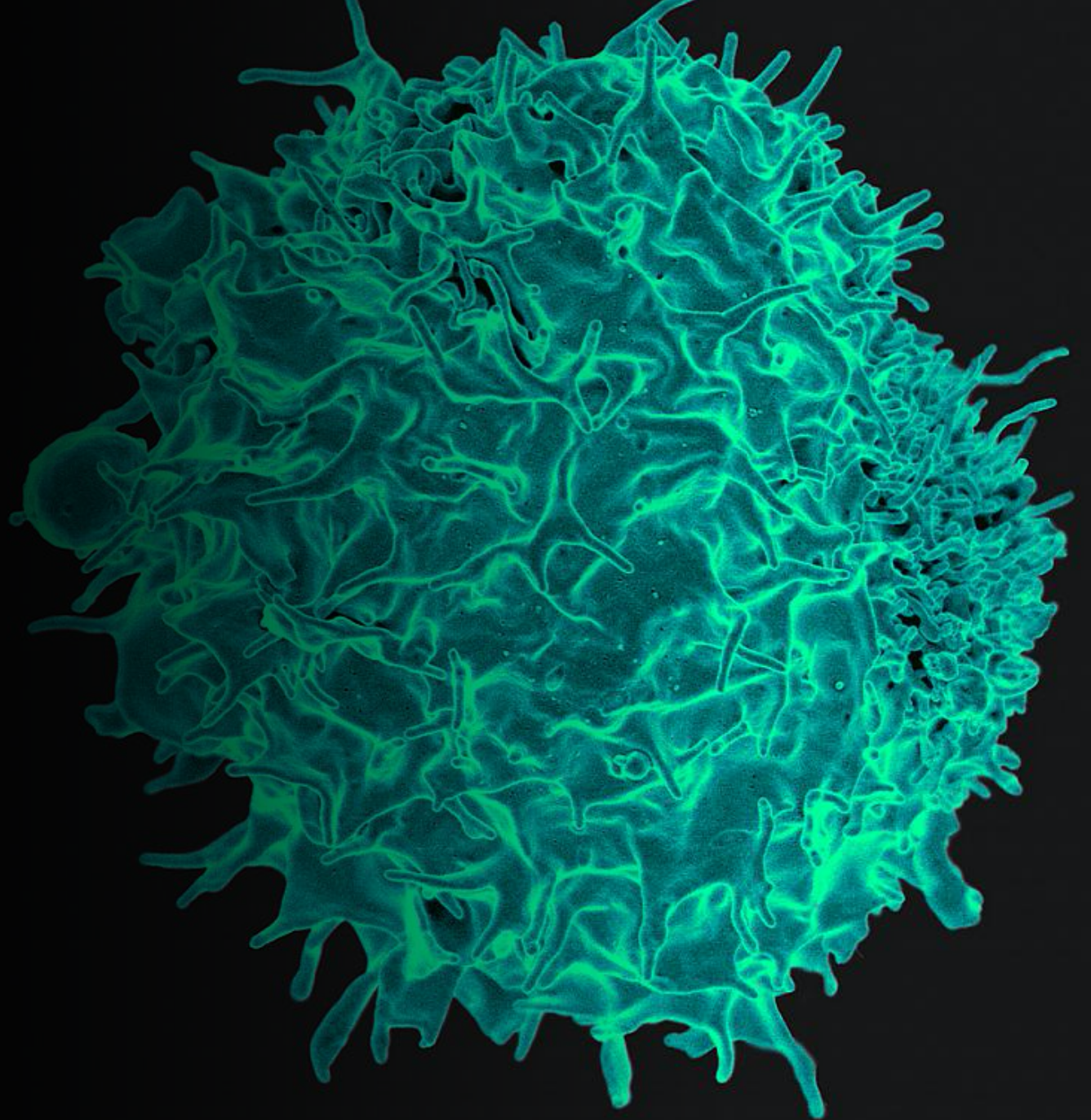
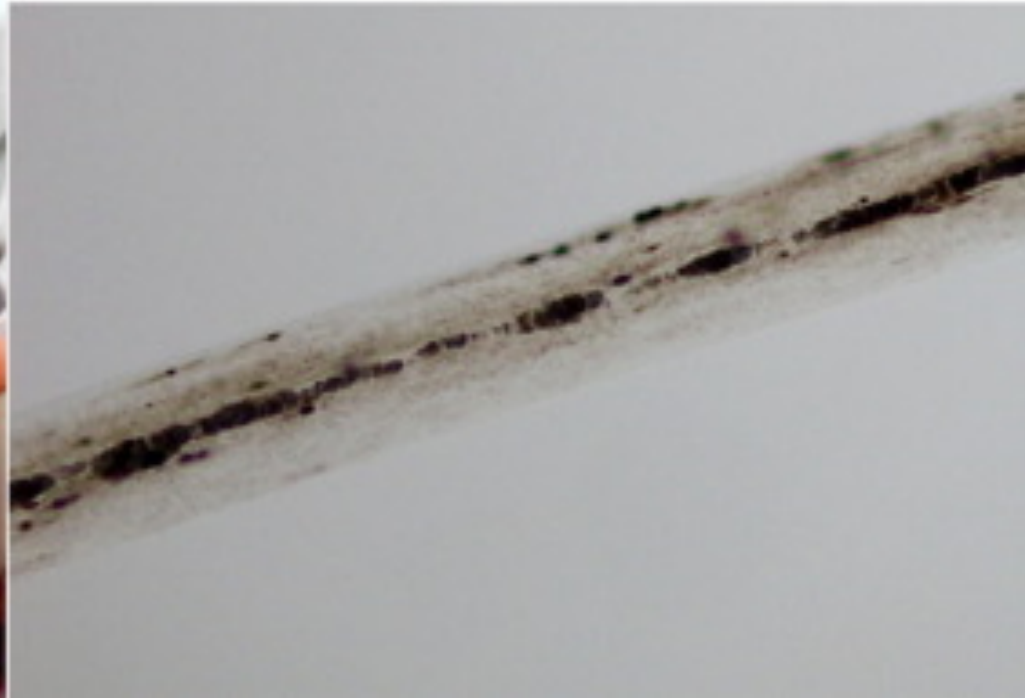


Griscelli Syndrome Type II and Rab27A

Presented By Gus Hermberg

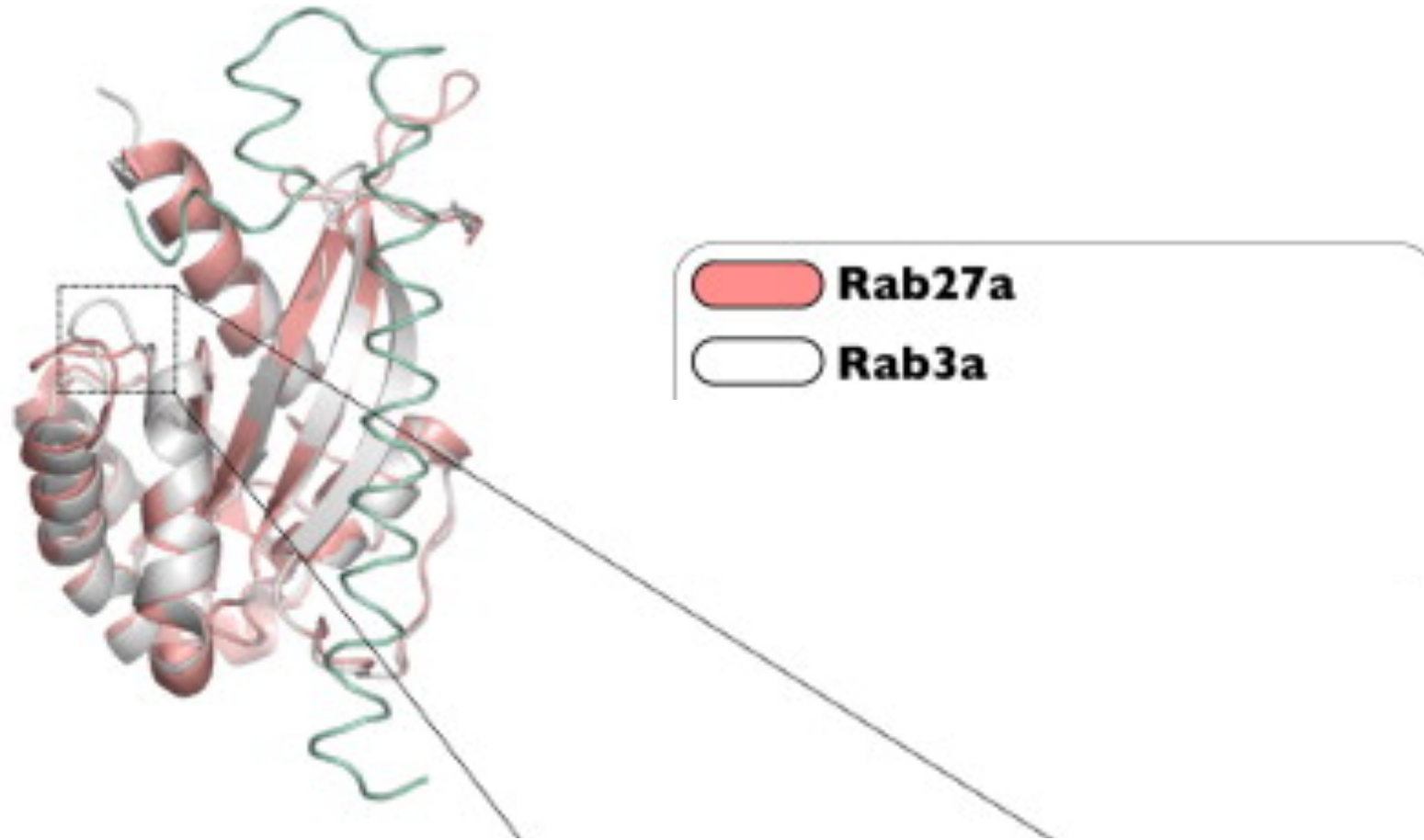


What is Griscelli Syndrome?



It is a rare genetic disorder recognizable from a combination of partial albinism with immunodeficiency.

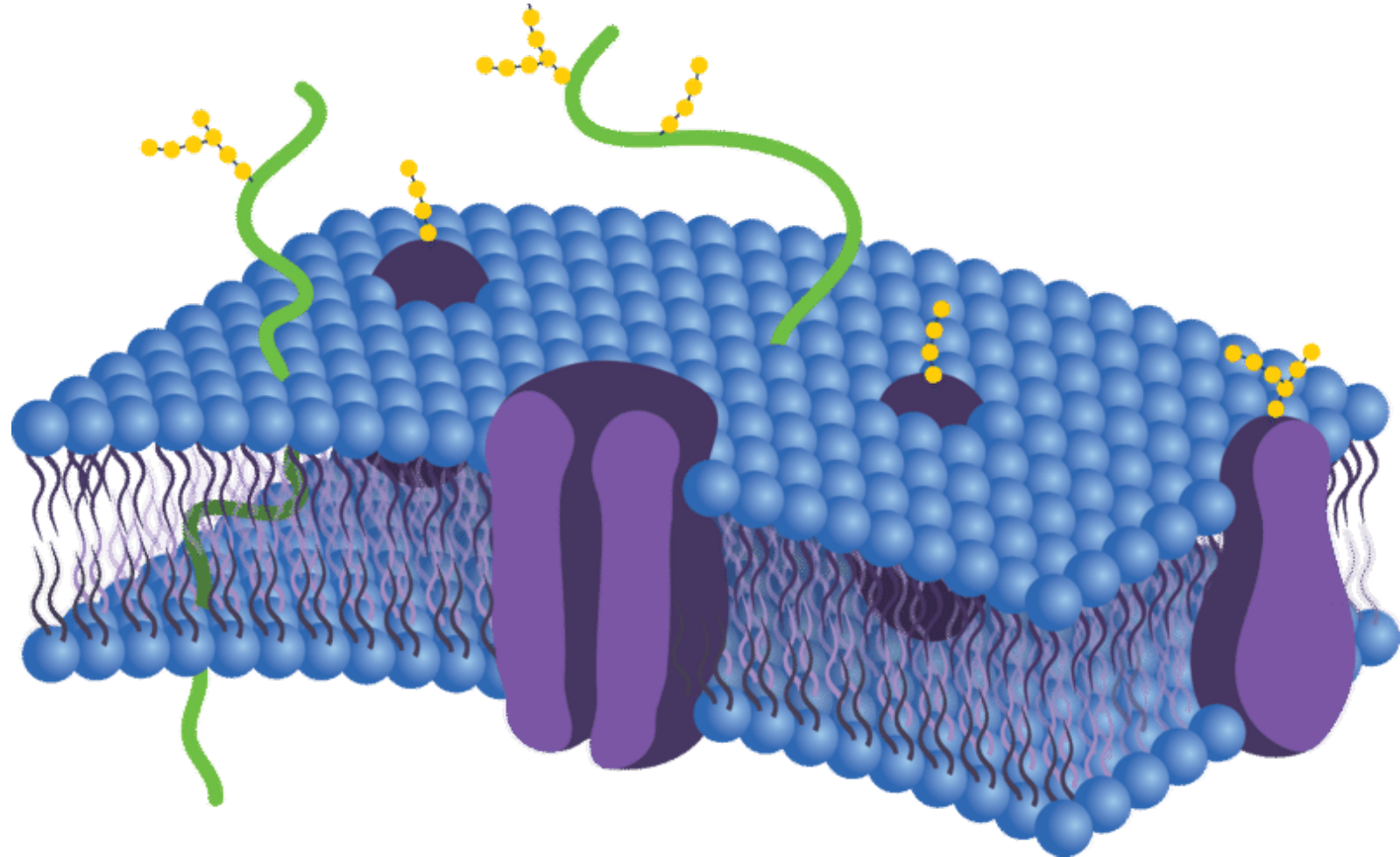
What is type II?



Type II is associated specifically with mutations in the protein encoding gene Rab27A.

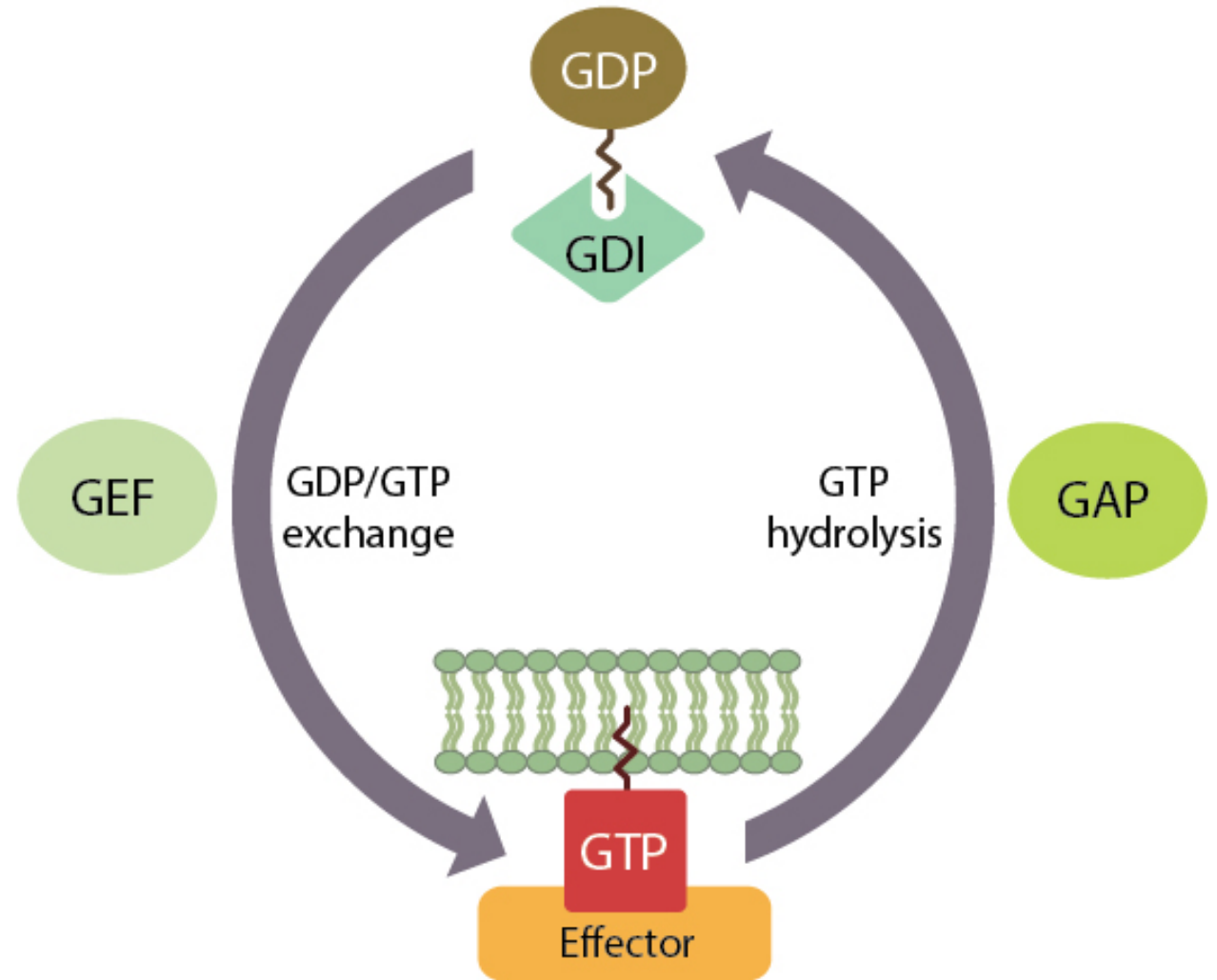
Where does Rab27A localize? Gene Ontology

The protein is found at the cell membrane.



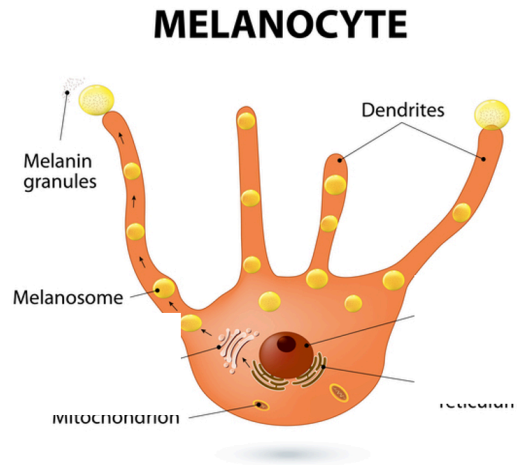
What is the molecular function? GO

As a GTPase it switches between active and inactive states as part of signal transduction.



What is the biological process? GO

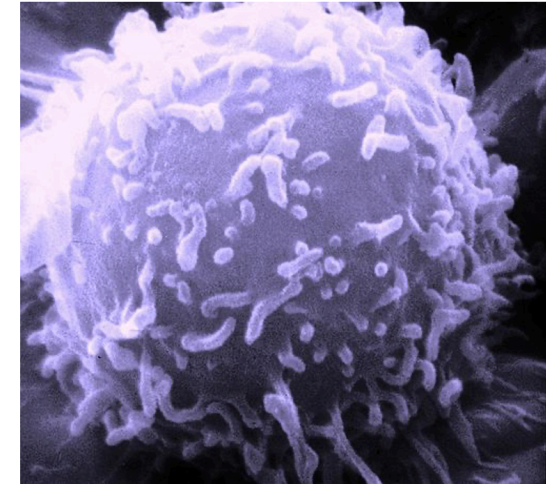
Why is albinism a symptom?



Inability to transport melanin outside of cells results in albinism.



Why is immunodeficiency a symptom?



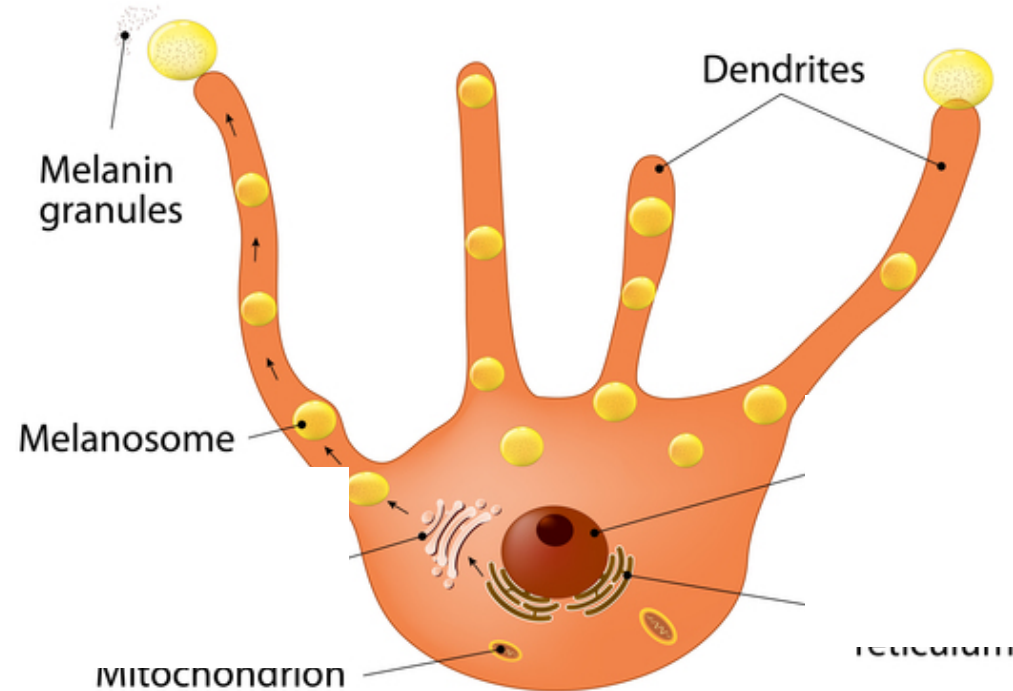
Disruption in cell transport means lymphocytes can't export key components of the lysosome.



Cellular Transport

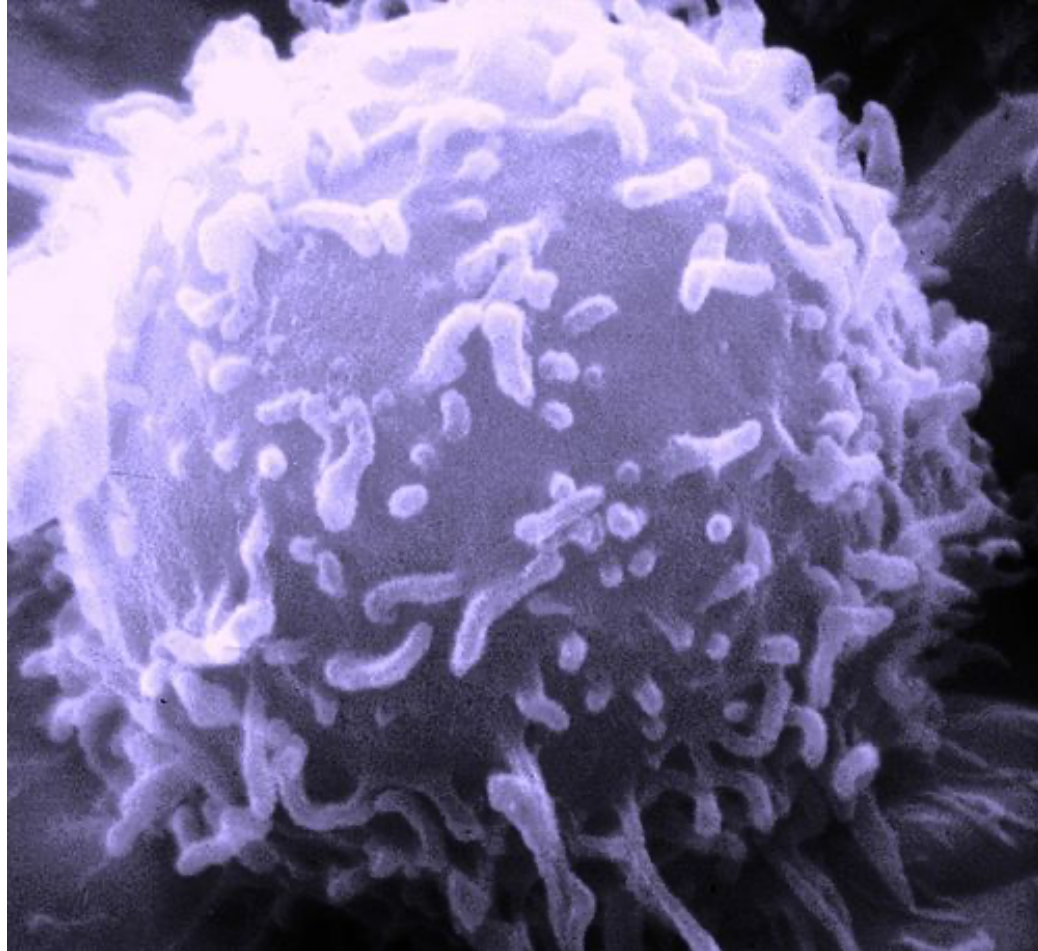
Why is albinism a symptom?

MELANOCYTE



Inability to transport melanin outside of cells results in albinism.

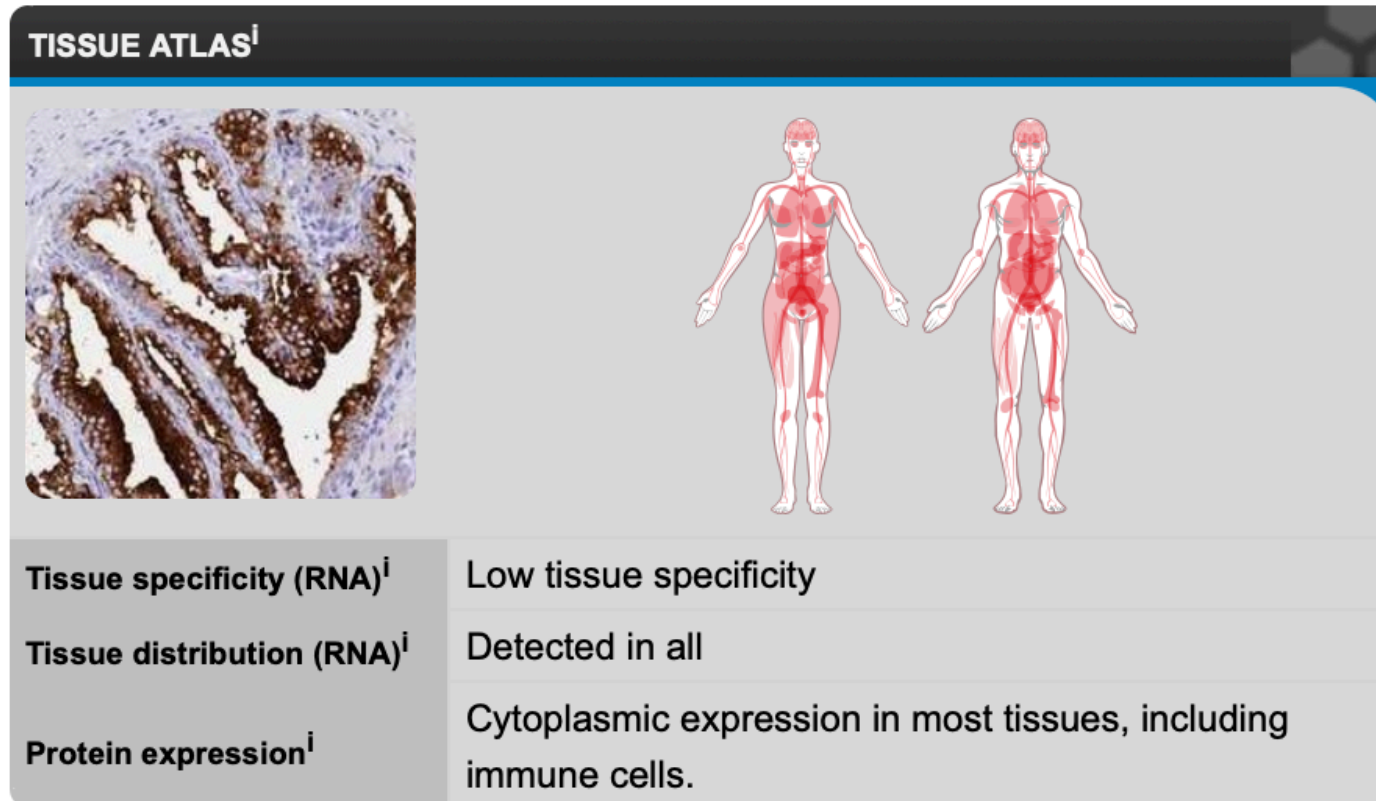
Why is immunodeficiency a symptom?



Disruption in cell transport means lymphocytes can't export key components of the lysosome.

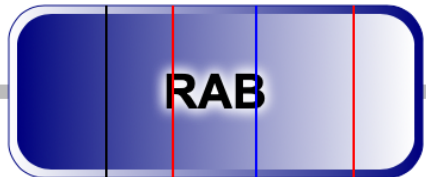
Where in the body is Rab27A expressed?

THE HUMAN PROTEIN ATLAS



Lack of tissue specific expression patterns raise interesting questions as to why the syndrome is seen most dramatically in 2 kinds of cells. This is in the proposed gap in knowledge to seek to address.

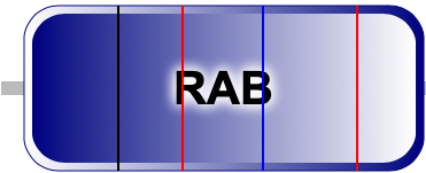
How conserved is the gene?



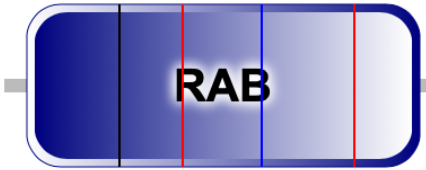
Humans



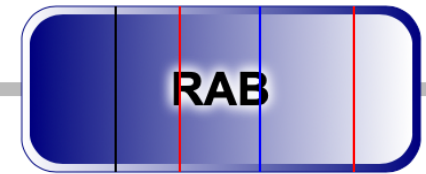
Rats



Dogs



Zebrafish



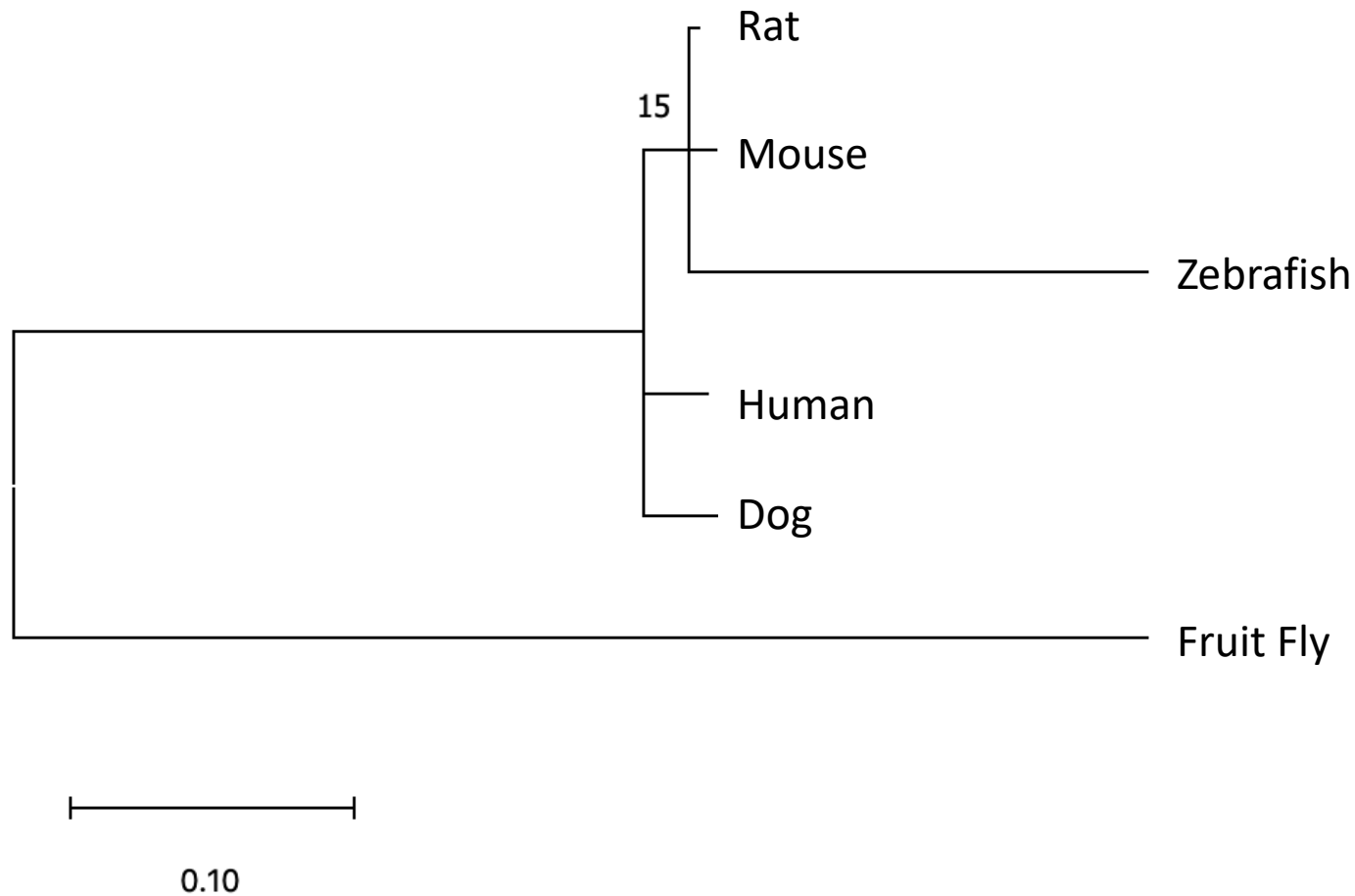
Mouse



Fruit Flies

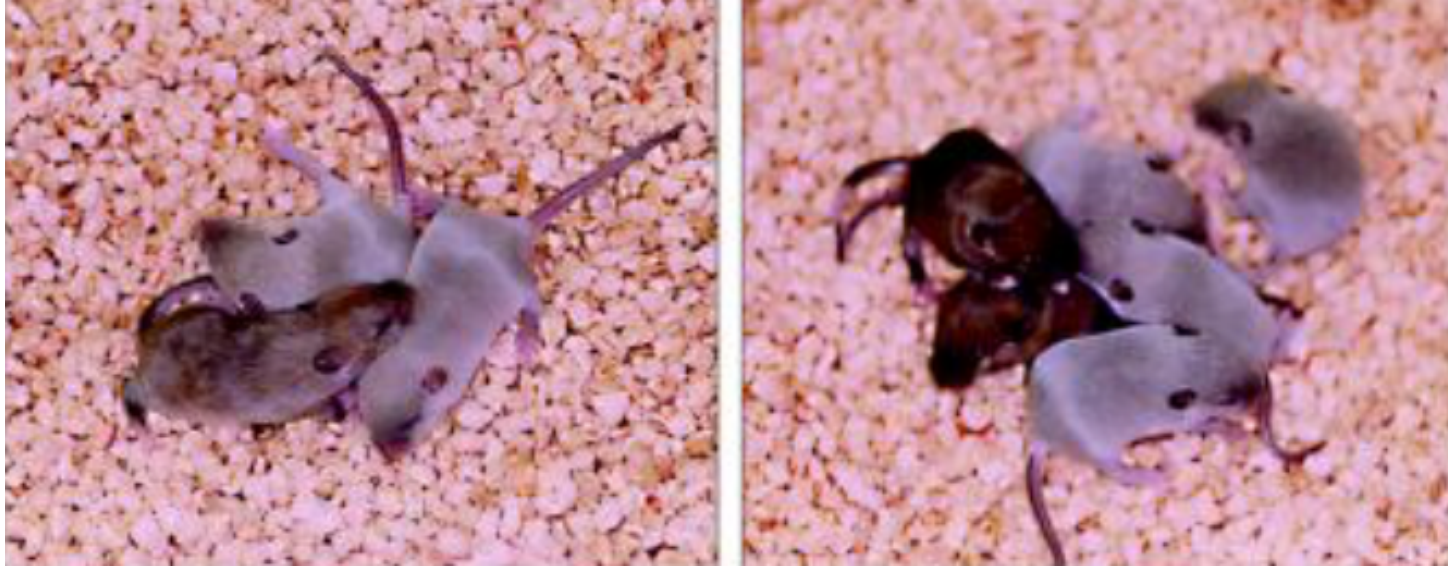
The simple and conserved architecture is promising for the use of model organisms.

What organisms have closely related proteins?

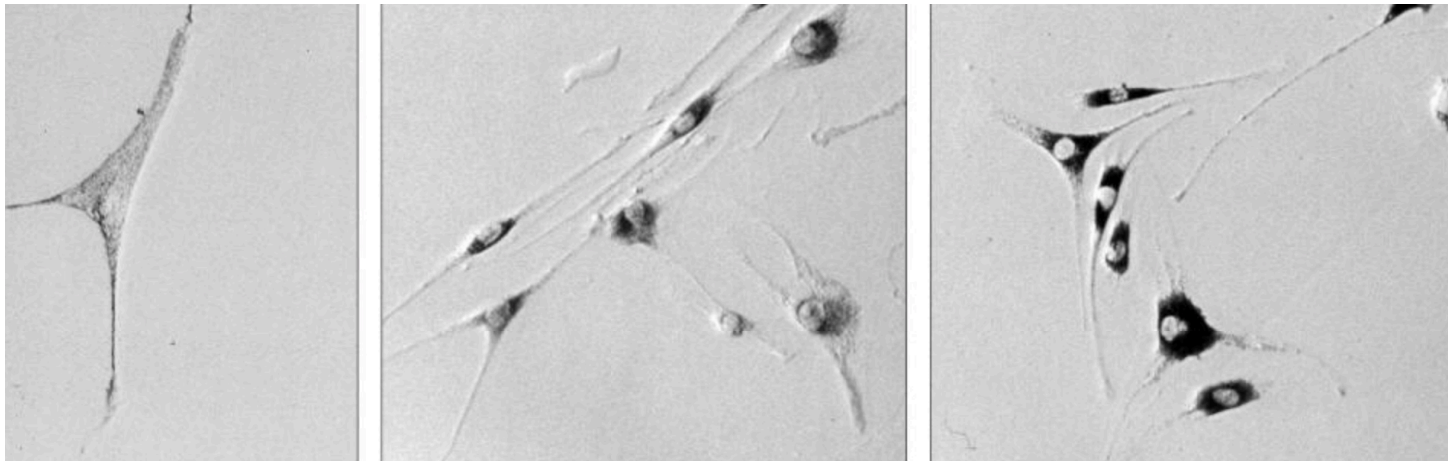


While the dog protein is more closely related to the human protein, there are significant

What are potential models for studies?

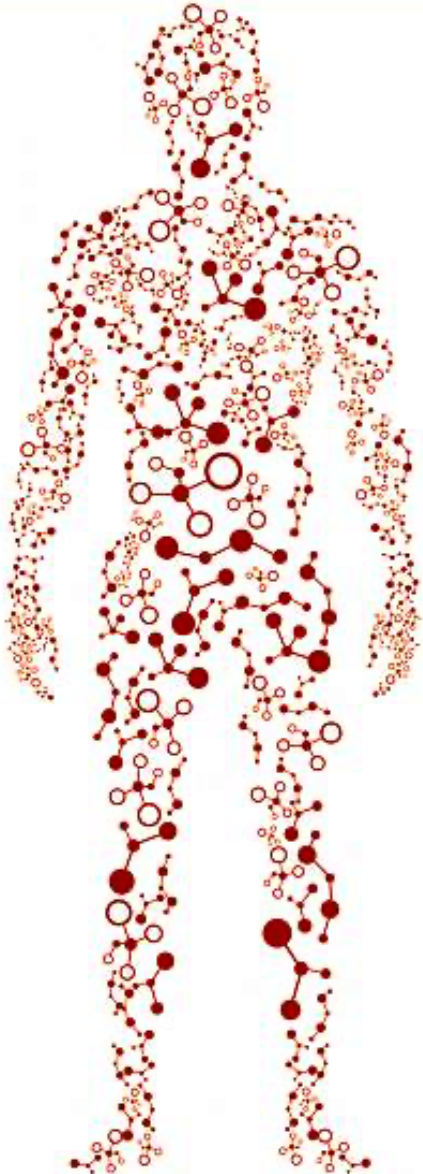


Mutant ashken mice provide an easy to detect albino phenotype. This phenotype is seen in the grey mice pictured.



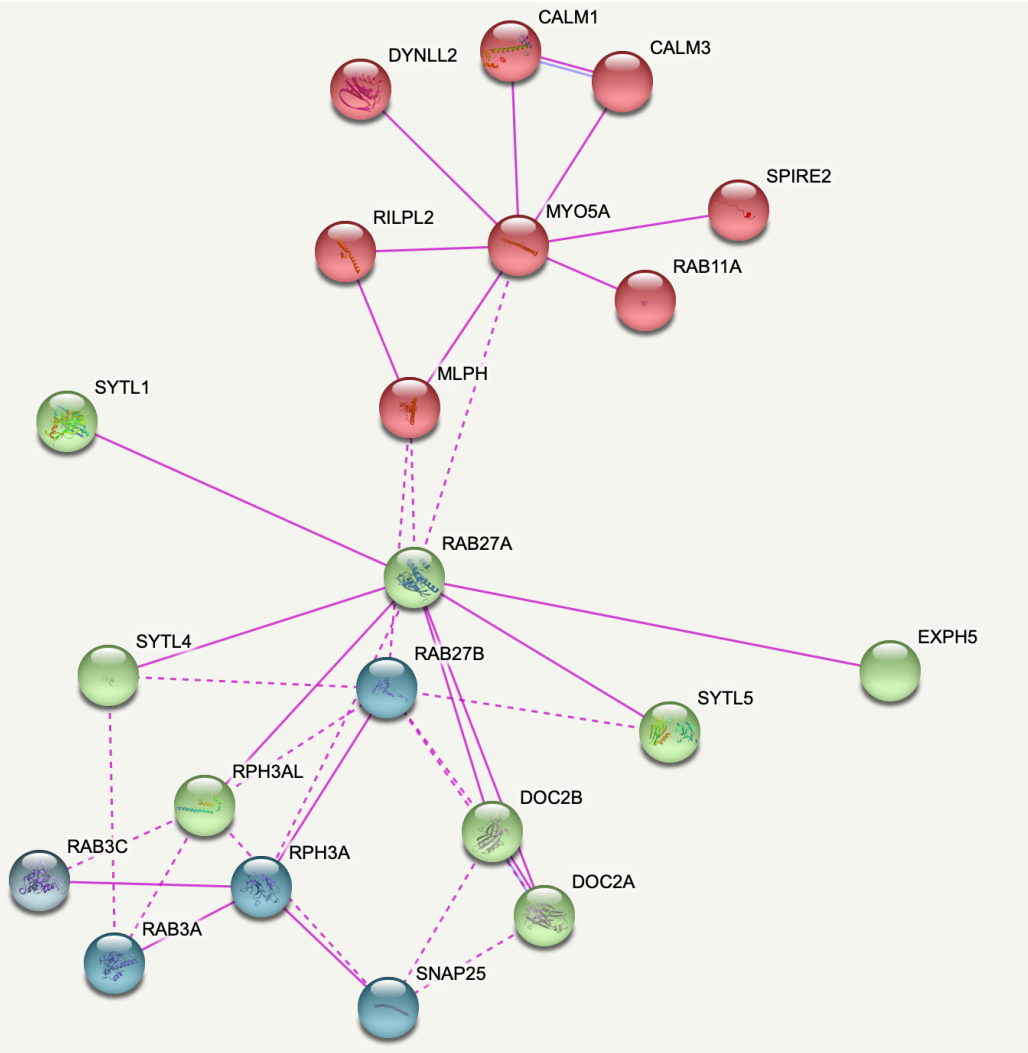
Cultured cell lines are easier to grow and maintain and allow failed transport to be seen trapped in the cells.

Aim #1 – What proteins does RAB27A interact with?



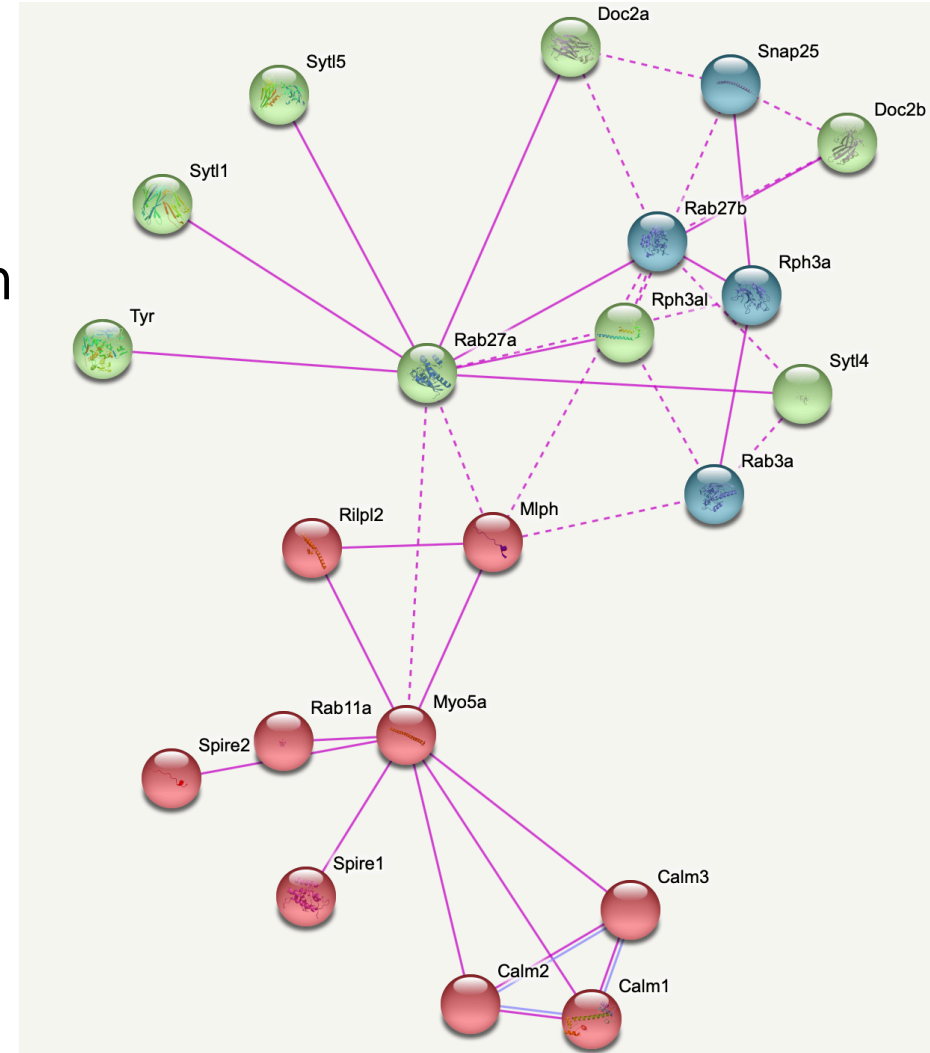
Protein interactions might shine light on why transport failure due to Rab27A mutations leads to specific phenotypes despite non-specific expression in the body.

What proteins are likely candidates for interaction?



Human Protein Interactions

Overlapping proteins between human and mouse networks allow results in mice to have implications for humans.



Mouse Protein Interactions

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Images

Title Slide: https://www.nih.gov/sites/default/files/styles/featured_media_breakpoint-large-extra/public/news-events/news-releases/2019/20190822-tcell_0.jpg?itok=I_NXMFAk×tamp=1566487121

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Slide 4: https://upload.wikimedia.org/wikipedia/commons/thumb/8/89/SEM_Lymphocyte.jpg/500px-SEM_Lymphocyte.jpg

Slide 6: https://dr282zn36sxxg.cloudfront.net/datastreams/f-d%3A21eb08bf8f5237a7e8c8ff22c216876df4b5a080b8ee01c25f922c0e%2BIMAGE_TINY%2BIMAGE_TINY.1

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