

Prader Willi Syndrome & Necdin

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A glowing blue DNA double helix structure is shown against a dark blue background. The DNA strands are translucent and emit a bright blue light, with several white, glowing spheres representing base pairs. The helix is positioned on the right side of the frame, curving upwards and then downwards.

What is Prader Willi Syndrome?



<http://www.aafp.org/afp/2005/0901/p827.html>

<http://www.pwcf.org/>

http://www.scielo.br/scielo.php?script=sci_arttext&pid=S0004-282X2002000600024

Necdin is mutated in Prader Willi Syndrome



MAGE

What is the **MAGE** Domain?

How well conserved is **Necdin**?



321 aa

MAGE

% Identity



321 aa

96%



325 aa

88%



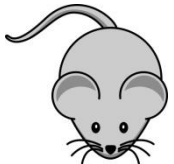
325 aa

87%



325 aa

85%



325 aa

81%

What does **Necdin** do and where?

Cellular Components

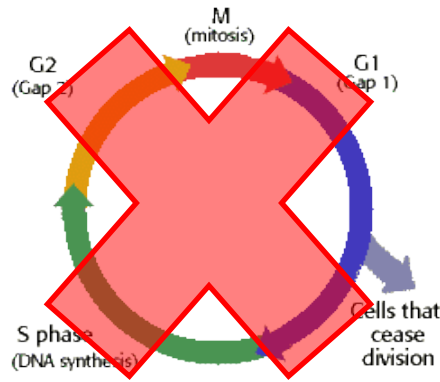
Cytoplasm



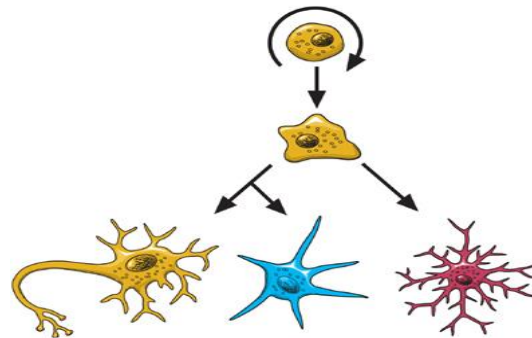
Nucleus

wiseGEEK

Biological Processes

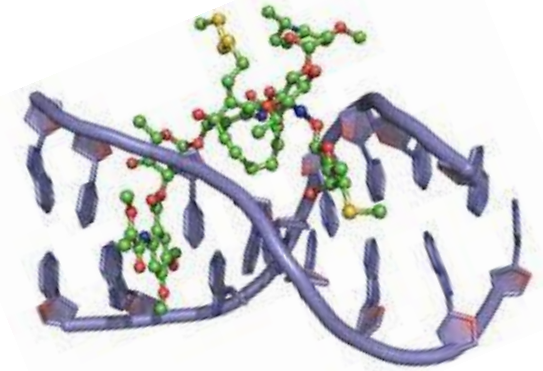


Cell Cycle Arrest



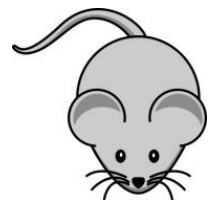
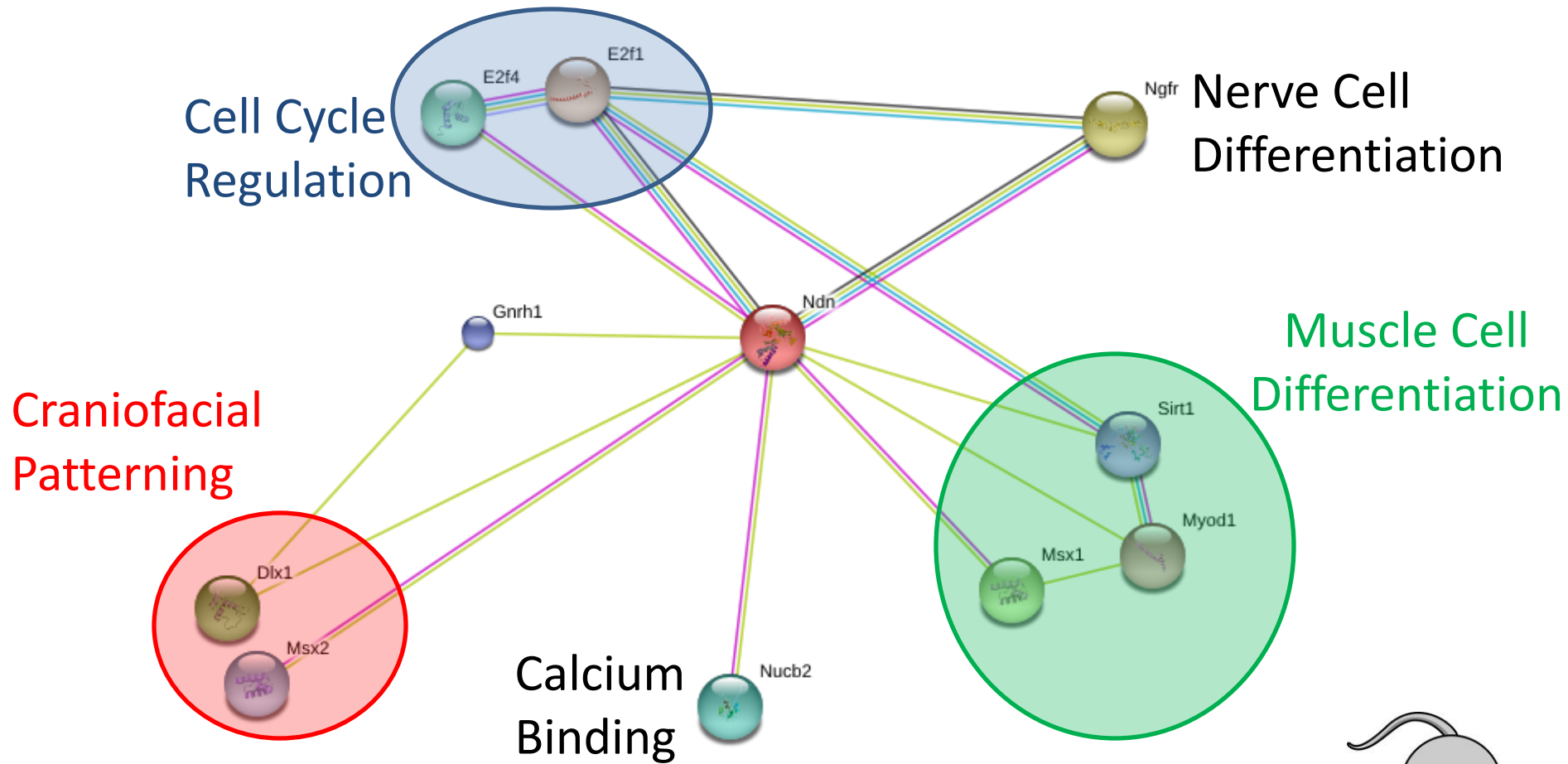
Nerve Cell Differentiation

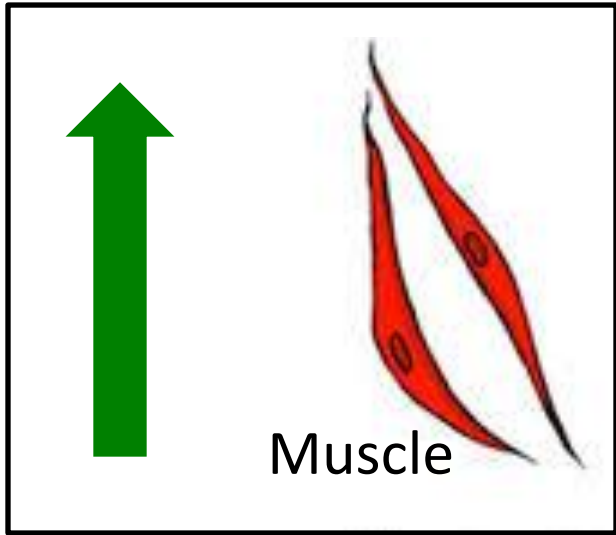
Molecular Function



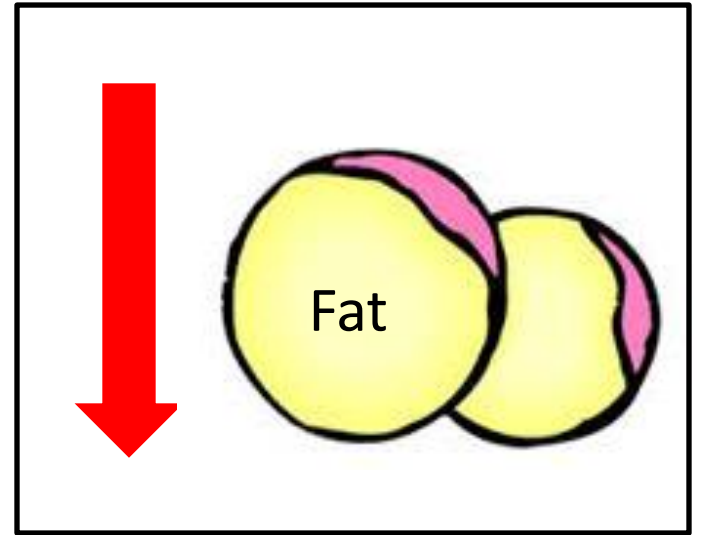
DNA Binding

What does **Necdin** interact with?

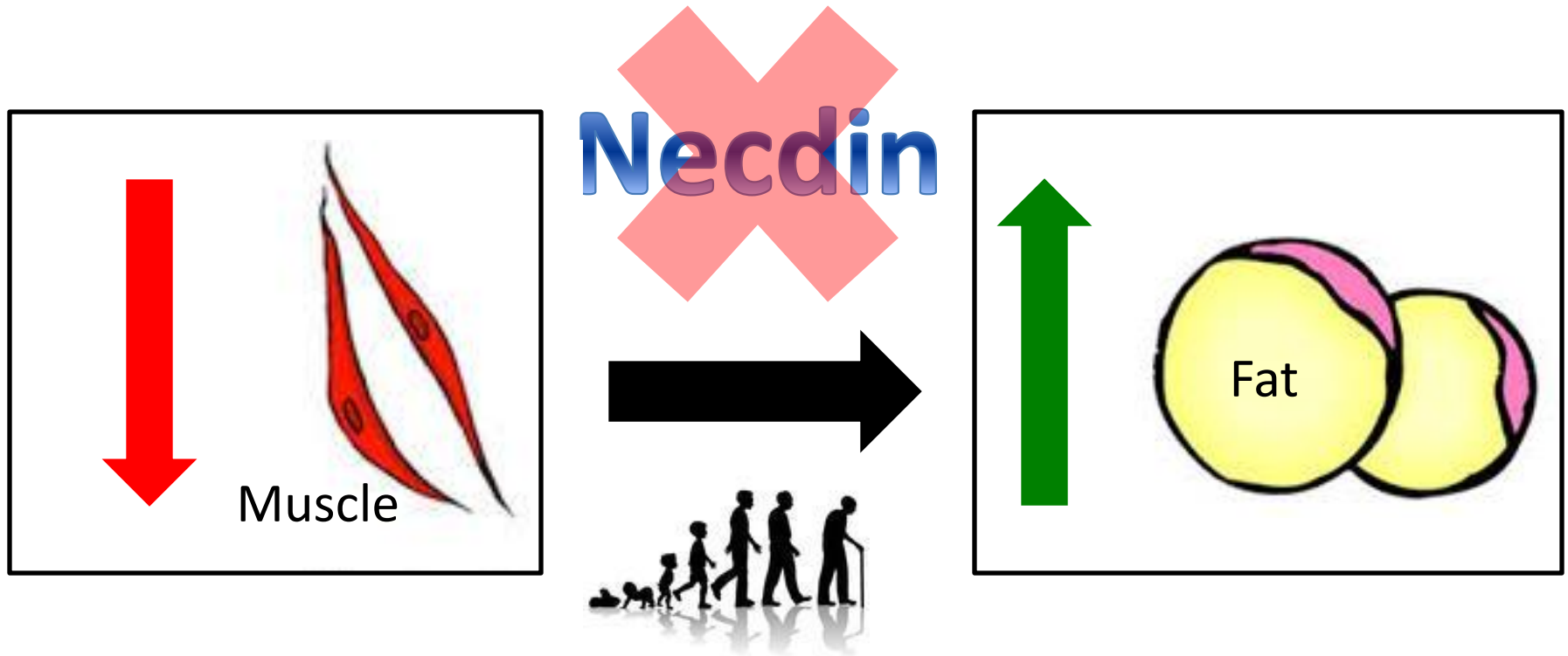




Necdin

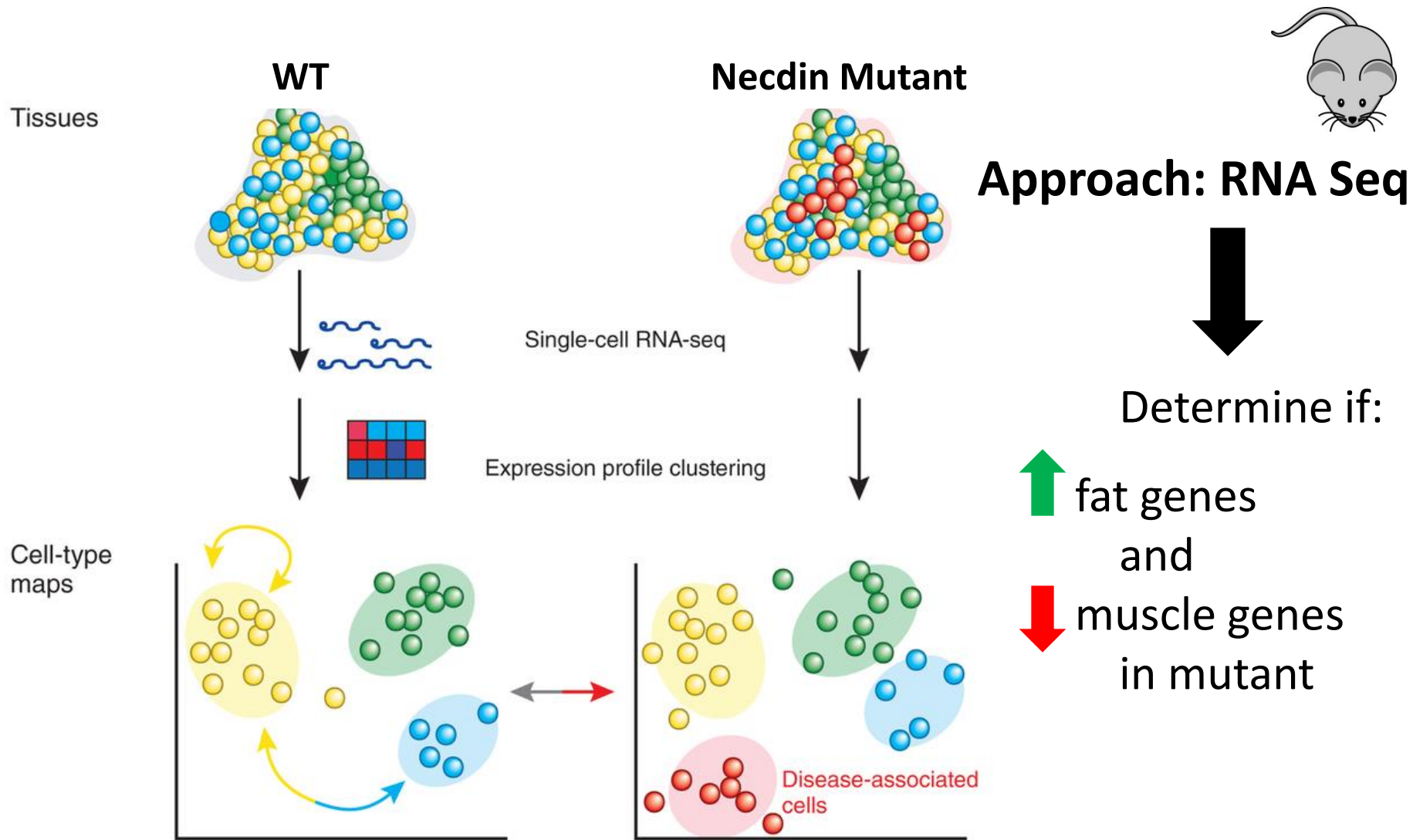


Knowledge Gap: What happens to **muscle** cell and **fat** cell differentiation throughout development in Prader Willi Syndrome patients?

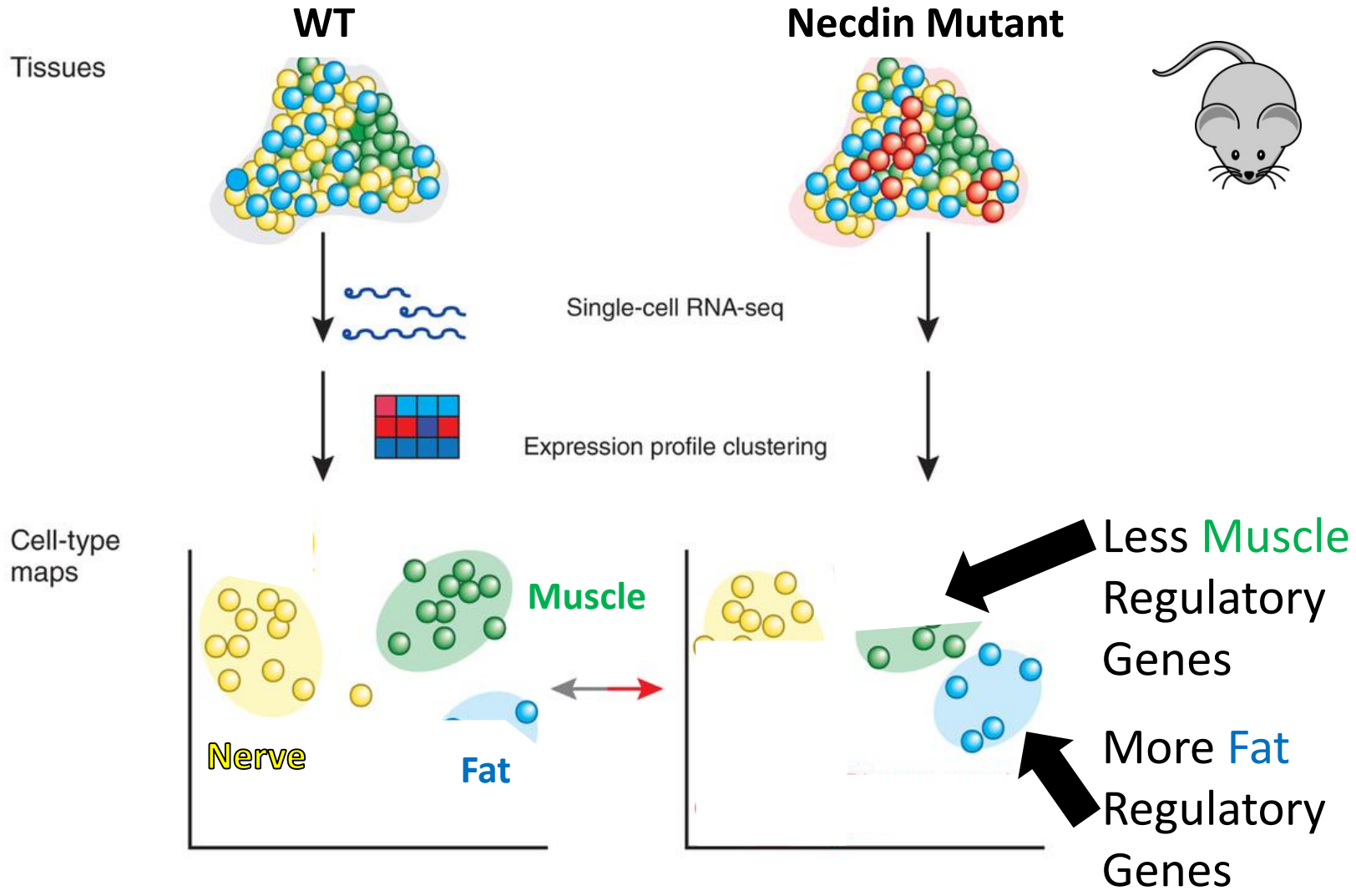


Hypothesis: The loss of necdin will **↓** **muscle** cell differentiation and **↑** **fat** cell differentiation at a certain point in development.

Aim 1: Are more fat cell associated genes and less muscle cell associated genes found in Necdin mutants?

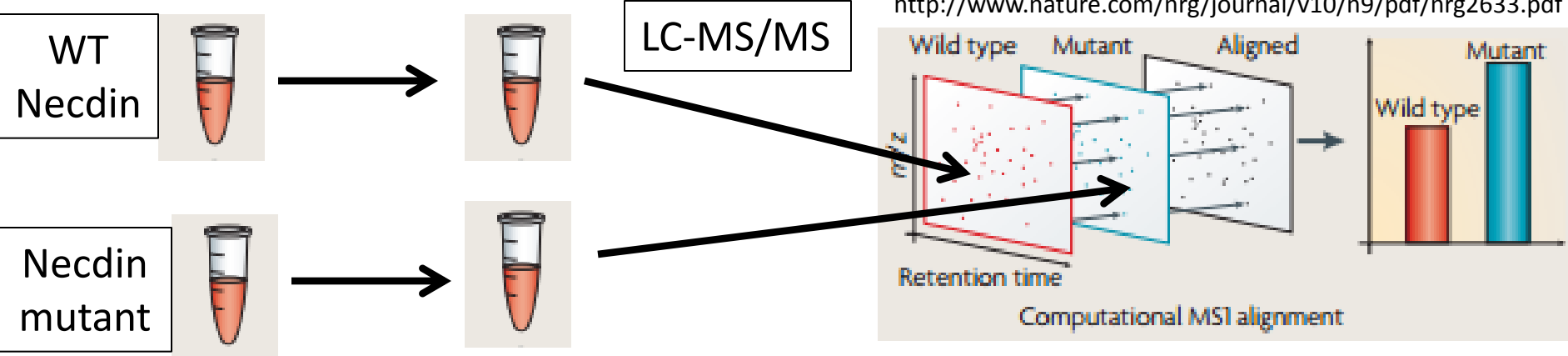


Aim 1: What is the expression of fat vs. muscle genes?



Hypothesis: Fat regulatory genes ↑ than muscle in mutant

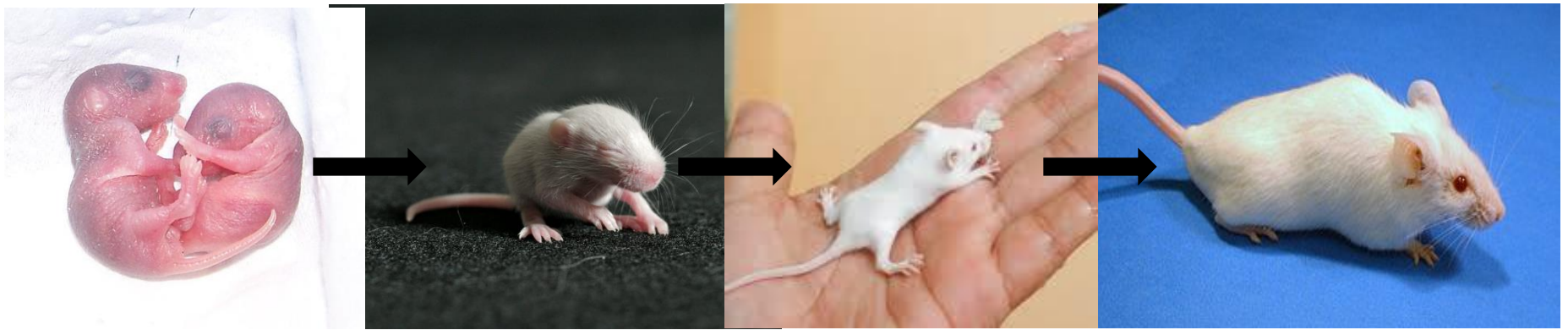
Aim 2: Is there overall muscle cell loss and fat cell accumulation at a certain stage in development?



Approach: Mass Spectrometry throughout development

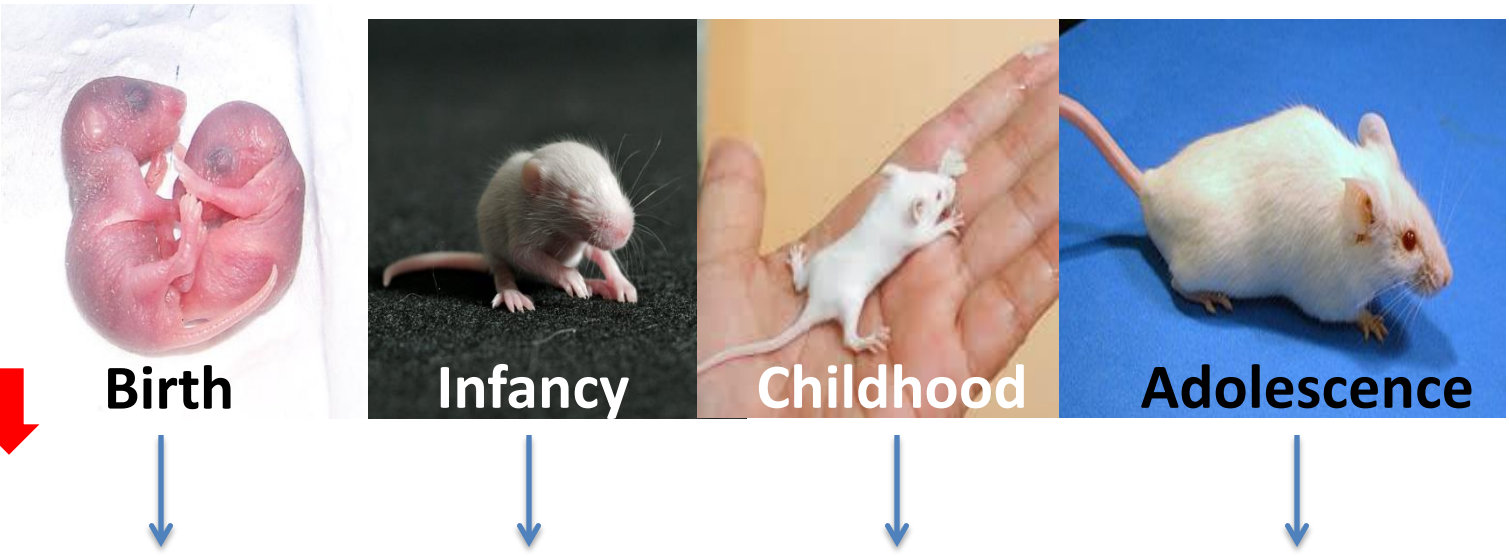


Information on timescale for diagnosis



Aim 2: Is there overall muscle cell loss and fat cell accumulation at a certain stage in development?

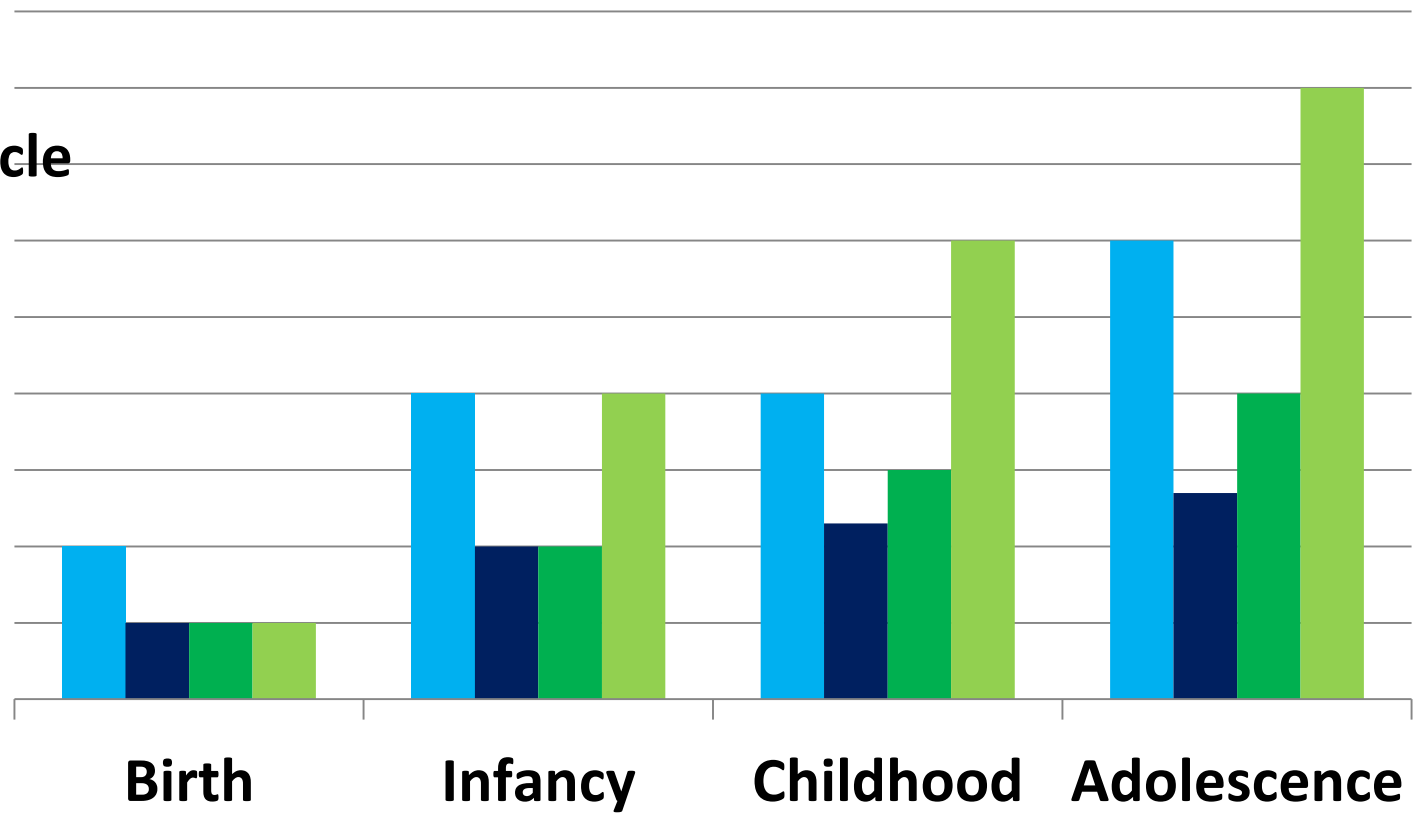
Hypothesis:
 Fat **↑** during development in mutant while Muscle **↓**



WT Muscle	Fast Growth	Fast Growth	Plateau	Fast Growth
WT Fat	Slow Growth	Slow Growth	Slow Growth	Slow Growth
Mutant Muscle	Decreased Growth	Slow Growth	Slow Growth	Slow Growth
Mutant Fat	Slow Growth	Fast Growth	Fast Growth	Fast Growth

Aim 2: Is there overall muscle cell loss and fat cell accumulation at a certain stage in development?

- WT Muscle
- Mutant Muscle
- WT Fat
- Mutant Fat

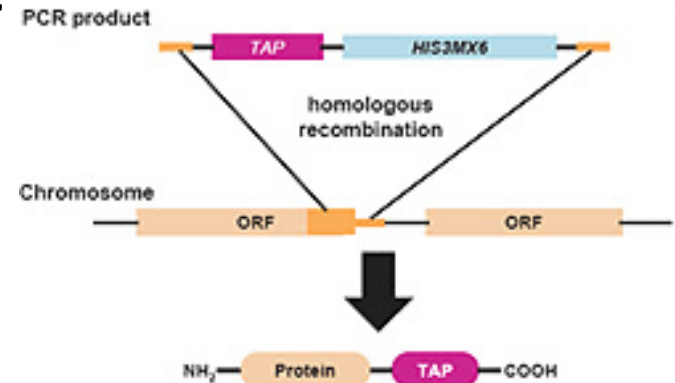
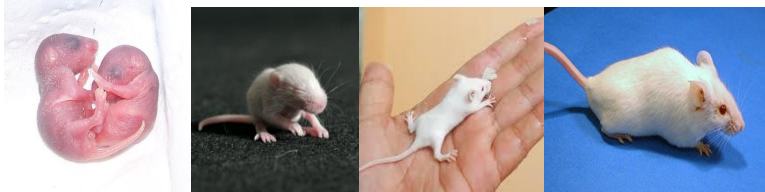


Hypothesis: **Fat** ↑ during development in mutant while **Muscle** ↓

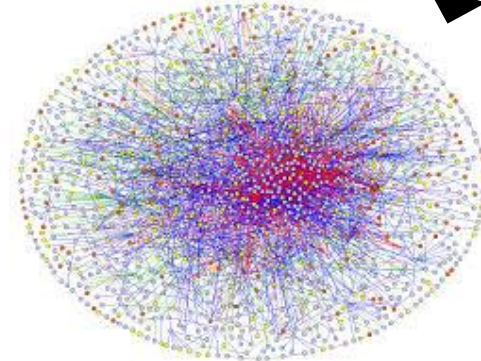
Aim 3: What are necdin interactions related to fat and muscle throughout development?

Approach:

Tap Tag throughout development

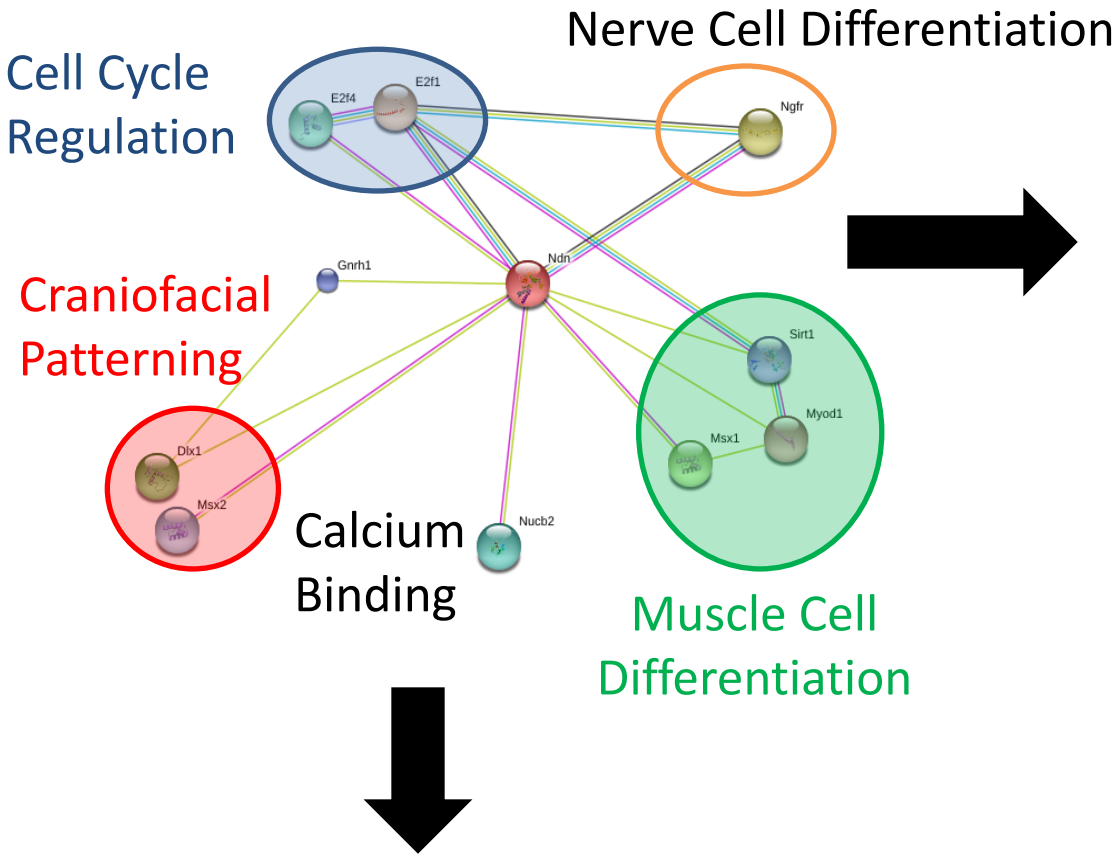


Determine Gene Ontology



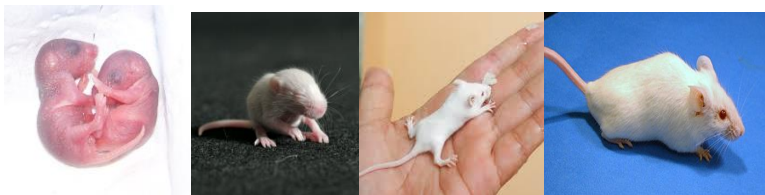
Create larger protein interaction network

Aim 3: What are necdin interactions related to fat and muscle throughout development?



Hypothesis: Necdin will interact with more muscle regulatory proteins, but new fat regulatory proteins will be found.

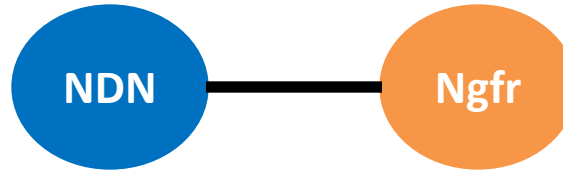
Example: **NGFR** could play a role in fat differentiation



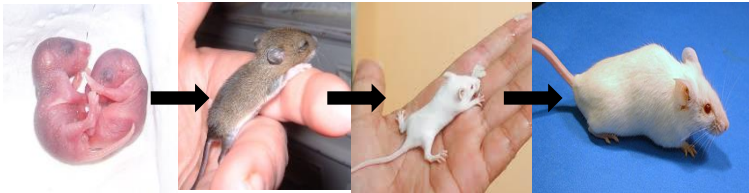
Hypothesis: Necdin will interact with different protein types at different stages of development

Future Directions

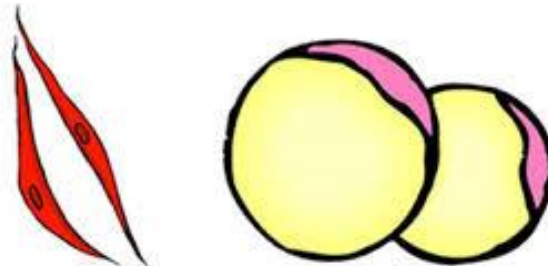
Determine relationship between Ngfr, Necdin, and fat differentiation



Create Diagnosis Plan using timeline information



Explore relationship of necdin in fat and muscle cell differentiation further



ANY
QUESTIONS
?

References

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