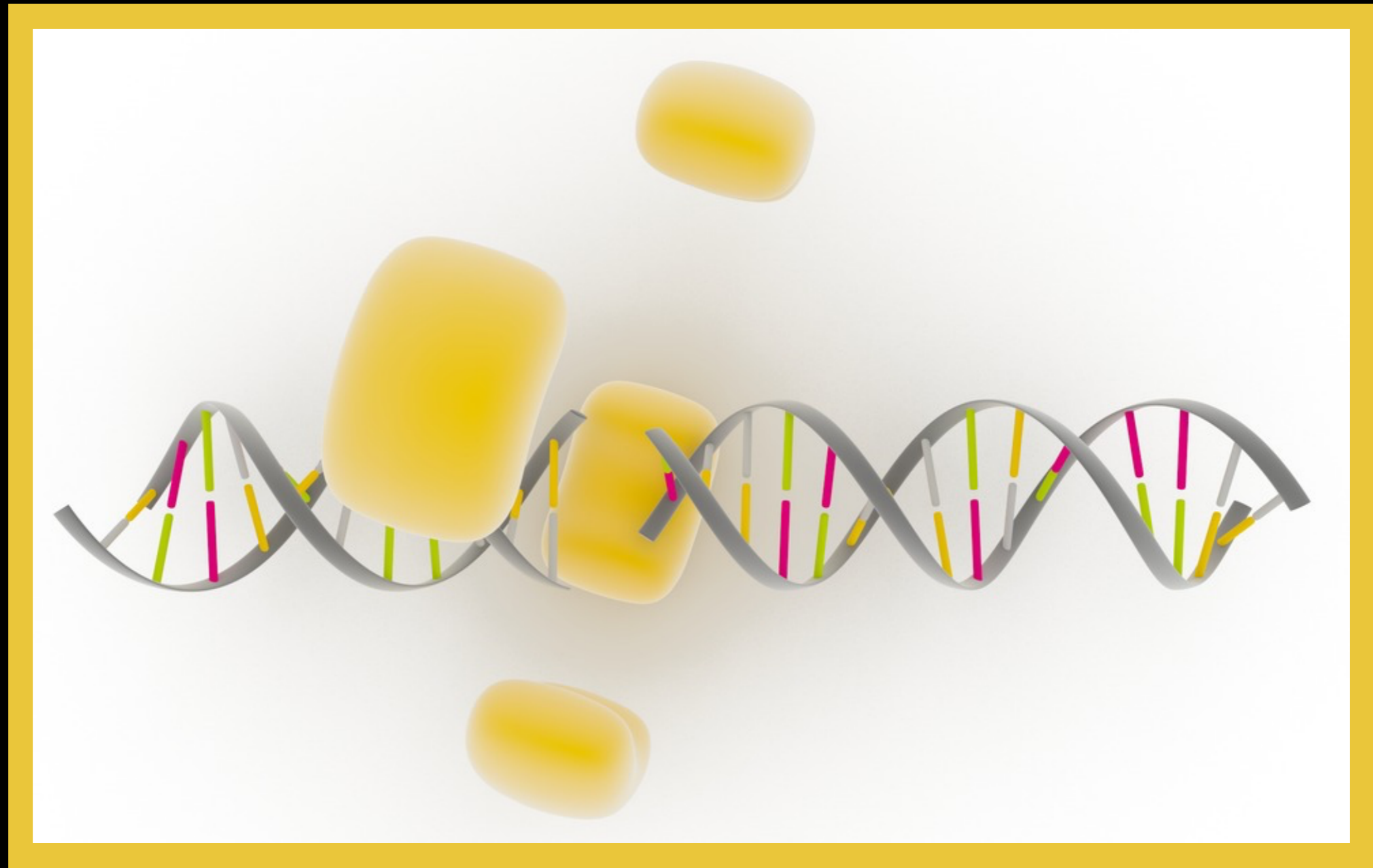
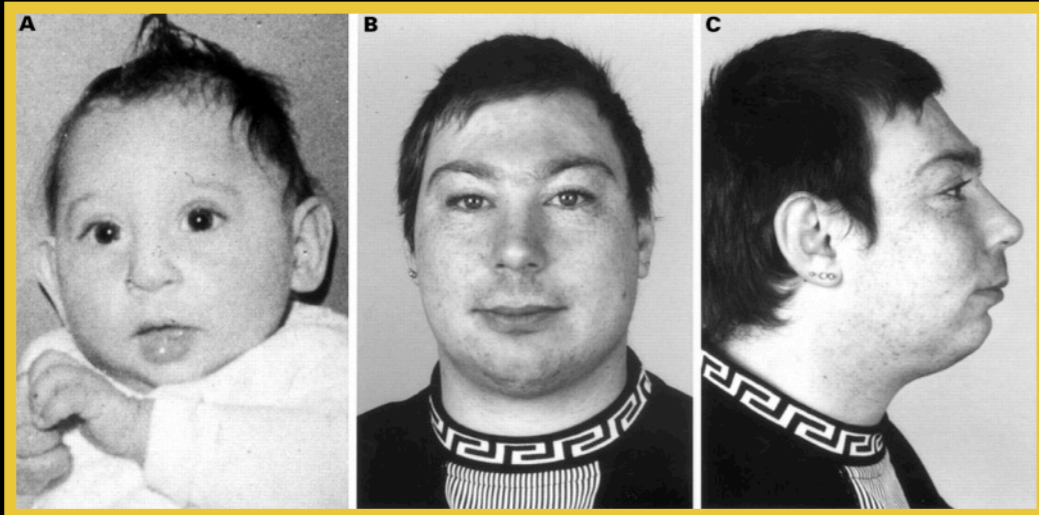


Nibrin & Nijmegen breakage syndrome



What is Nijmegen breakage syndrome (NBS)?



Abnormal physical features

Intellectual disability

Immunodeficiency

Premature ovarian failure

Cancer predisposition



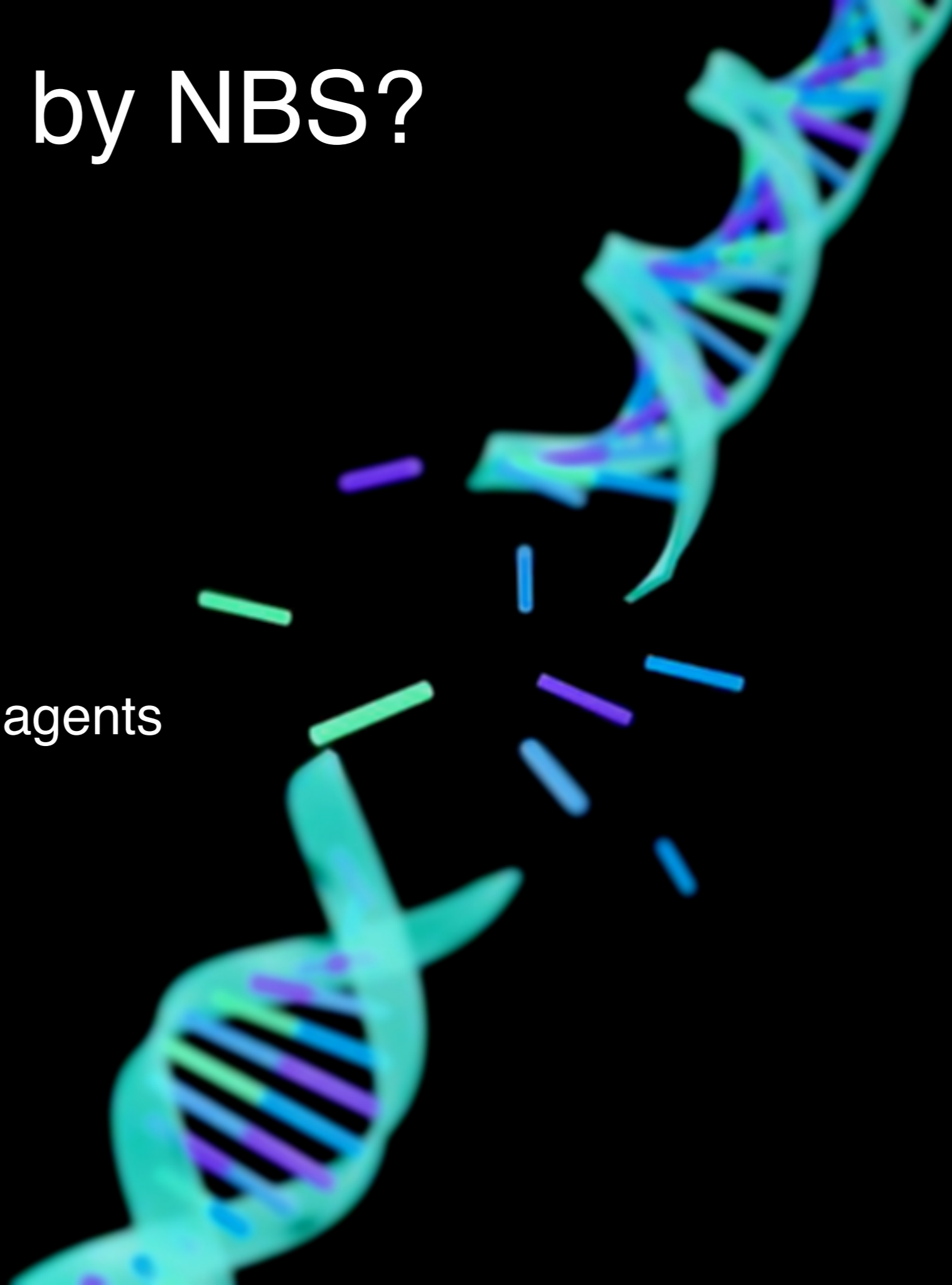
What is affected by NBS?

Chromosomes

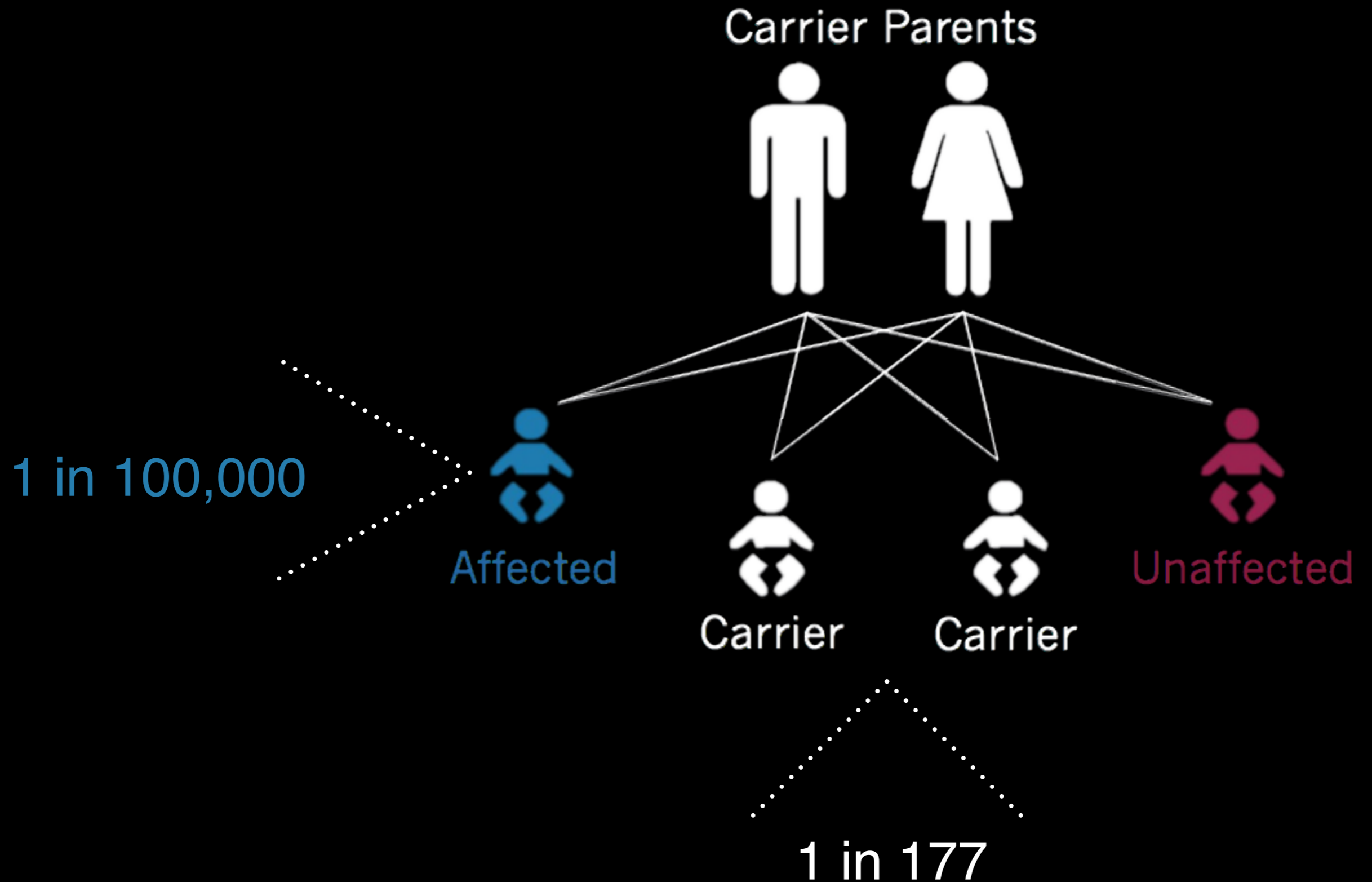
Telomeres

Cell cycle checkpoints

Sensitivity to DNA-damaging agents

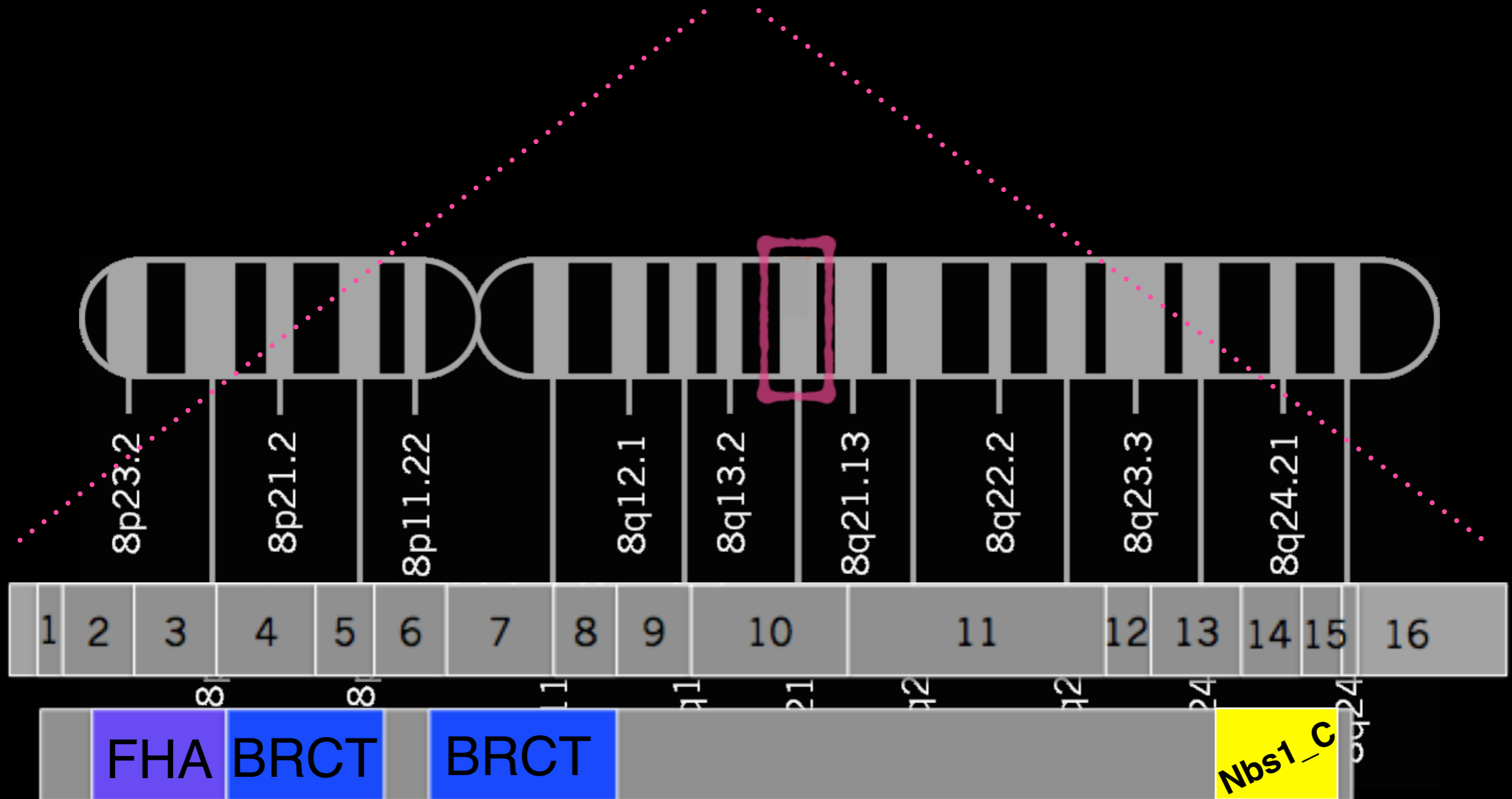


How is NBS inherited?

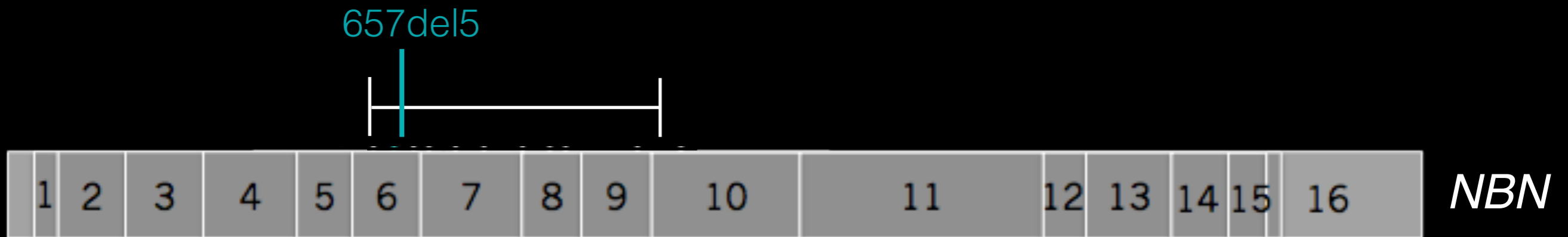


Nibrin is associated with NBS

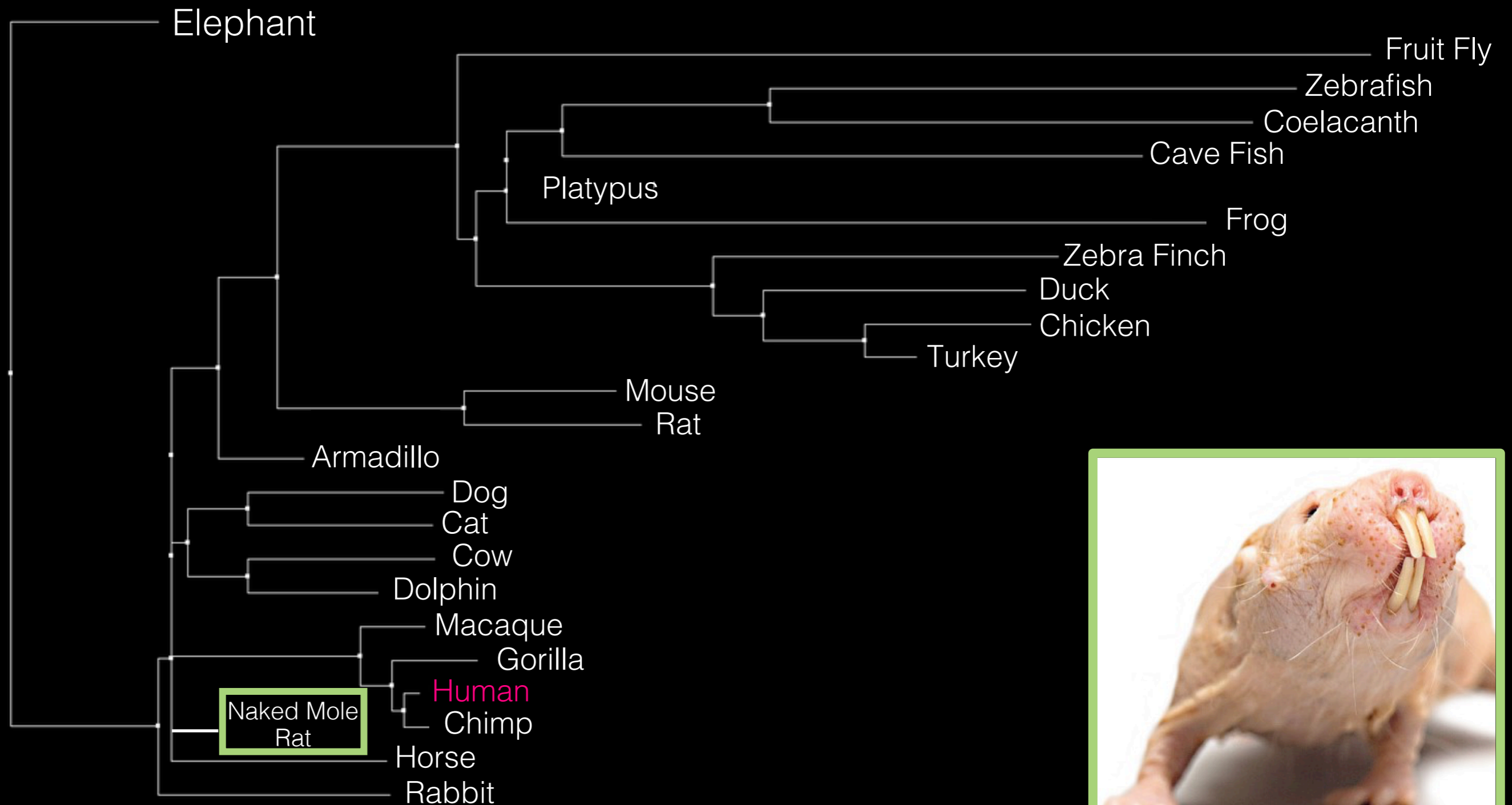
(NBN)



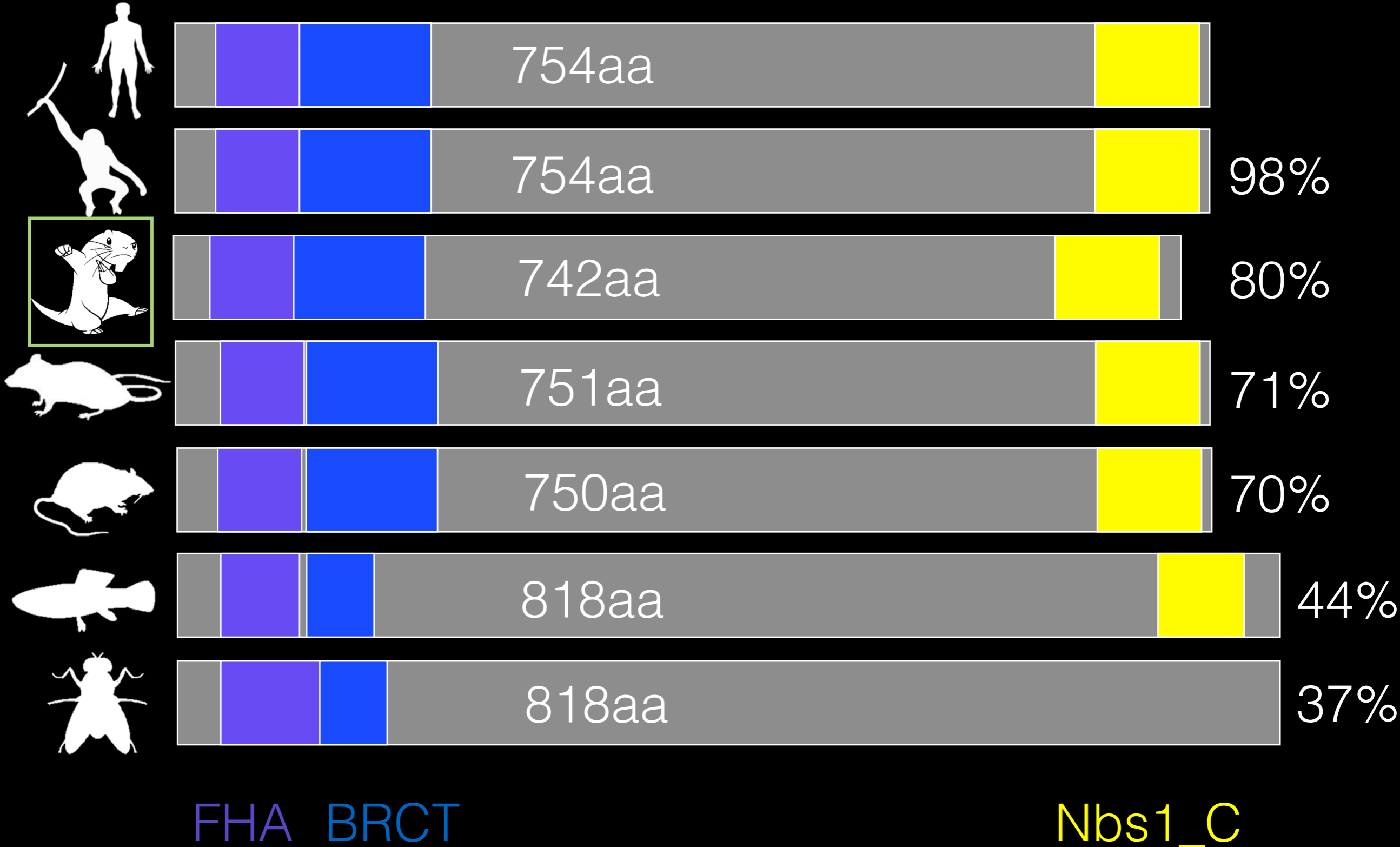
What mutations are found in Nibrin?



What is **Nibrin** phylogeny?



Is Nibrin conserved?



What does Nibrin do?

Rad50

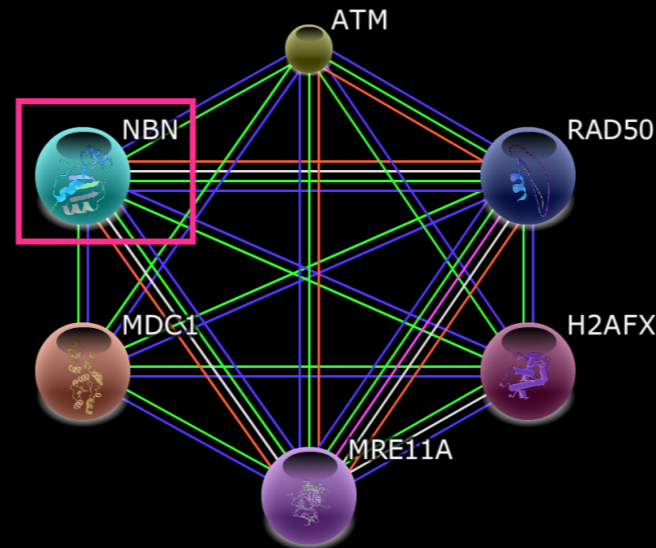
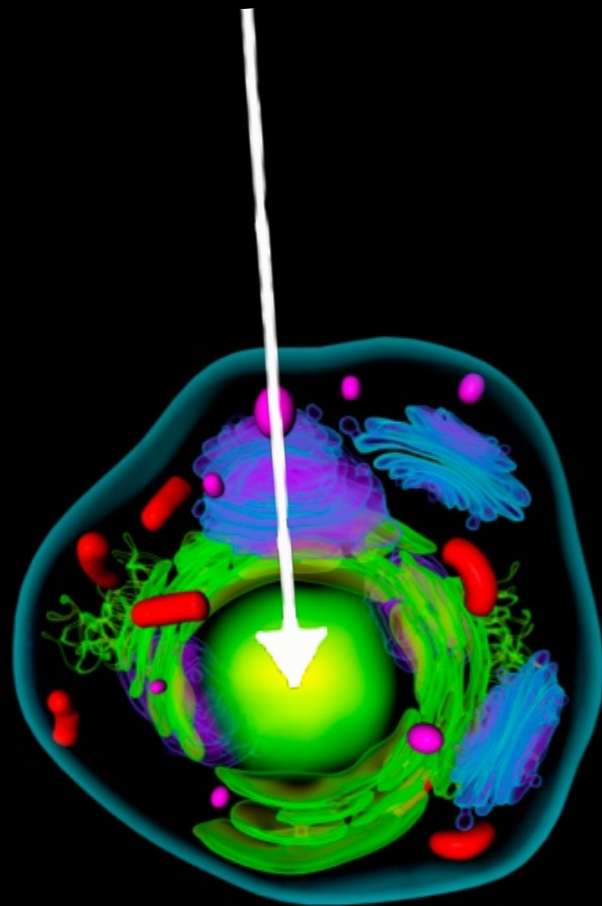
NBN

Mre11

Cellular
Components

Molecular
Functions

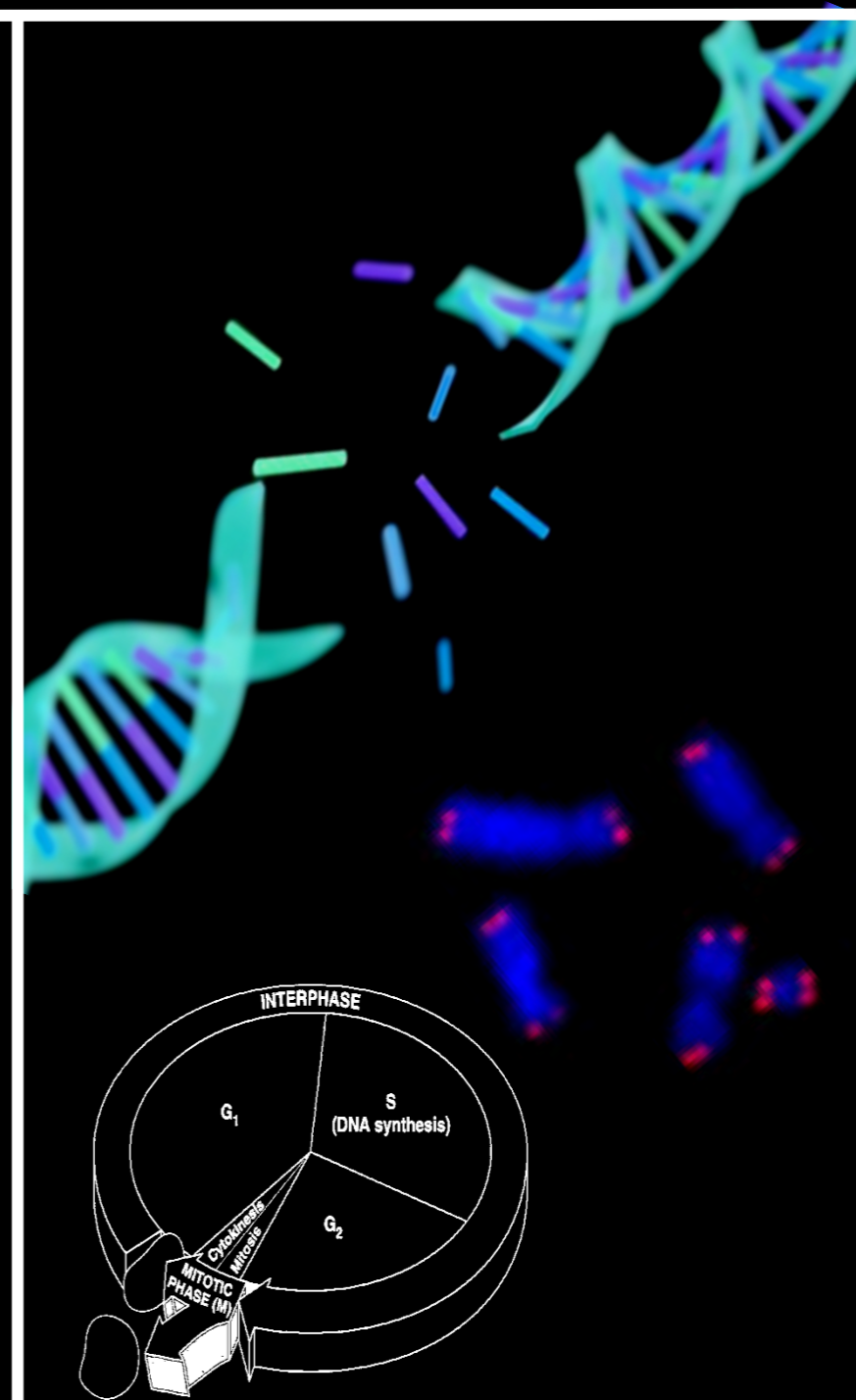
Biological
Processes



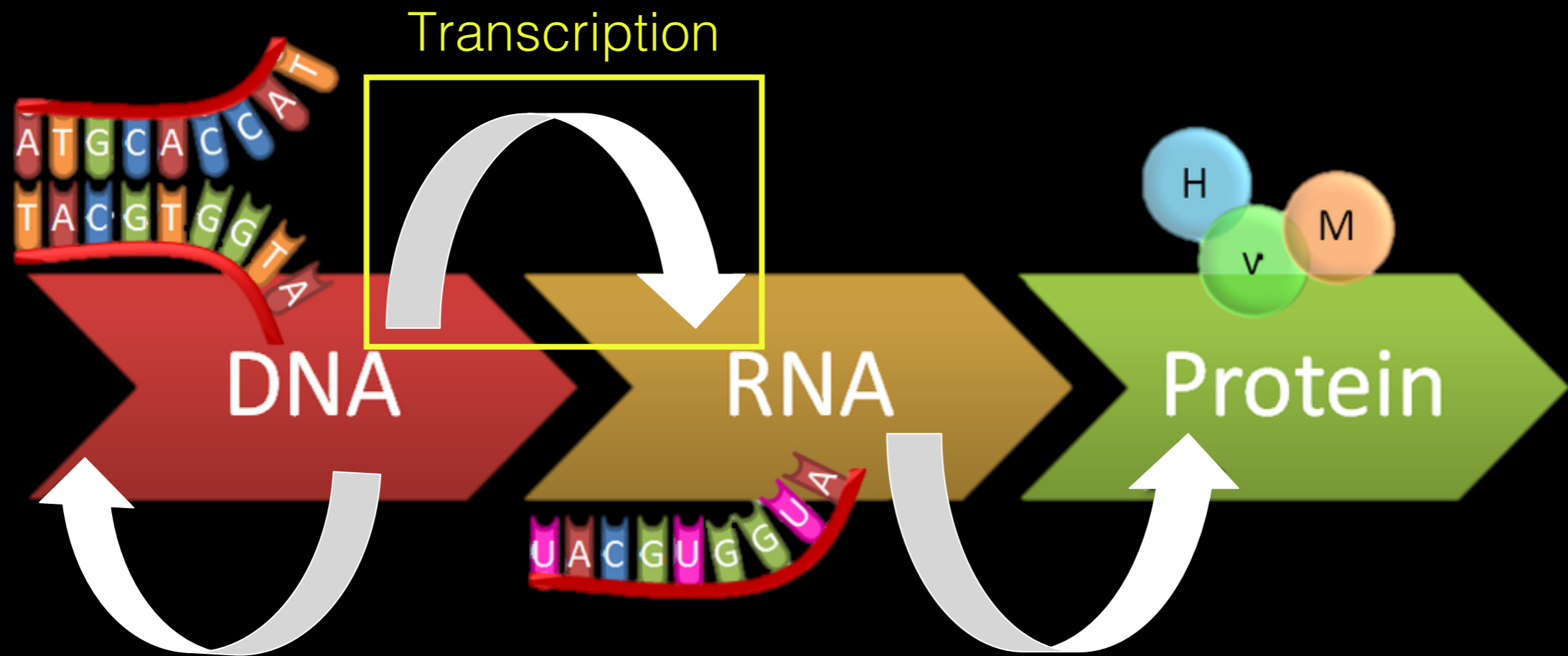
Protein binding



FHA
BRCT
Nbs1_C



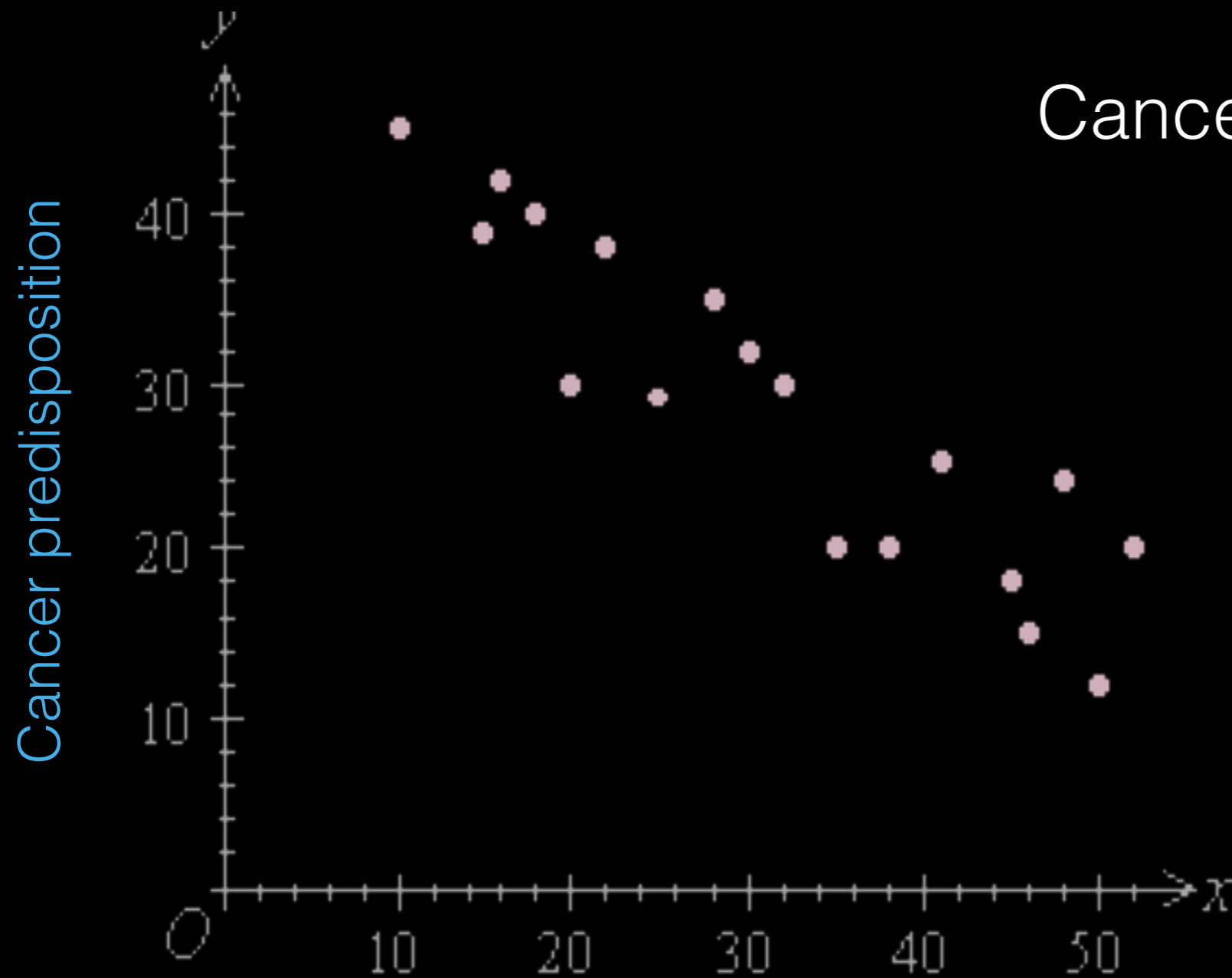
Gap in knowledge



What are the molecular mechanisms that regulate *NBN* expression?

Hypothesis

As expression of *NBN*



Cancer predisposition

Expression of *NBN*

• Individual

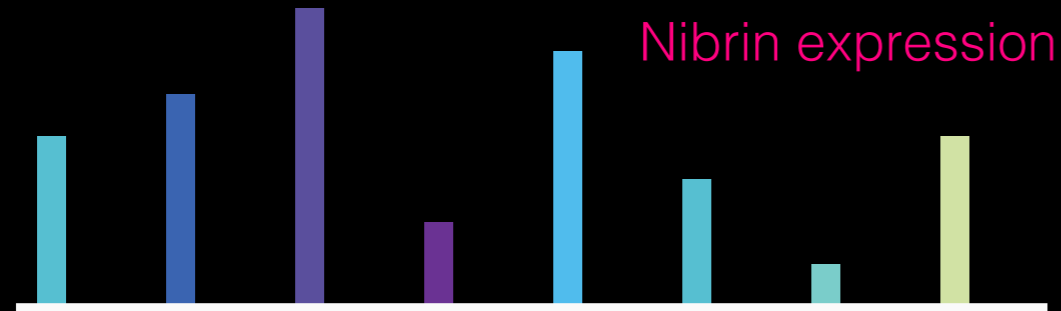
Aim 1: Identify SNPs directly affecting *nibrin* expression levels.

Hypothesis & Approach:



Next generation sequencing

+



Quantitative Mass Spectrometry

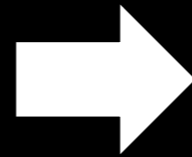
Correlation?

Aim 1: Identify SNPs directly affecting *nibrin* expression levels.

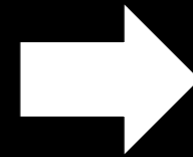
Rationale:



SNP Manipulation



Nibrin
Expression



Cancer
Predisposition

Aim 2: Identify transcription factors (TF) that regulate *nibrin* expression.

Hypothesis & Approach:



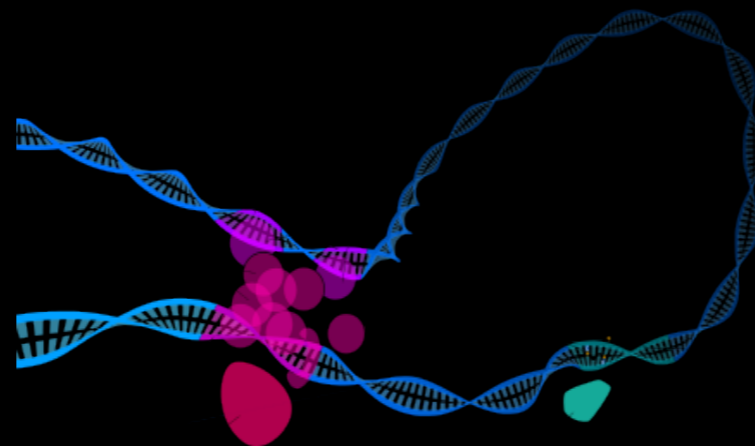
Wild Type



High



TF Mutant



CRISPR-based screen
& CRISPR-Cas9



Influenced



Knockout



CRISPR-Cas9

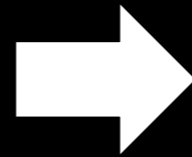


Aim 2: Identify transcription factors (TF) that regulate *nibrin* expression.

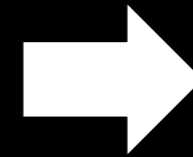
Rationale:



TF Manipulation



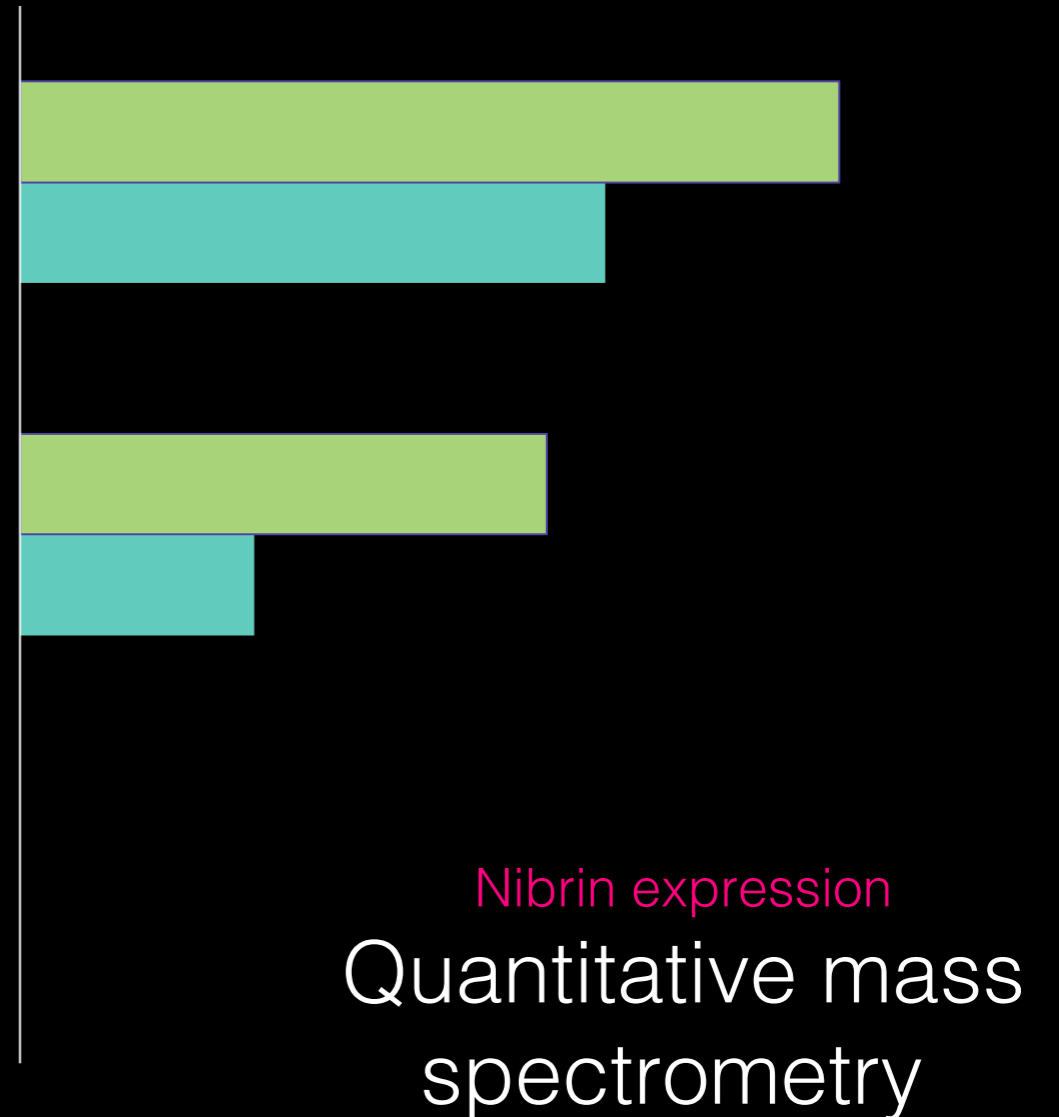
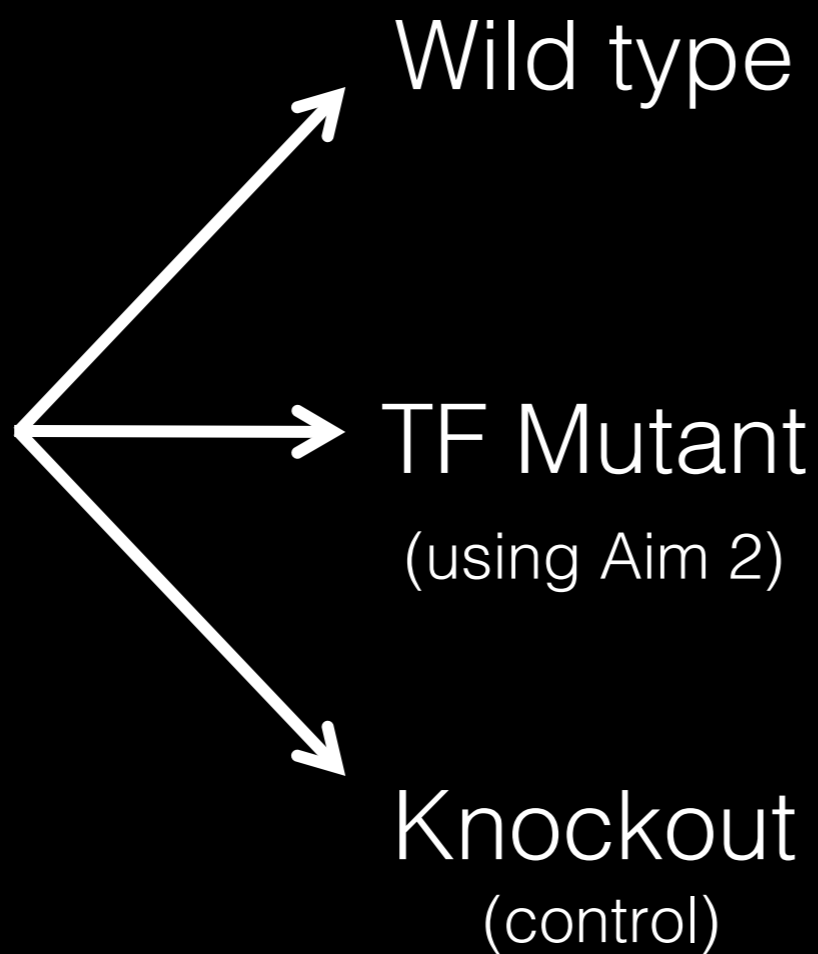
Nibrin
Expression



Cancer
Predisposition

Aim 3: Determine *nibrin* expression levels in naked mole-rats.

Hypothesis & Approach:

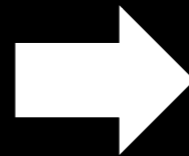


Aim 3: Determine *nibrin* expression levels in naked mole-rats.

Rationale:



Nibrin
Expression



Cancer
Predisposition

Future Directions

Long-term goal: Help those affected by NBS

Overall goal: Help the population by screening for Nibrin-related cancer.



References

Pictures by slides

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