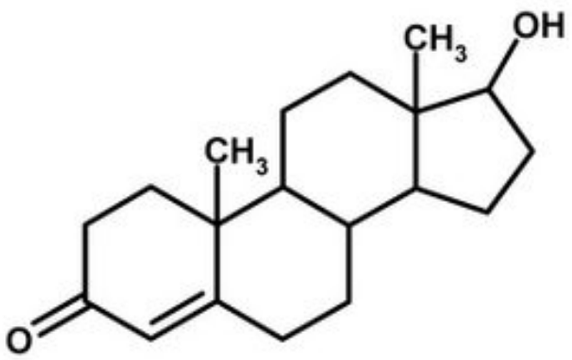


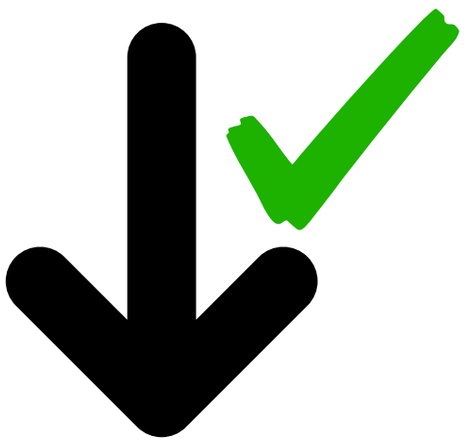
PCOS

Prenatally androgenized rats display PCOS phenotype

The knowledge gap

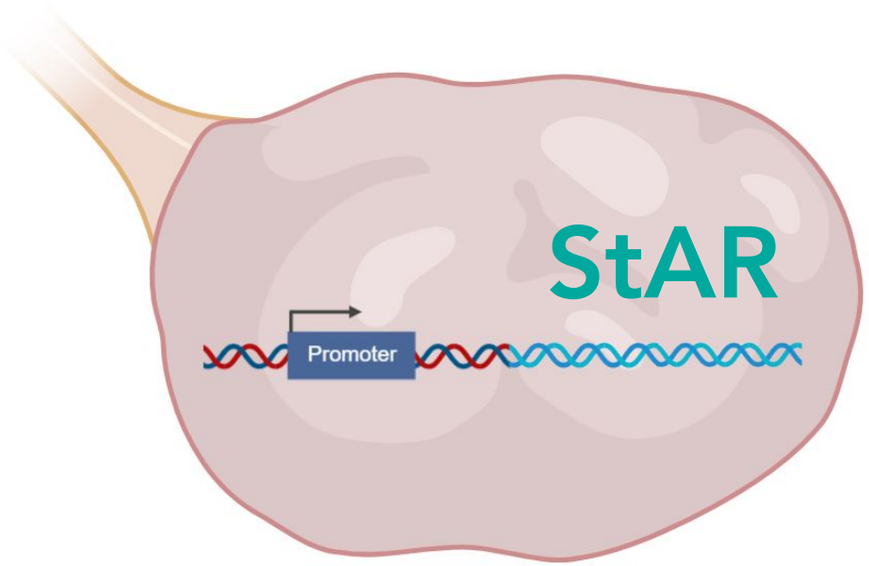


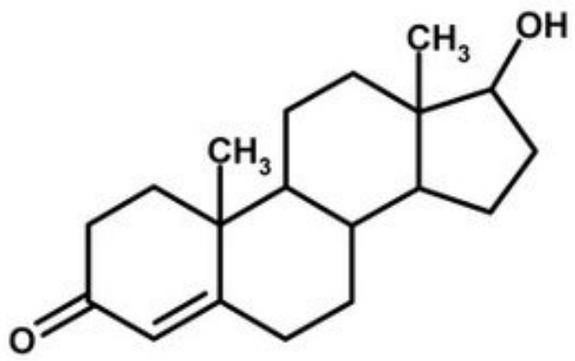


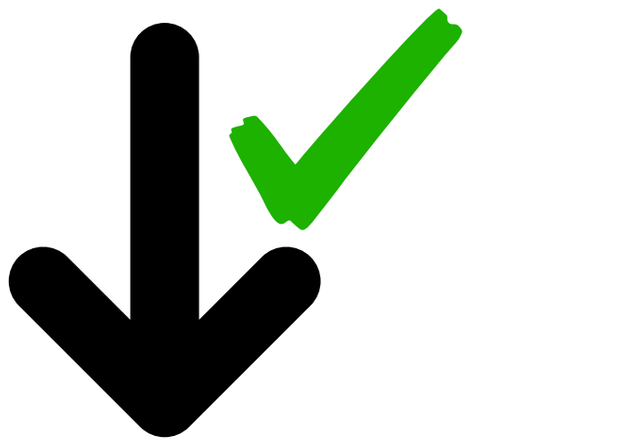


The knowledge gap

Regulating factors







What is the primary goal?

To better understand what factors regulate StAR expression and testosterone levels in PCOS

Aim 1

Determine what sequences within the StAR promoter are conserved and contribute to testosterone levels in ovaries

Aim 2

Identify differentially regulated genes in a PCOS model that are important for StAR expression and testosterone levels in ovaries

Aim 3

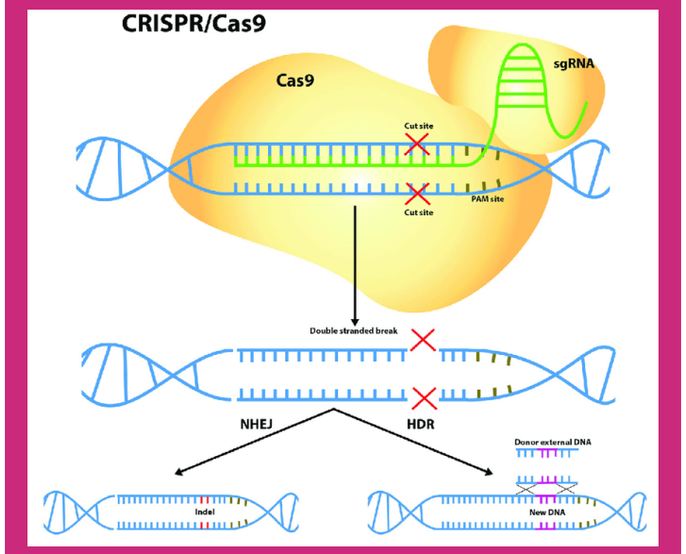
Identify direct protein interactions with the StAR promoter and protein that impact testosterone levels within ovaries

Aim 1: Determine what sequences within the StAR promoter are conserved and contribute to testosterone levels in ovaries

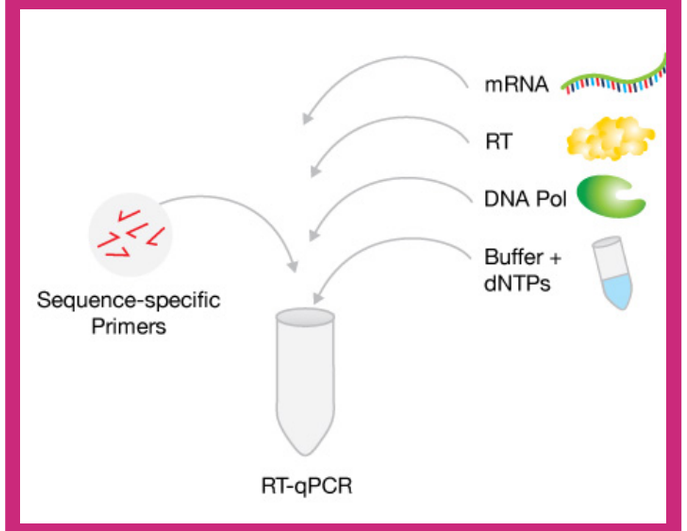
Identify conserved regions and variants

illumina®

Mutagenize



Measure StAR expression



Hypothesis: mutating conserved regions of the StAR promoter will result in differential expression of StAR and testosterone levels

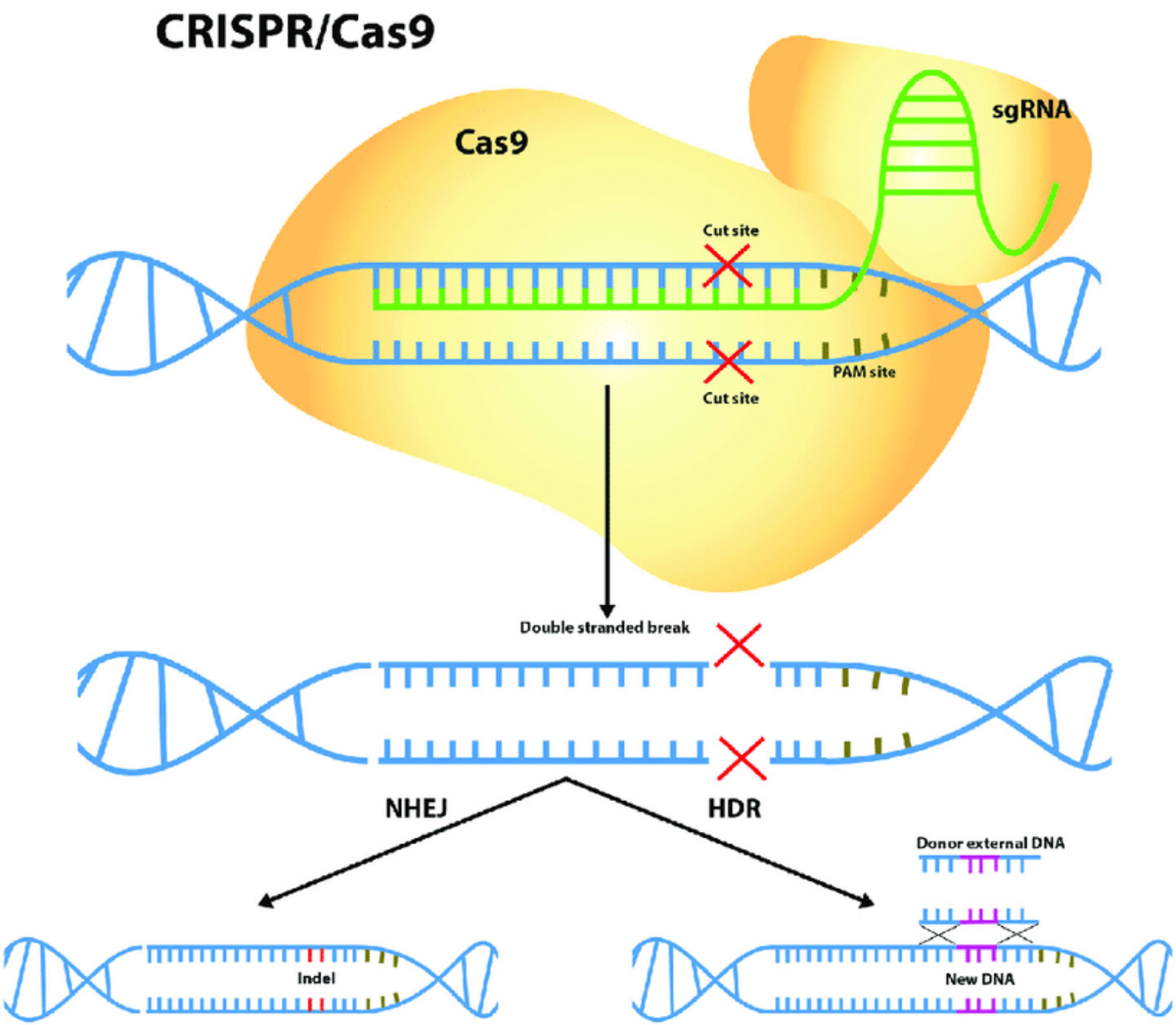
Aim 1

Identify conserved regions and variants

illumina®

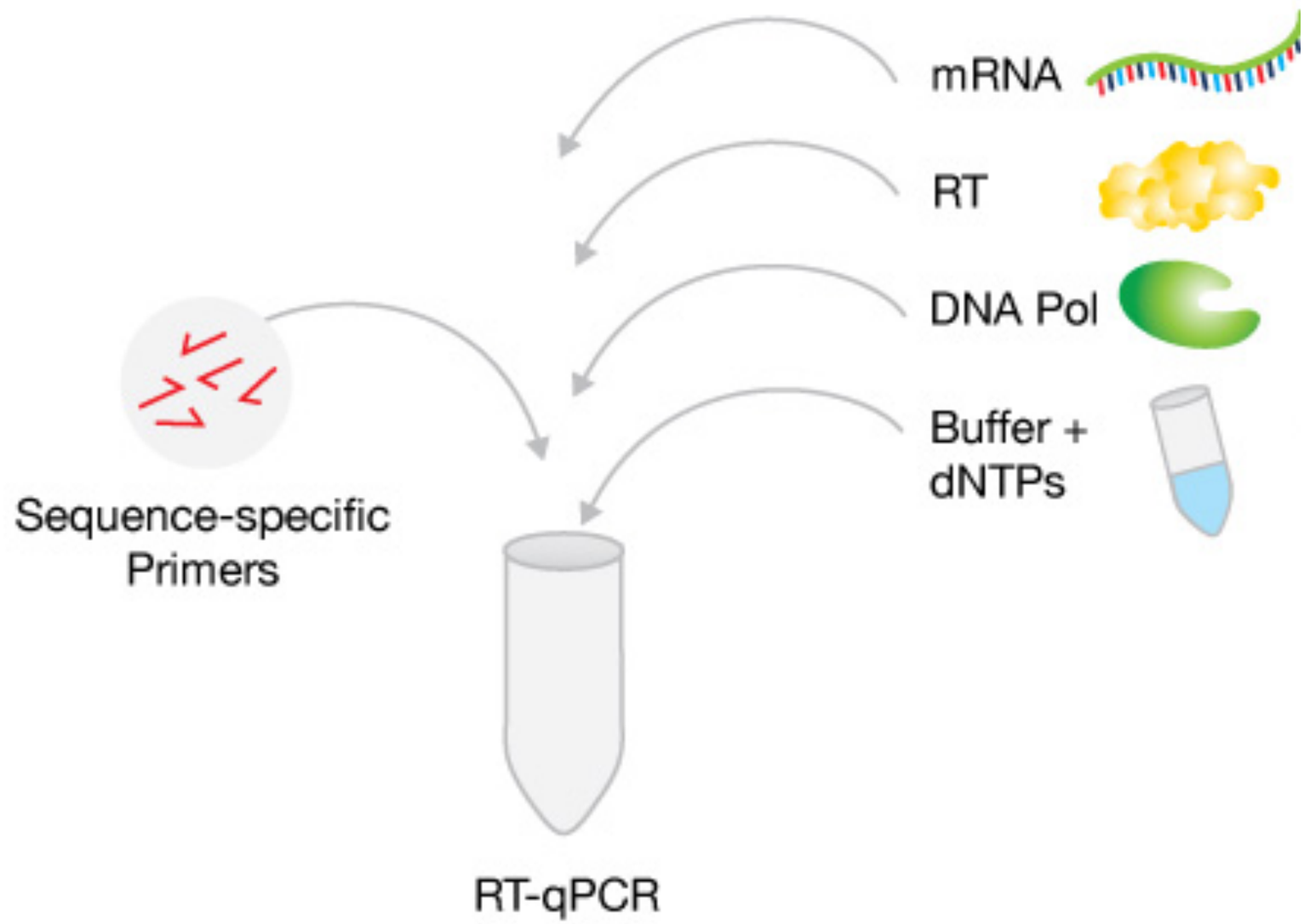
Aim 1

Mutagenize



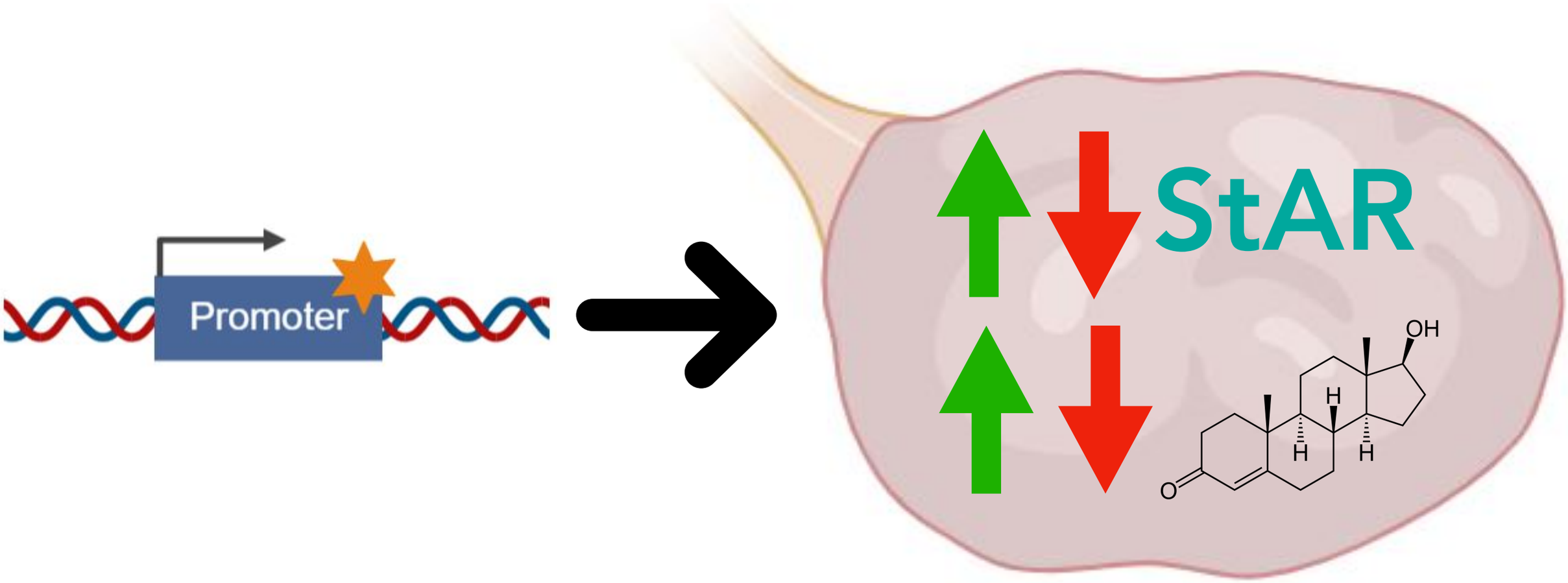
Aim 1

Measure StAR expression



Aim 1

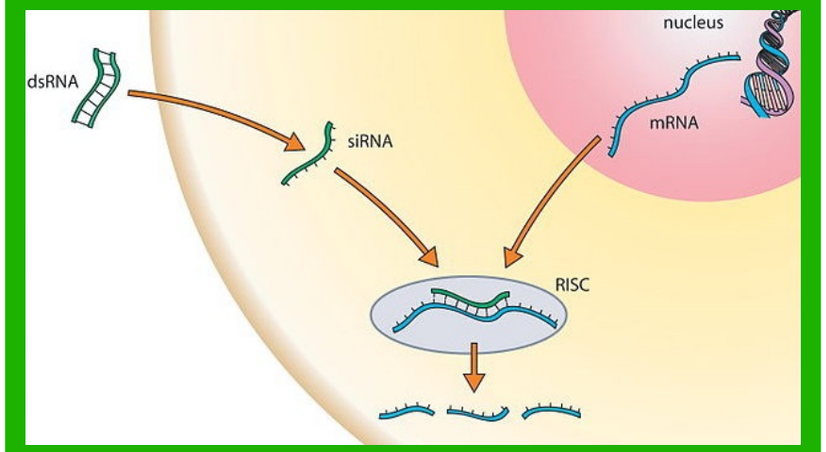
Expectation



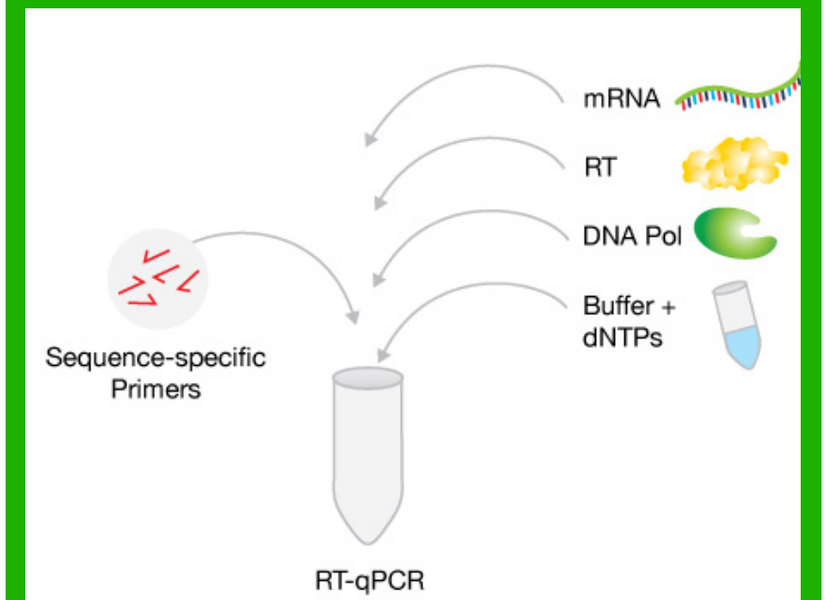
Hypothesis: mutating conserved regions of the StAR promoter will result in differential expression of StAR and testosterone levels

Aim 2: Identify differentially regulated genes in a PCOS model that are important for StAR expression and testosterone levels in ovaries

Identify candidate genes



Measure expression of candidate genes

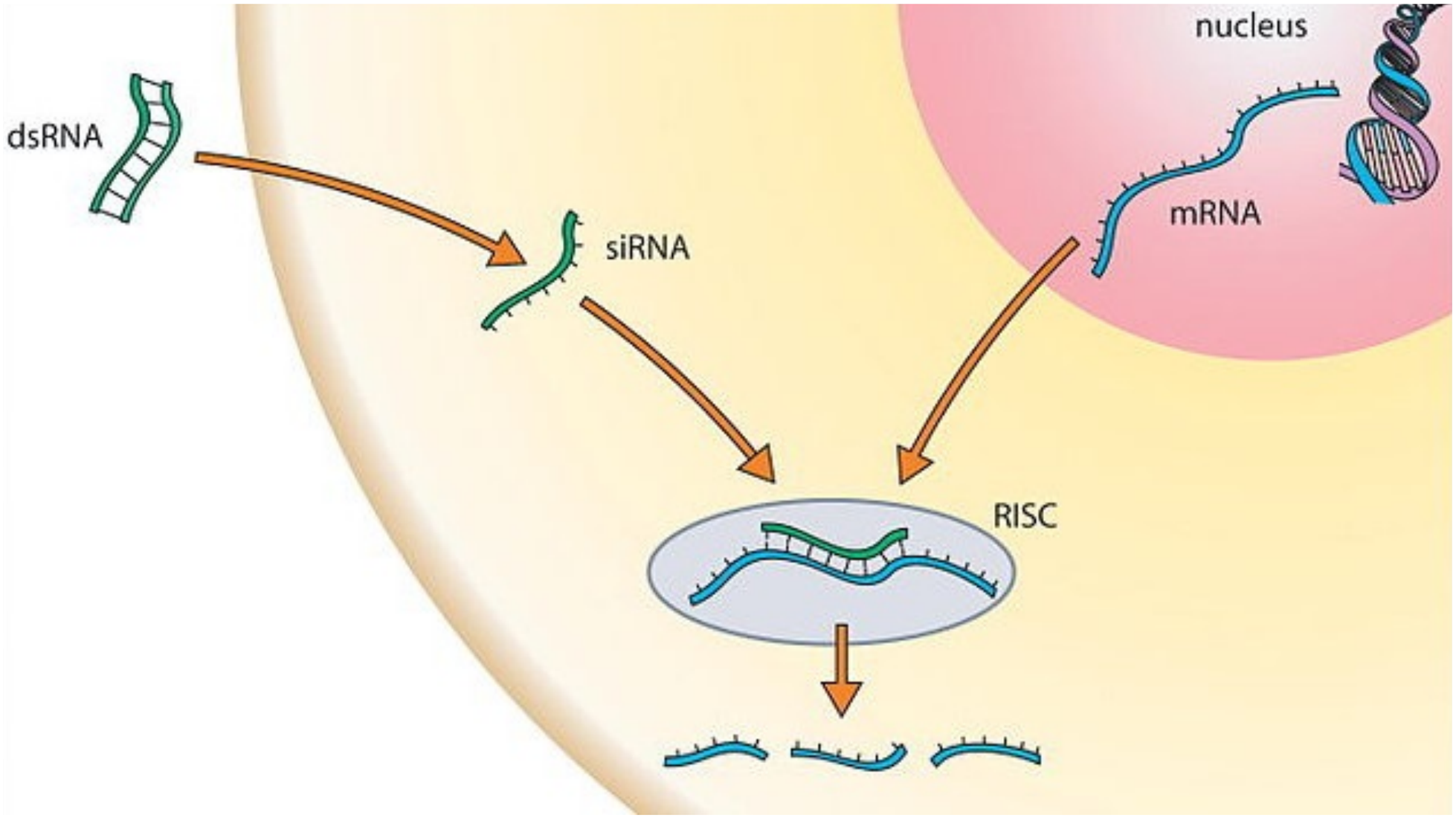


Hypothesis: one or more of the candidate genes identified in the RNAi screen will be differentially regulated in a PCOS model.

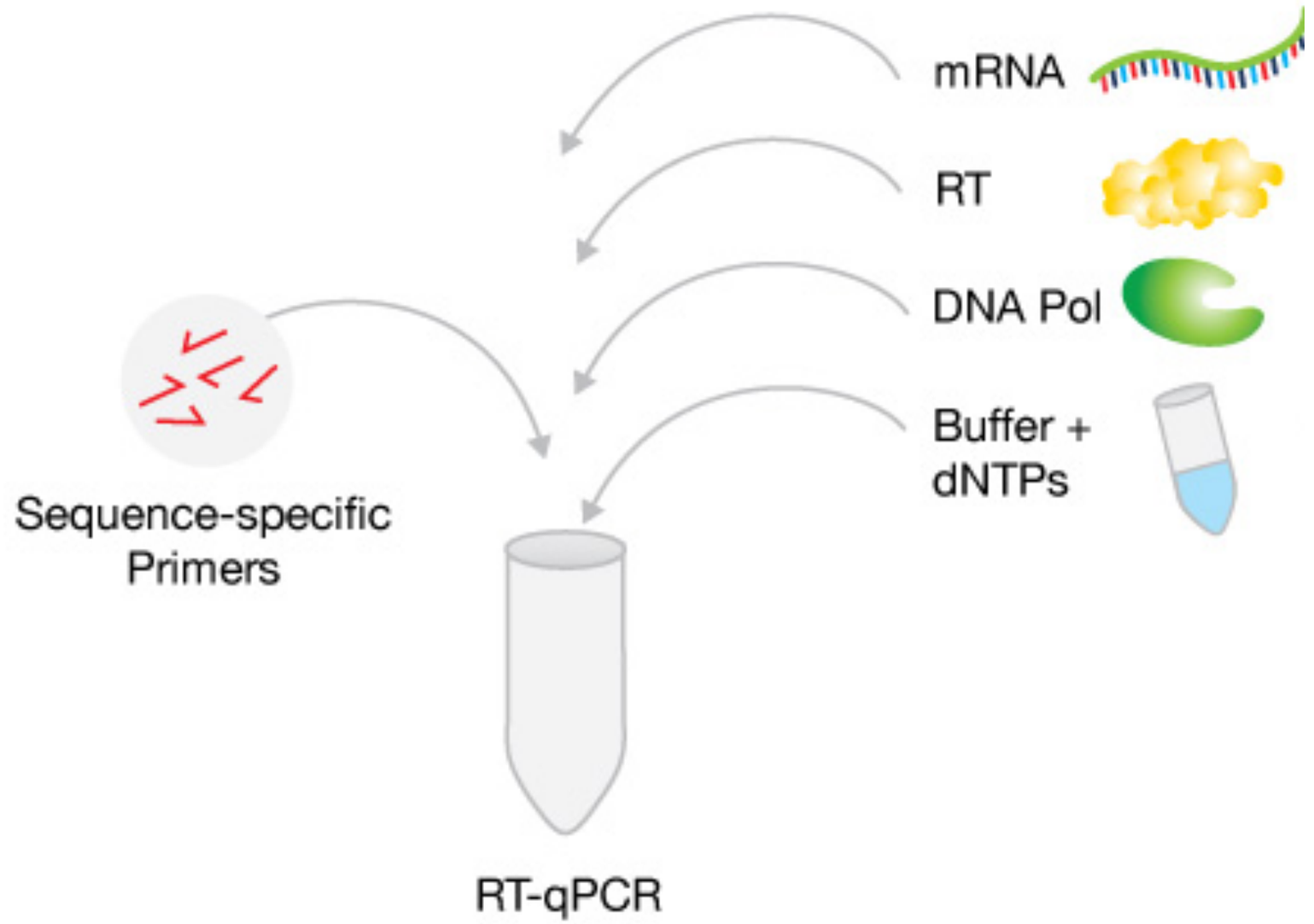
Aim 2

Identify candidate genes

RNAi

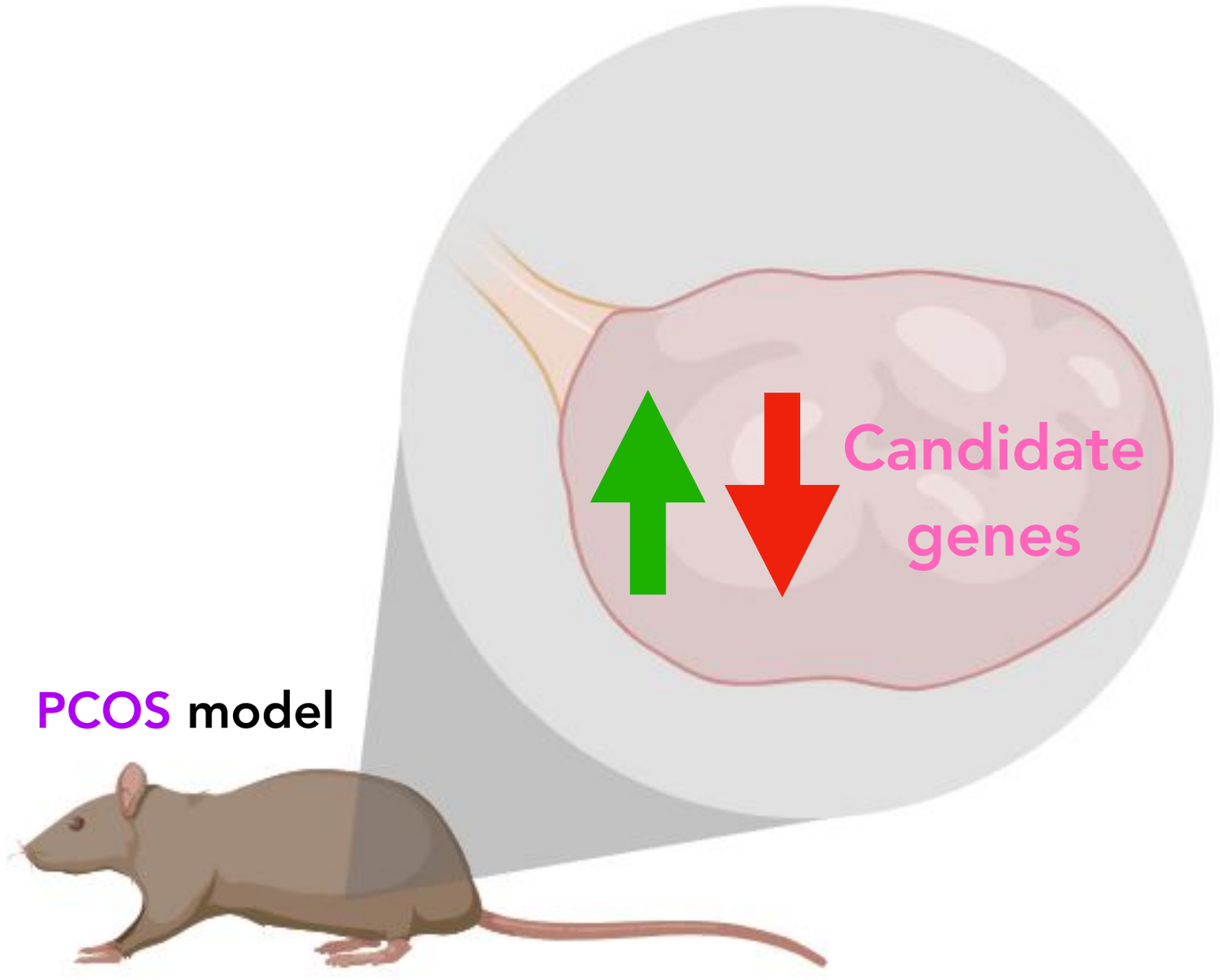


Aim 2 Measure expression of candidate genes



Aim 2

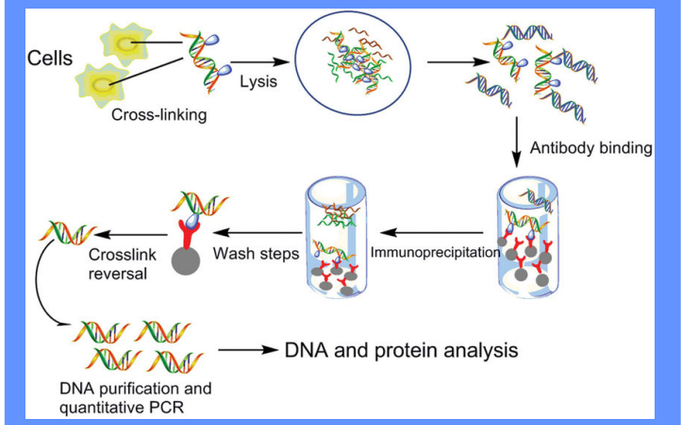
Expectation

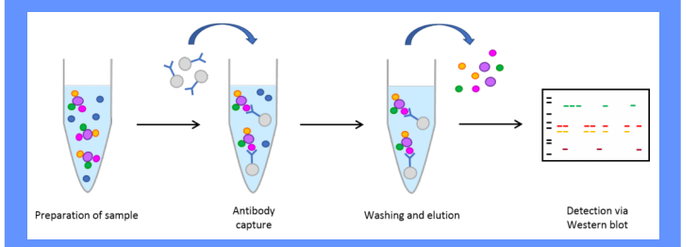


Hypothesis: one or more of the candidate genes identified in the RNAi screen will be differentially regulated in a PCOS model.

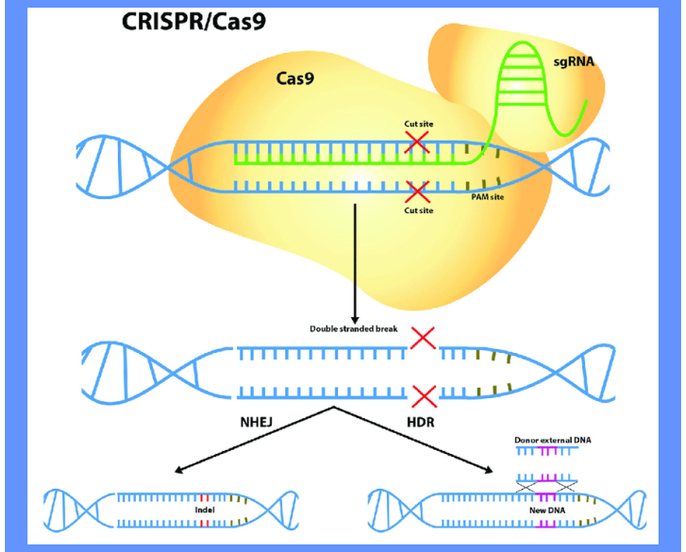
Aim 3: Identify direct protein interactions with the StAR promoter and protein that impact and testosterone levels within ovaries

Identify binding proteins

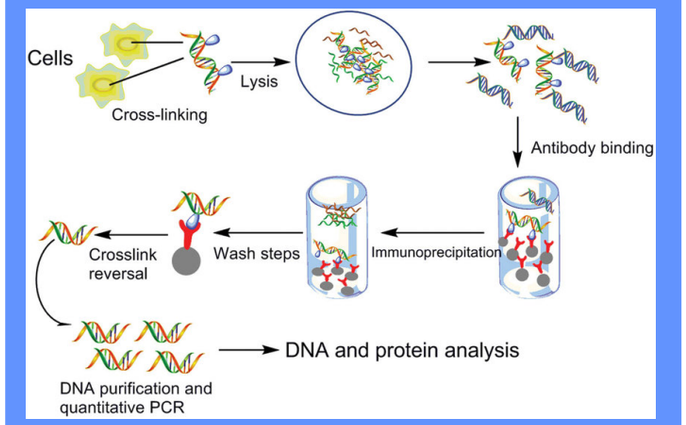


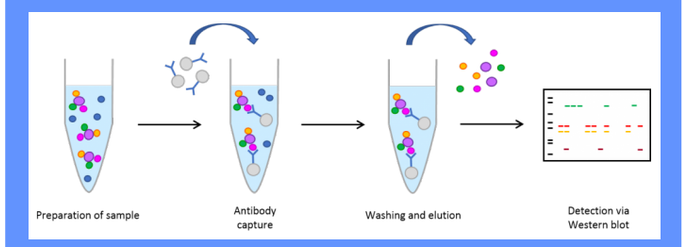


Mutagenize



Determine if mutation affects binding



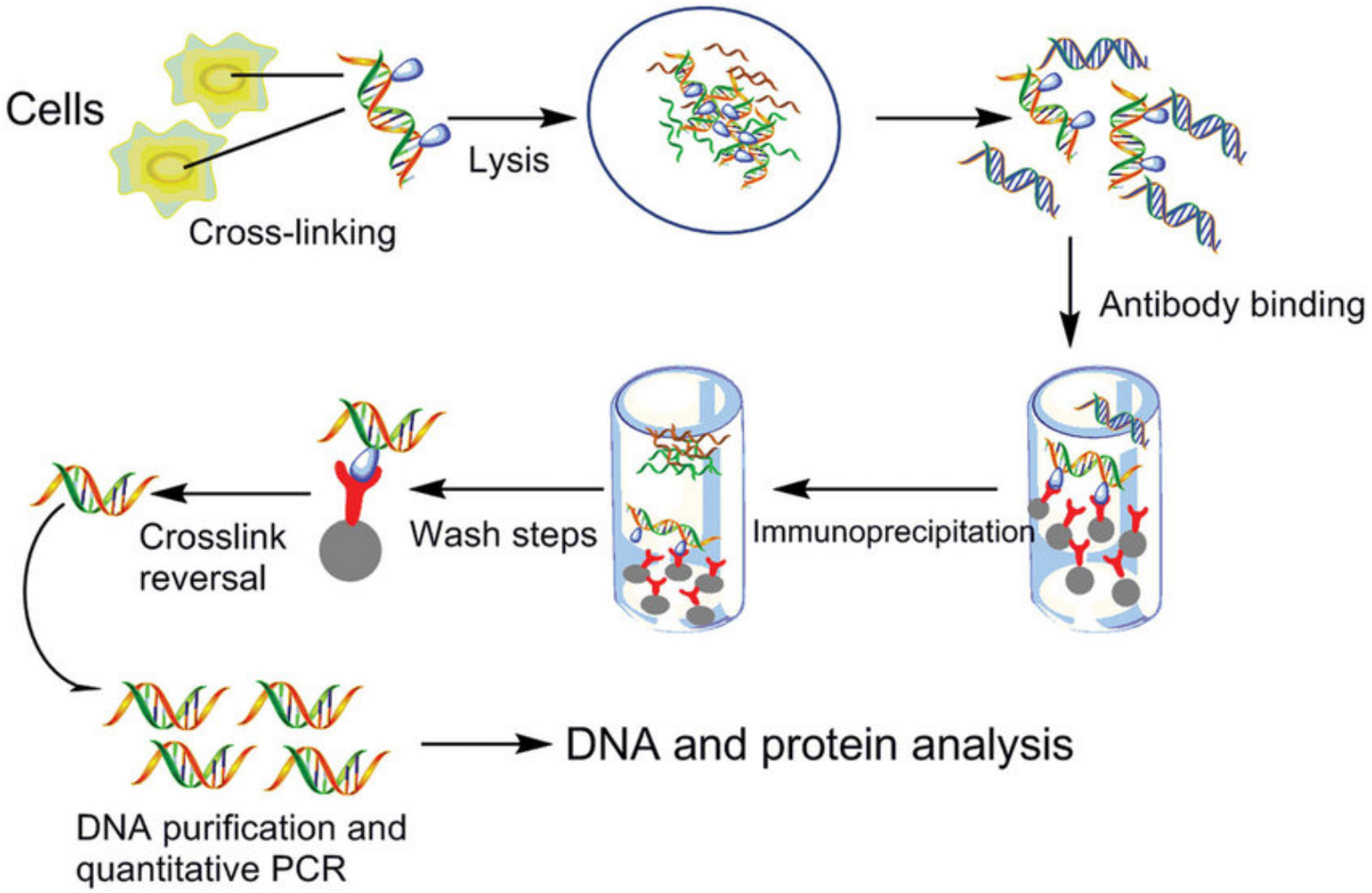


Hypothesis: mutating conserved regions of the StAR promoter will result in a lack of protein binding on the StAR promoter.

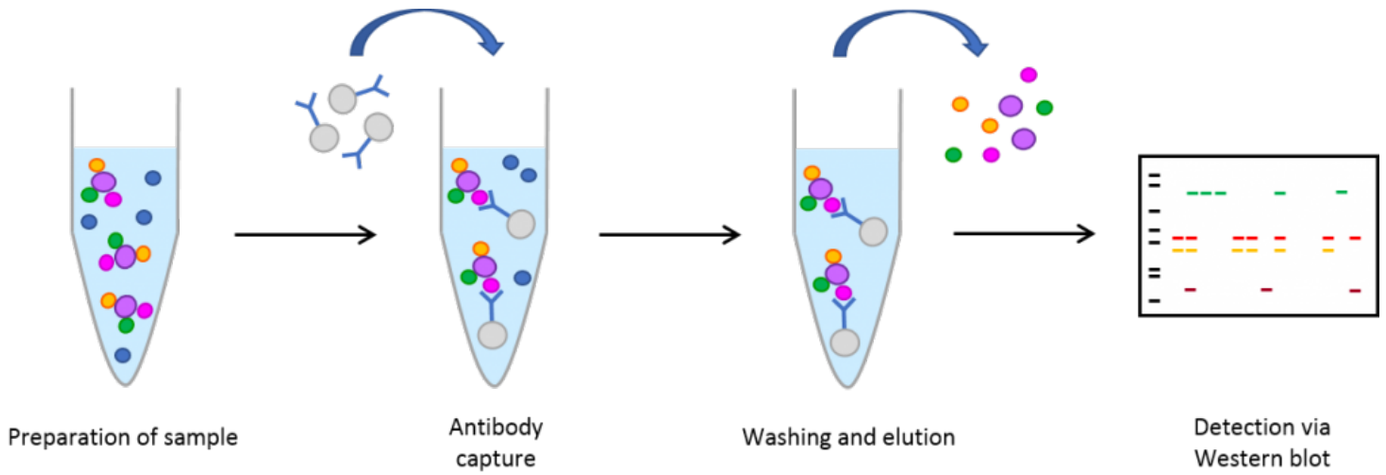
Aim 3

Identify binding proteins

ChIP

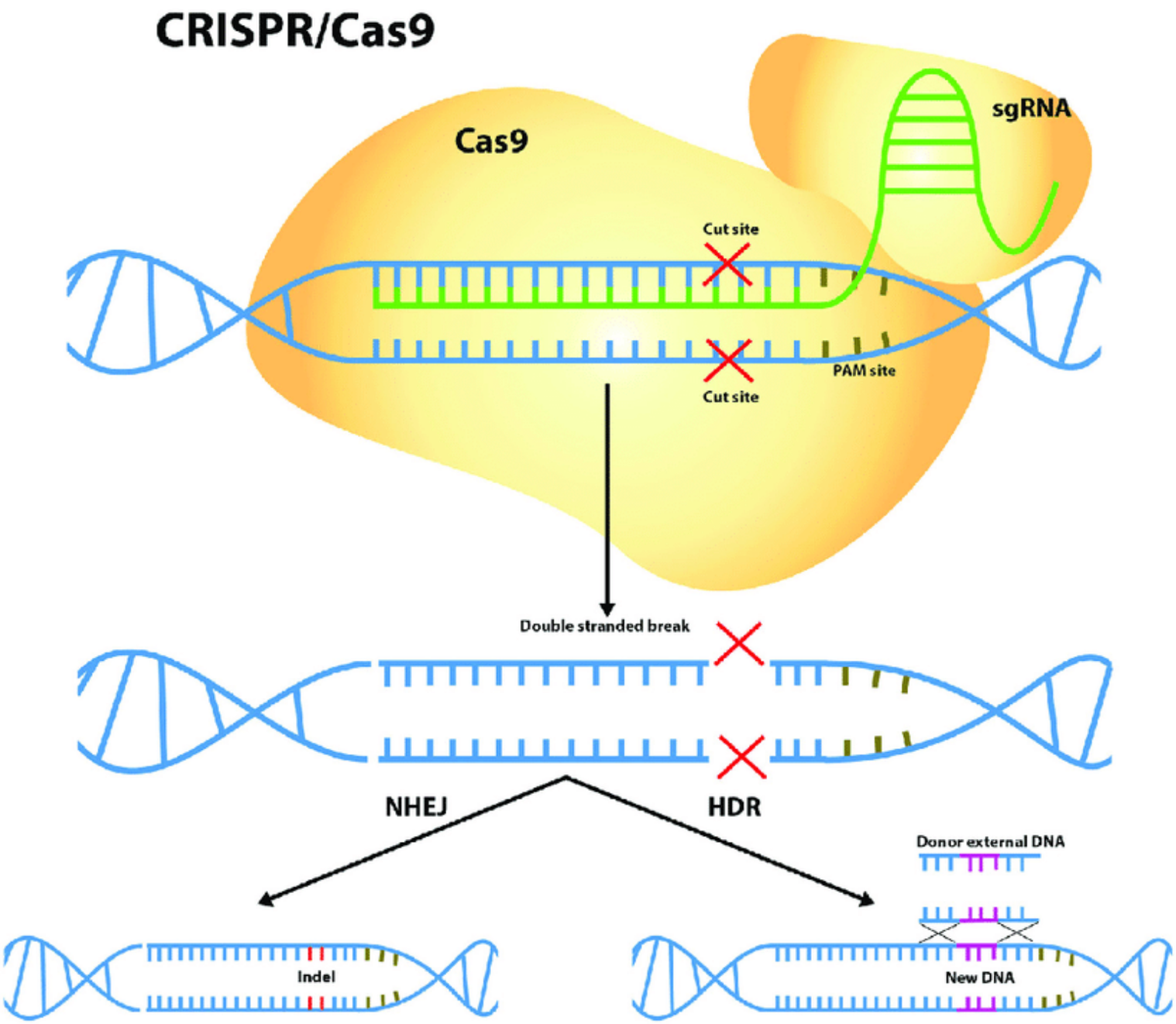


CoIP



Aim 3

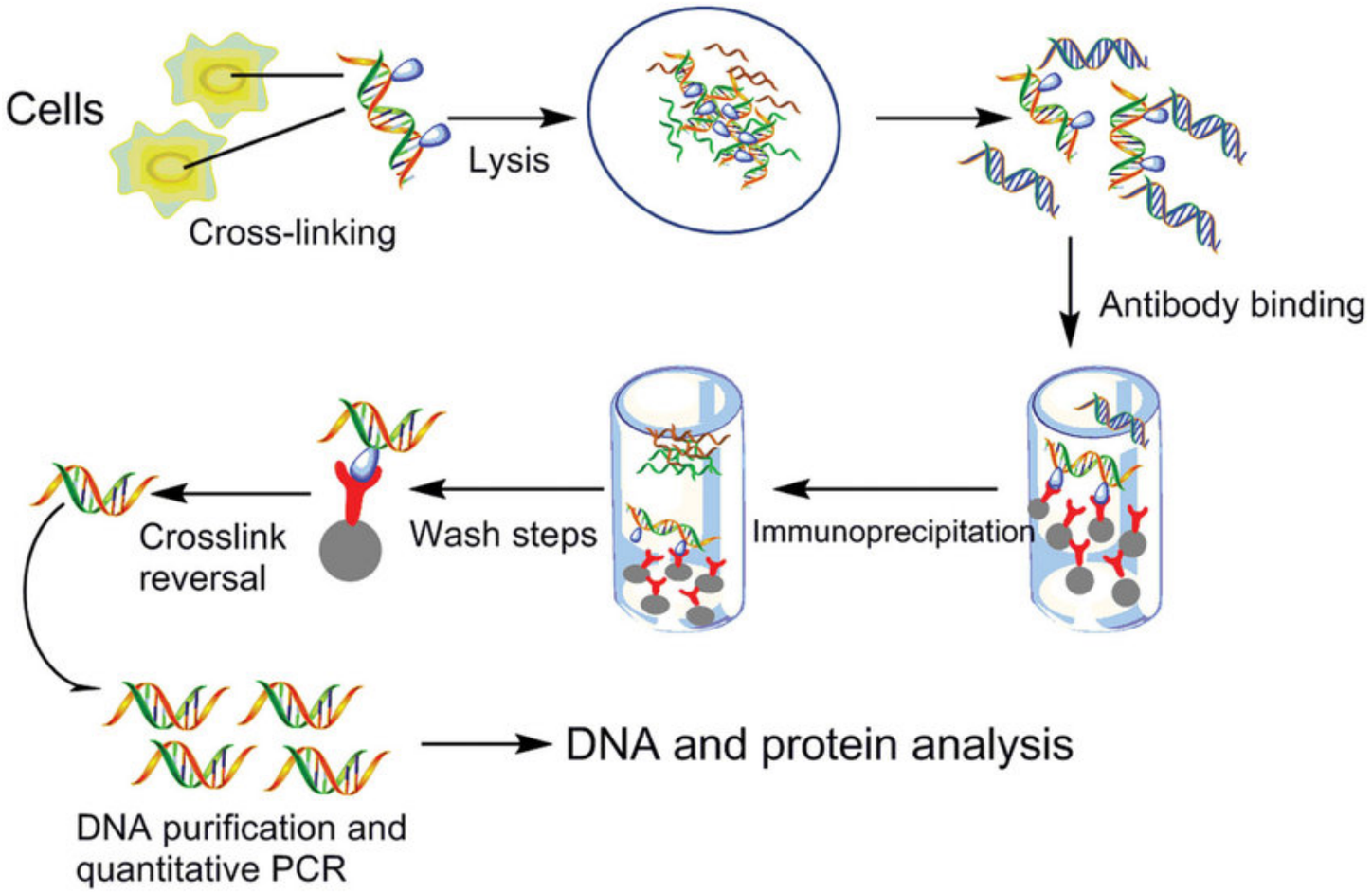
Mutagenize



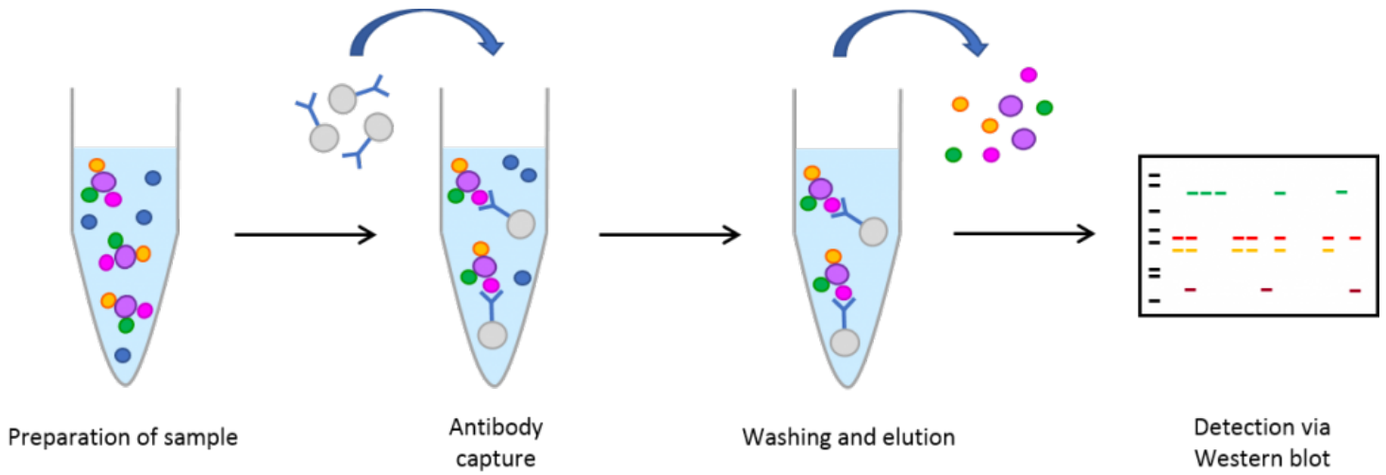
Aim 3

Determine if mutation affects binding

ChIP

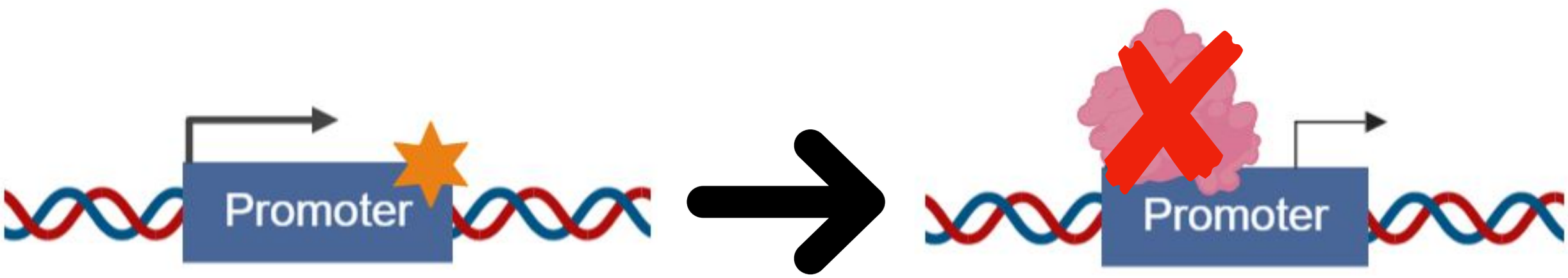


CoIP



Aim 3

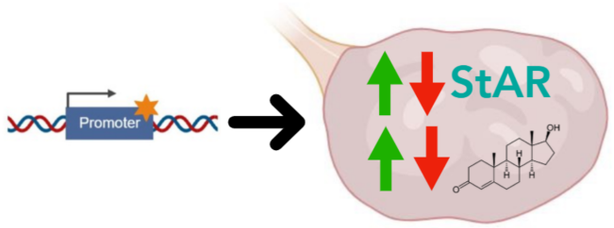
Expectation



Hypothesis: mutating conserved regions of the StAR promoter will result in a lack of protein binding on the StAR promoter.

Summary

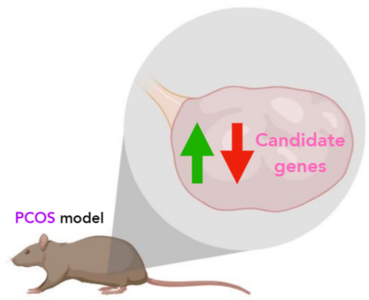
Aim 1 Expectation



Hypothesis: mutating conserved regions of the StAR promoter will result in differential expression of StAR and testosterone levels

Confirmation that alterations of the StAR promoter impact regulation of StAR expression and testosterone levels

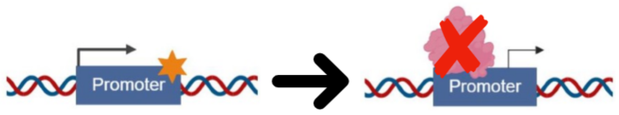
Aim 2 Expectation



Hypothesis: one or more of the candidate genes identified in the RNAi screen will be differentially regulated in a PCOS model.

Identification of candidate genes involved in regulating StAR and if they are differentially regulated in PCOS model.

Aim 3 Expectation



Hypothesis: mutating conserved regions of the StAR promoter will result in a lack of protein binding on the StAR promoter.

Identification of proteins that directly bind the StAR promoter or protein to regulate StAR expression

Future Research

Protein-protein interactions

Other symptoms


Questions?

References

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