



EB RESEARCH
PARTNERSHIP



Kindler Syndrome



National Institutes of Health
Turning Discovery Into Health

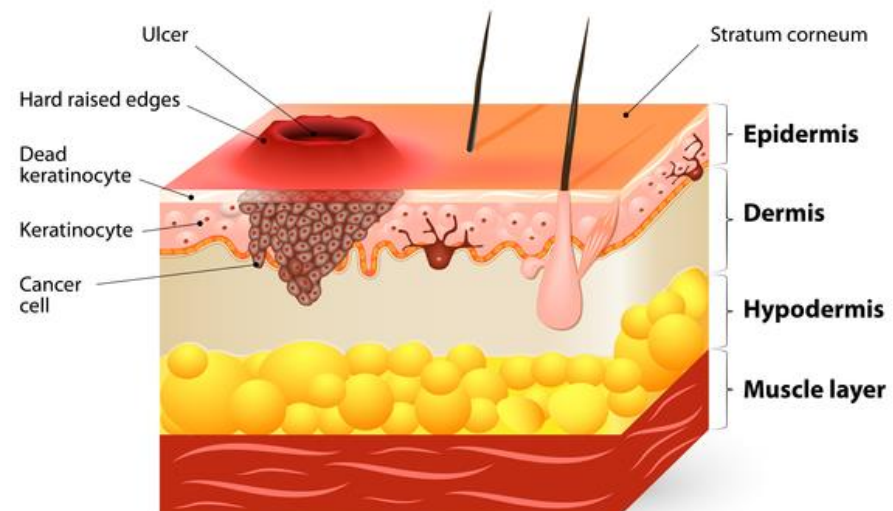


Kindler syndrome is a skin condition with some severe phenotypes. Some of the following images may be graphic.

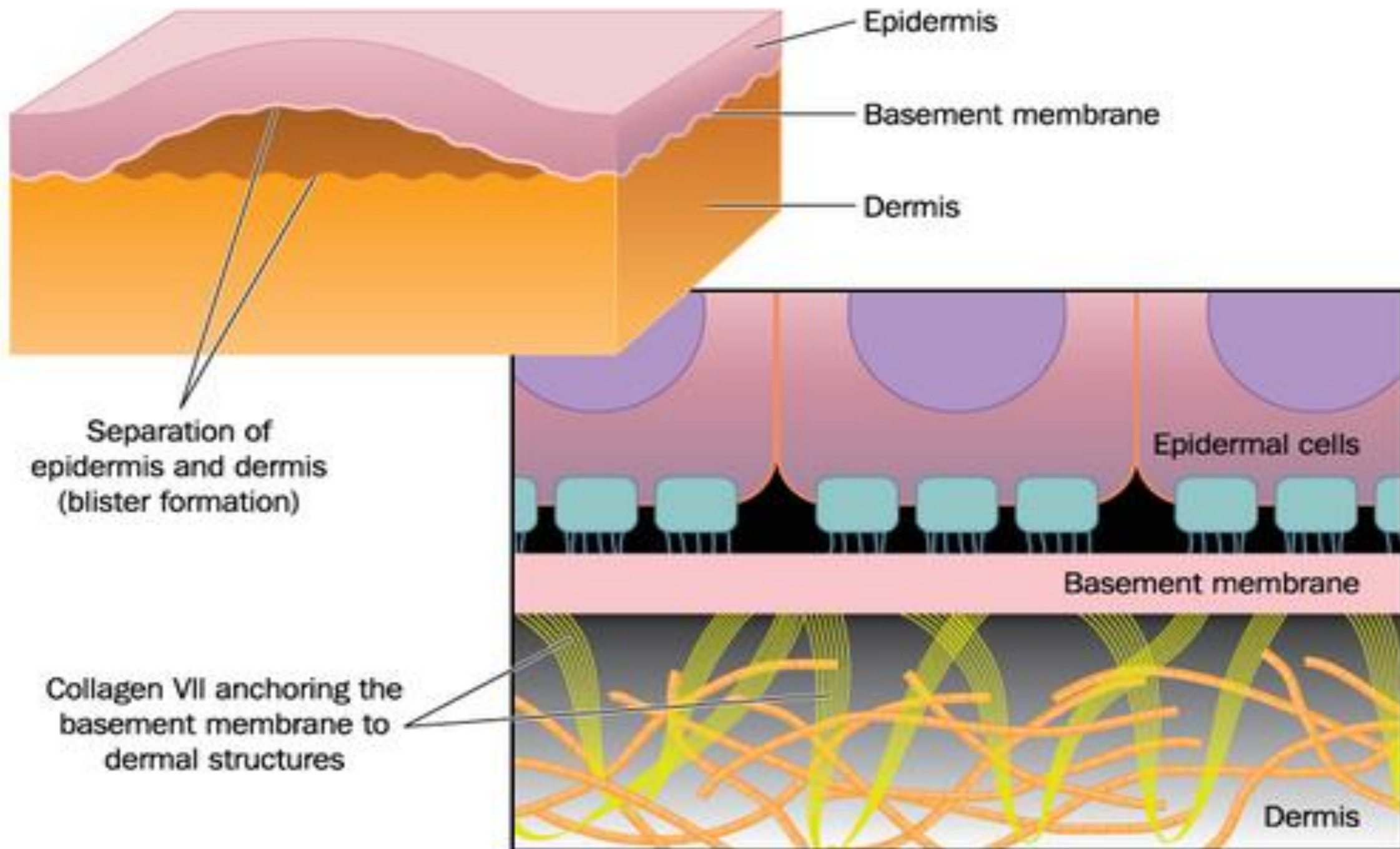
What is Kindler Syndrome?



Squamous-cell carcinoma



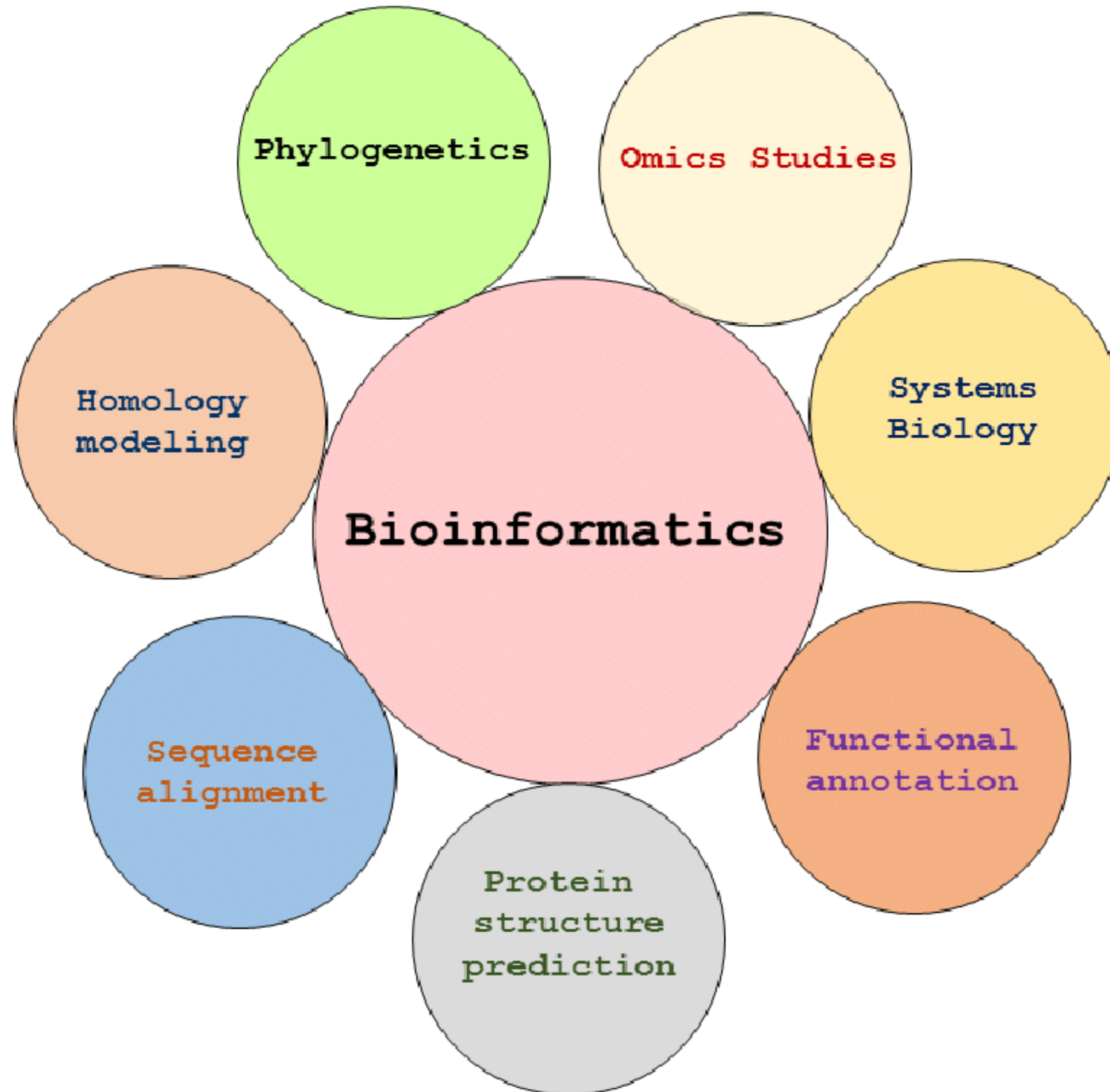
What causes Kindler Syndrome?



How To Treat
Kindler's
Syndrome?

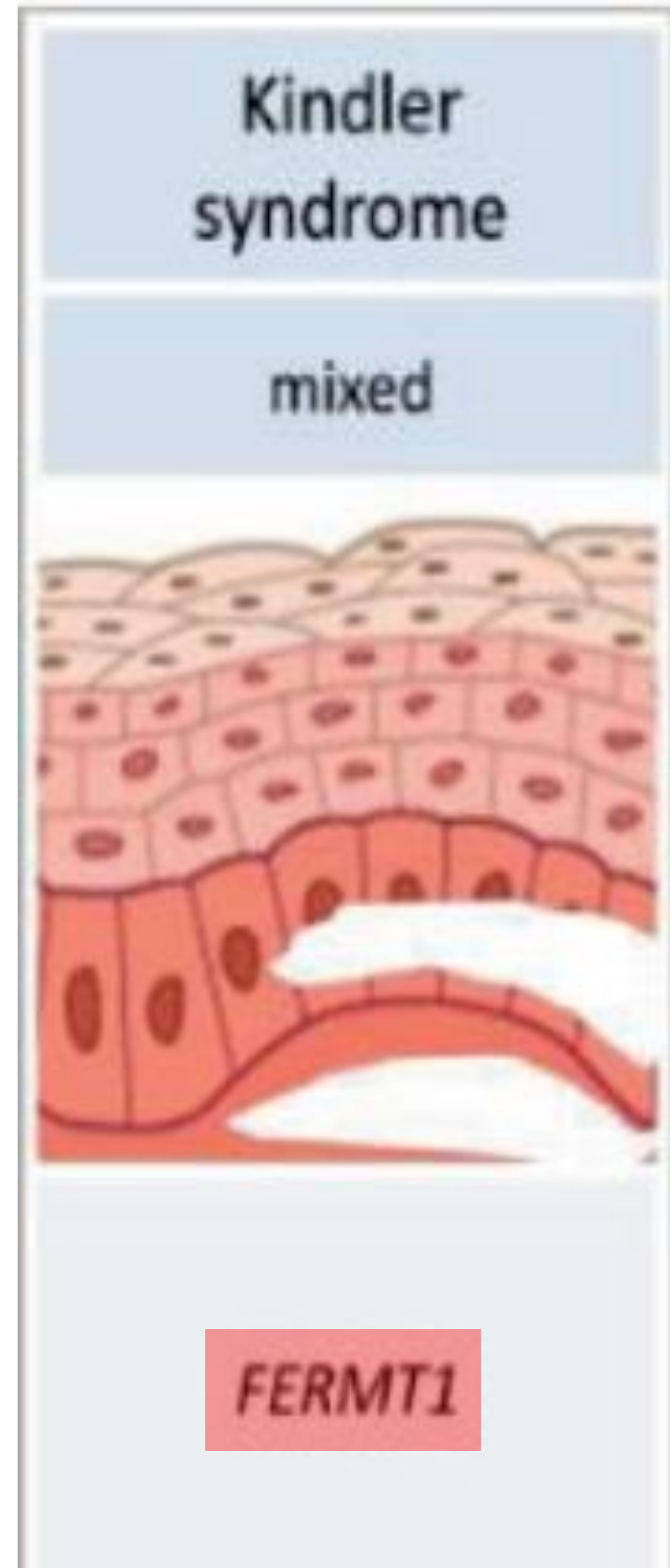


How can we better understand Kindler syndrome?

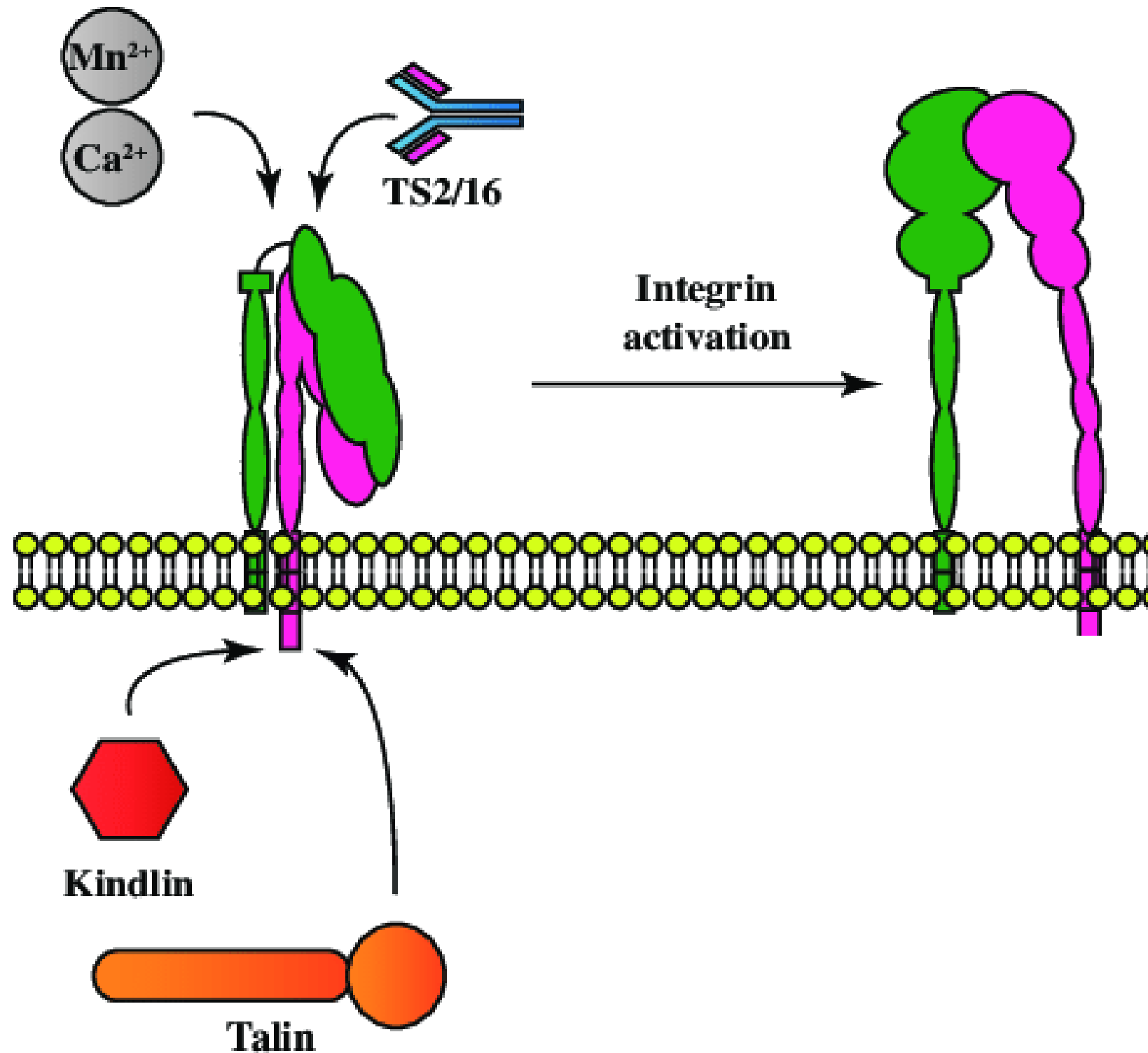


What gene causes Kindler Syndrome?

FERMT1 encodes kindlin-1

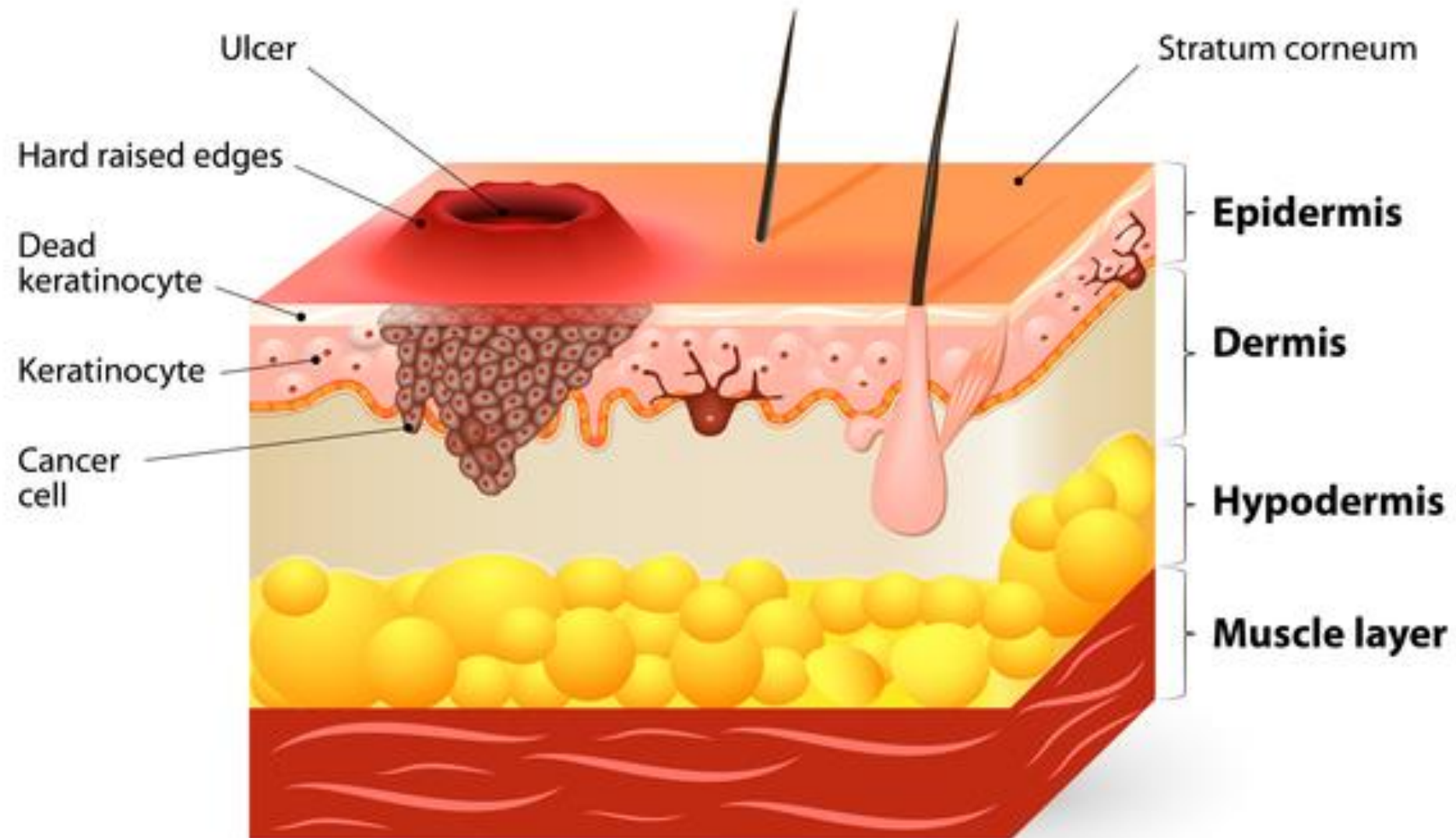


What is kindlin-1's function?



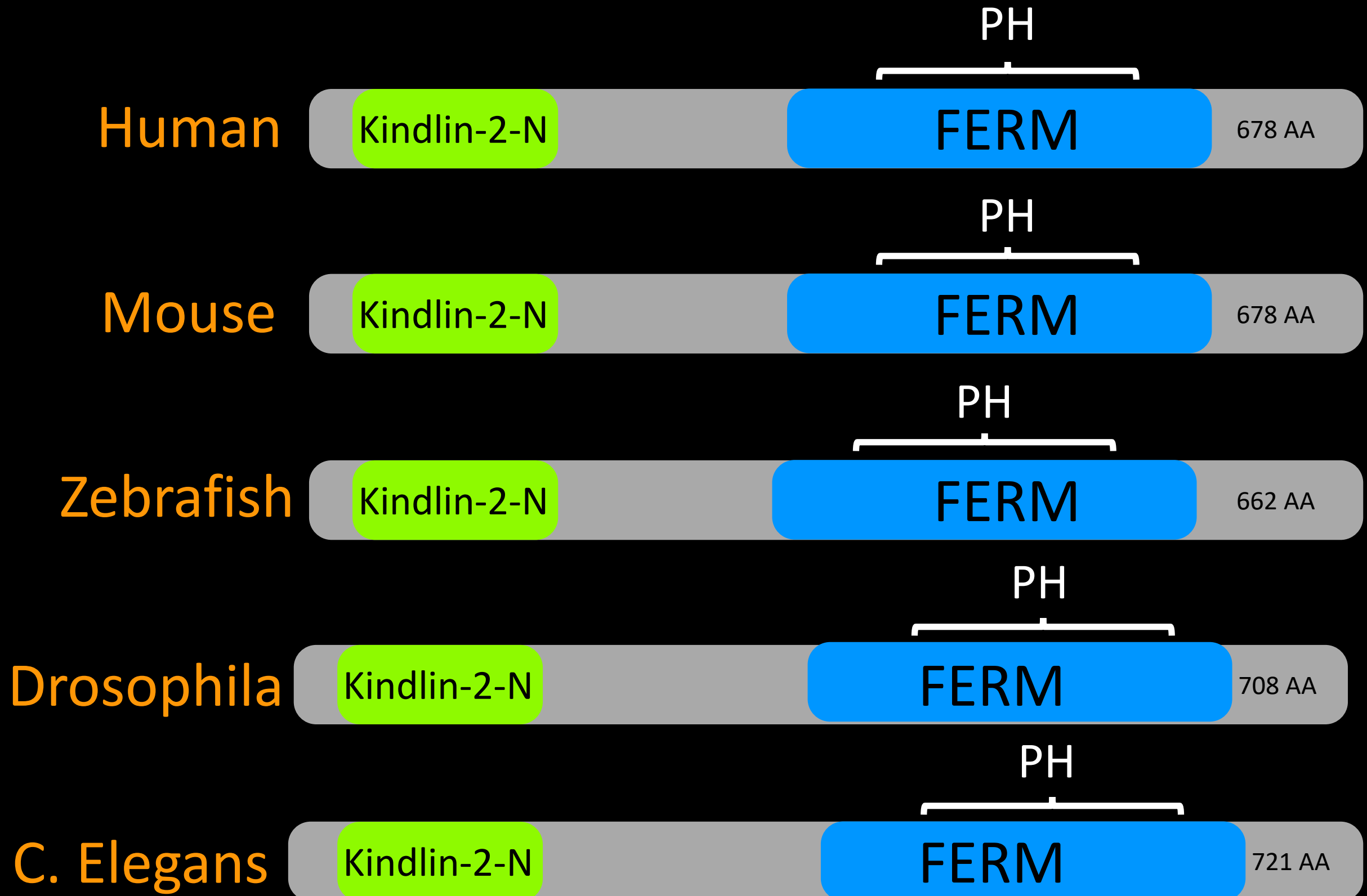
What is the gap in knowledge?

Squamous-cell carcinoma

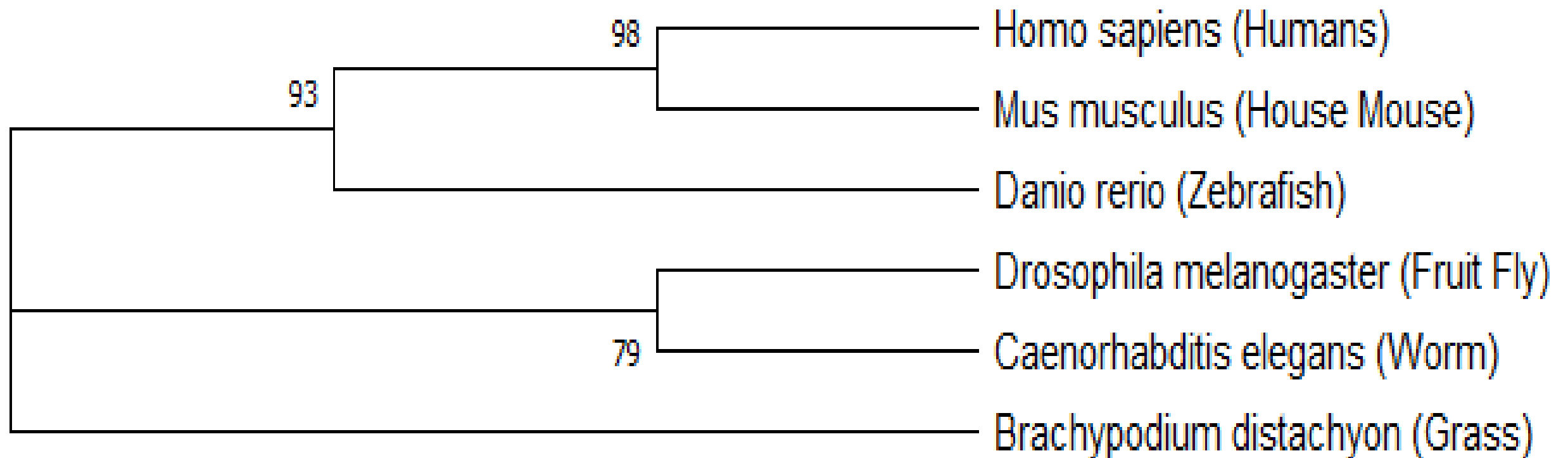


Why does Kindler Syndrome lead to development of squamous-cell carcinomas in older patients?

FERMT1 is highly conserved across model organisms



How can we study FERMT1?



Which model organism will be used?



Danio rerio

Inexpensive

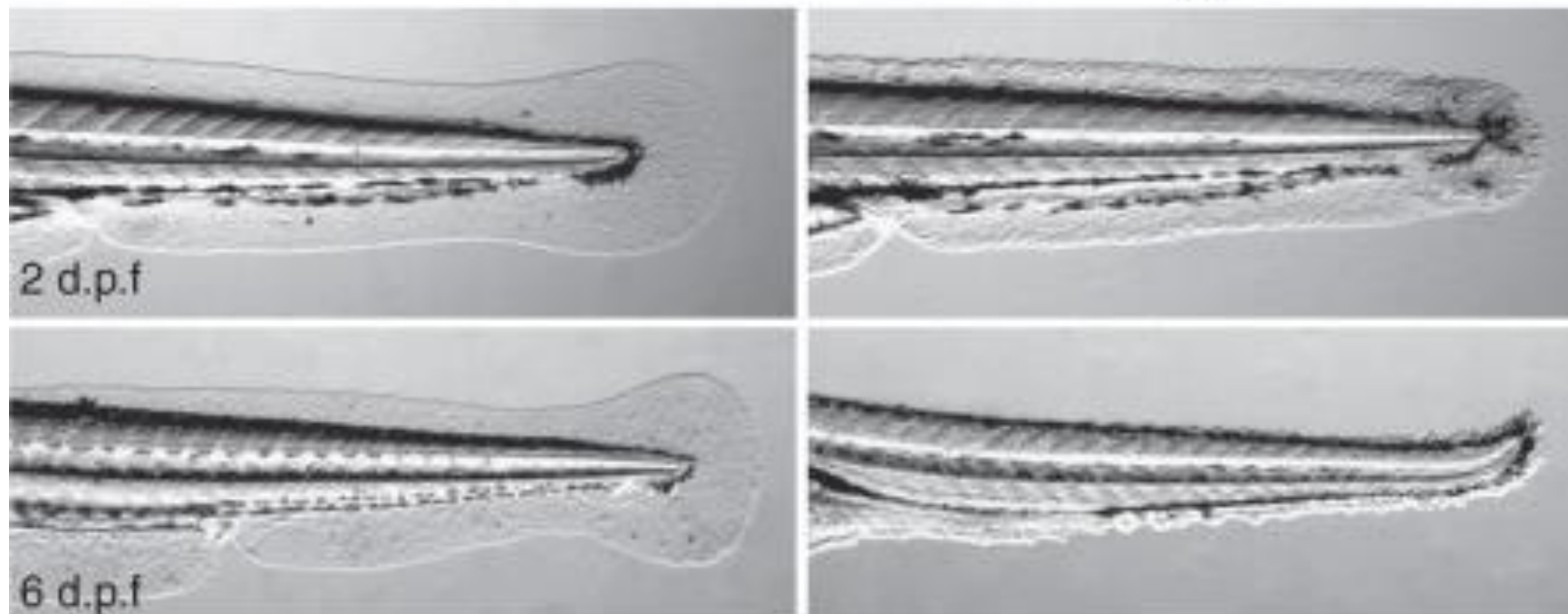
Shows phenotype

Homologous gene

Similar function

Wild Type

kindlin mutant



Primary Goal

Determine what FERMT1's role is in cancer development of Kindler Syndrome patients

AIM 1

Identify highly conserved residues of FERMT1

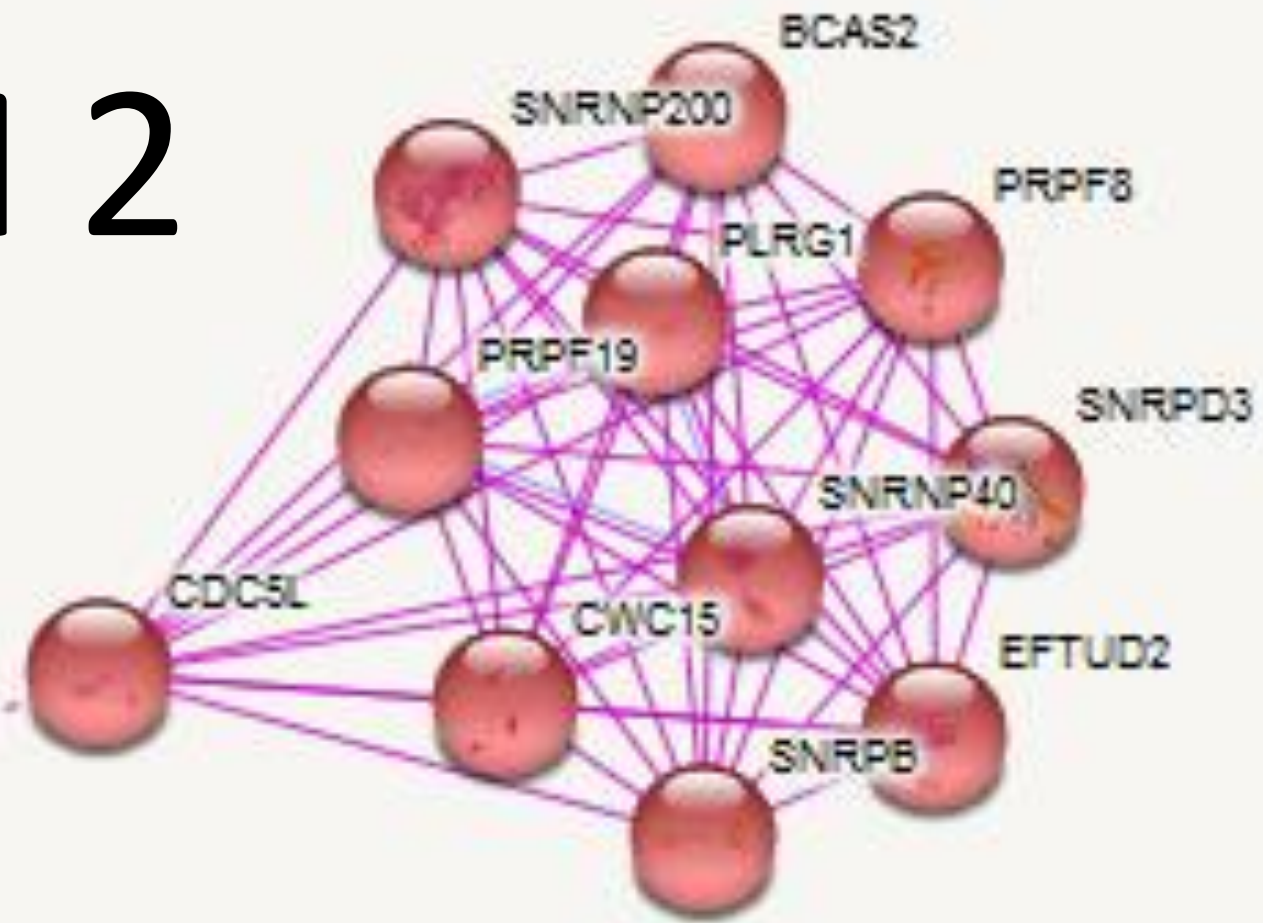
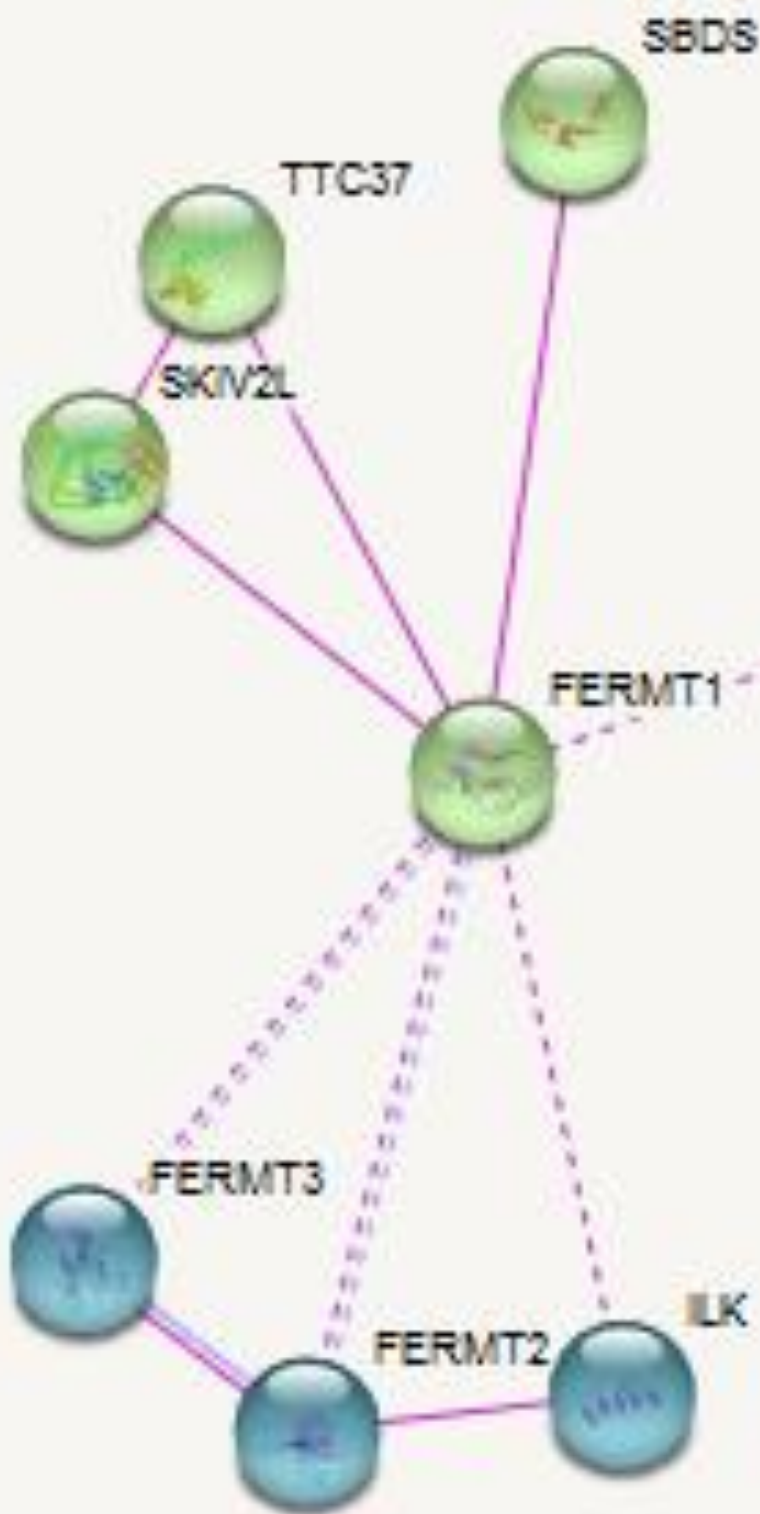
AIM 2

Analyze protein interaction networks

AIM 3

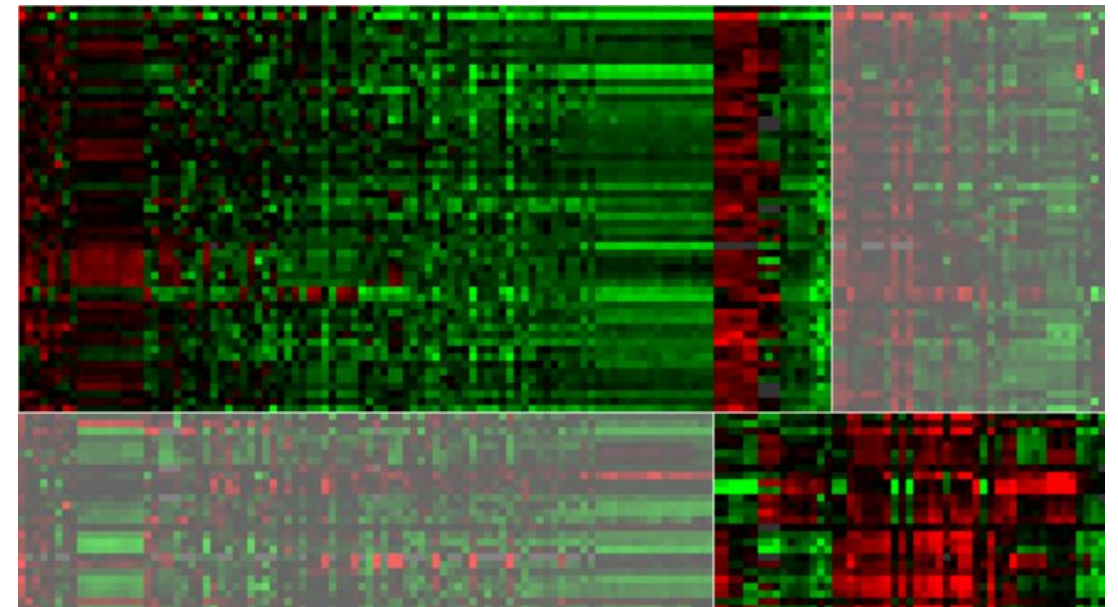
Analyze the transcriptome in FERMT1 mutants

AIM 2



**Use protein
interaction networks
to find an explanation
for cancer phenotype**

AIM 3



Mutate FERMT1 using CRISPR-Cas9

Verify mutants with the fin phenotype

Analyze the transcriptome for transcription alterations

Does timing of kindlin-1 mutation affect phenotype?



WT



Knockdown WT at adolescence



**Recovered phenotype?
(No cancer)**

References

Epidermis Picture: <https://ghr.nlm.nih.gov/condition/kindler-syndrome>

Kindler Syndrome picture: <https://www.debra.org.uk/uk-funded-projects/sonnenberg-kindler-syndrome>

Kindler Knee: https://www.researchgate.net/figure/Clinical-features-of-Kindler-syndrome-a-b-Poikiloderma-with-hyperpigmentation-and_fig1_229161951

How to treat: <https://www.lybrate.com/topic/how-to-treat-kindler-s-syndrome/4dd0715e83fa2628d34f85008f42581e>

Worm: <http://haasegen564s17.weebly.com/homology.html>

Hands: <https://www.vectorstock.com/royalty-free-vector/silhouette-hand-helping-hand-vector-631062>

Kindler hands: https://link.springer.com/chapter/10.1007/978-3-662-45698-9_43

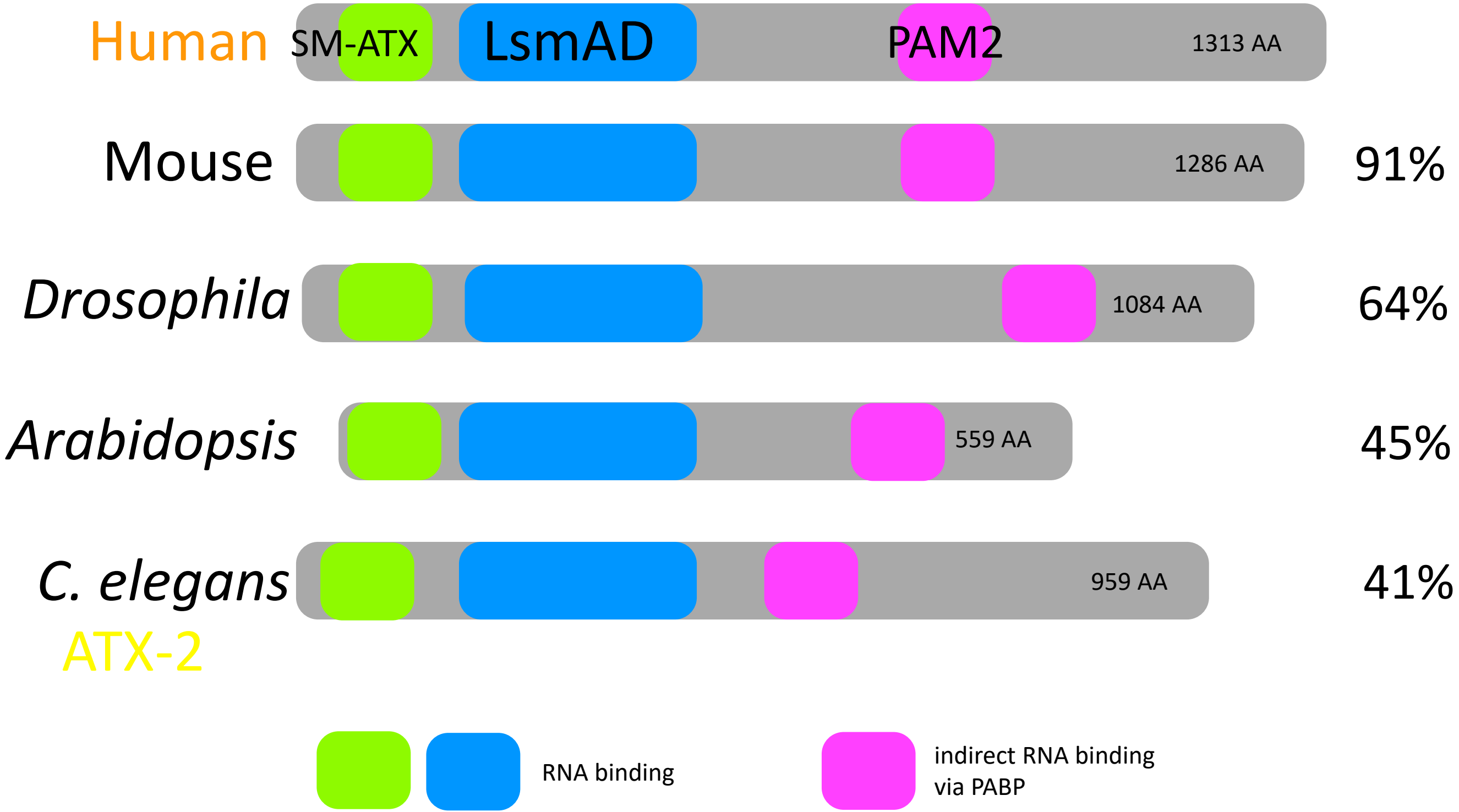
Zebrafish: https://www.google.com/url?sa=i&url=https%3A%2F%2Fgtgc2016.sciencesconf.org%2Fconference%2Fgtgc2016%2FYvesClement_2016.07.01_GTGC.pdf&psig=AOvVaw3OSzzPEah2nDhbn3ibyZrP&ust=1582740105733000&source=images&cd=vfe&ved=0CAMQjB1qFwoTCliz08Ck7ecCFQAAAAAdAAAAABBP

Kindlin-1 function: https://www.researchgate.net/figure/Molecular-mechanisms-for-integrin-activation-Integrins-exist-in-two-activation-states-on_fig4_323191947

Zebrafish embryo: <http://sitn.hms.harvard.edu/art/2014/zebrafish-embryo-development/>

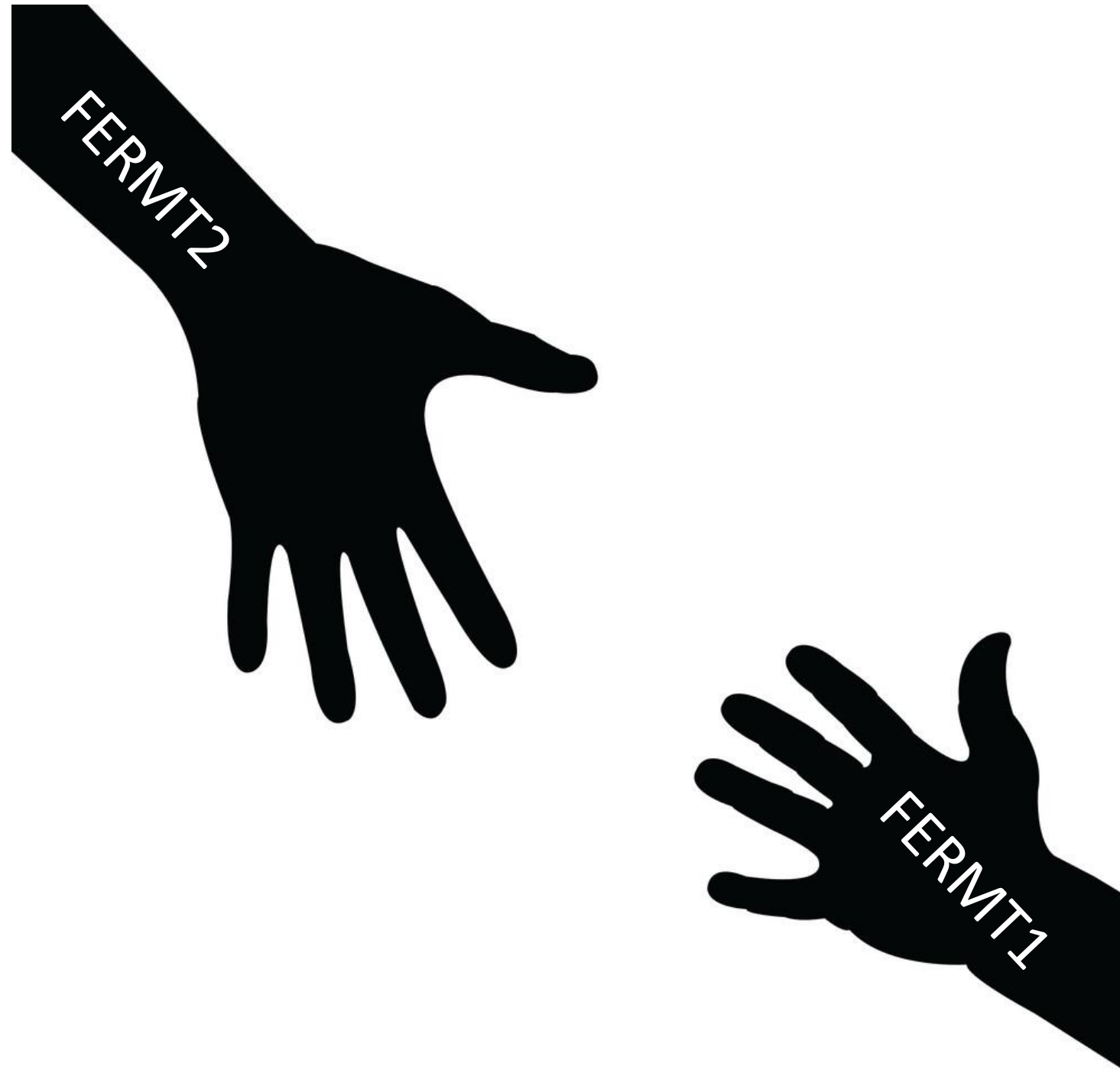
Zebrafish adult: <http://www.sleepreviewmag.com/2019/10/zebrafish-study-sheds-light-sleep-regulated-brain/>

Ataxin-2 is a conserved RNA Binding Protein



ATX-2

How can we recover kindlin-1 function?



YES! Kindlin-2 function recovers function lost by kindlin-1 mutations

How does kindlin-1 expression change over time?

