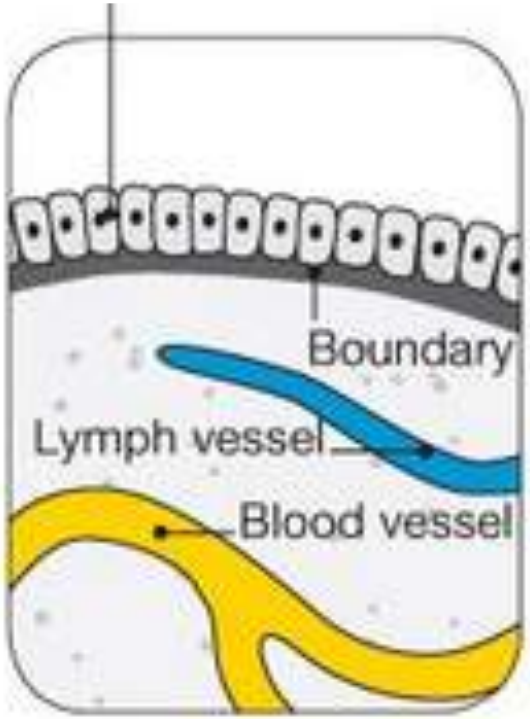
Lung Cancer

WISCONSIN
UNIVERSITY OF WISCONSIN–MADISON

Ryan Brown

What is cancer?



Normal cells

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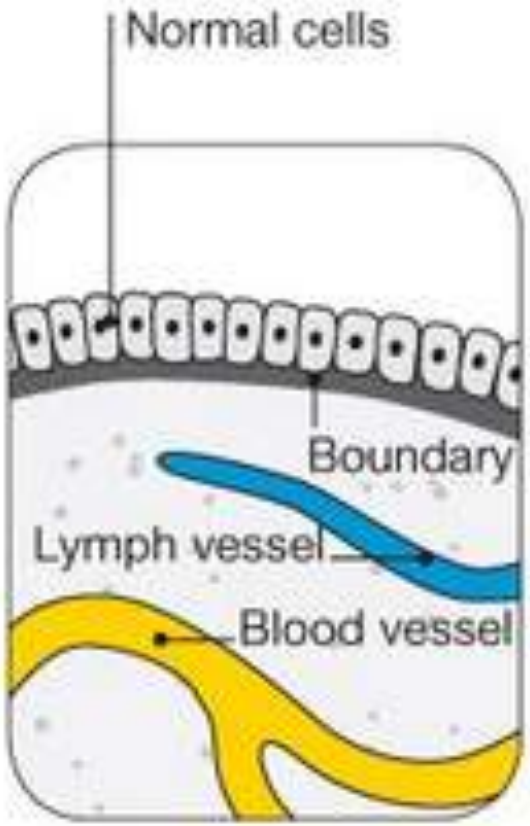

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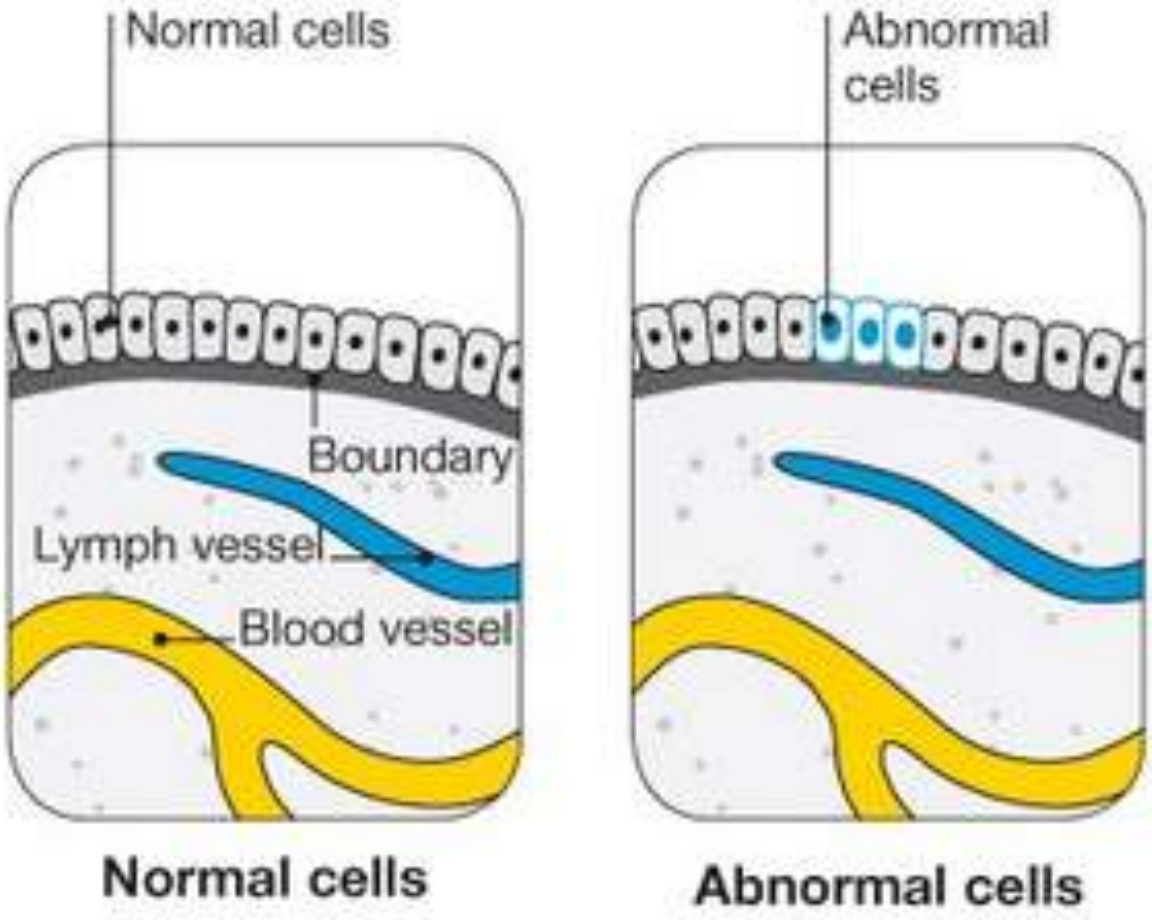

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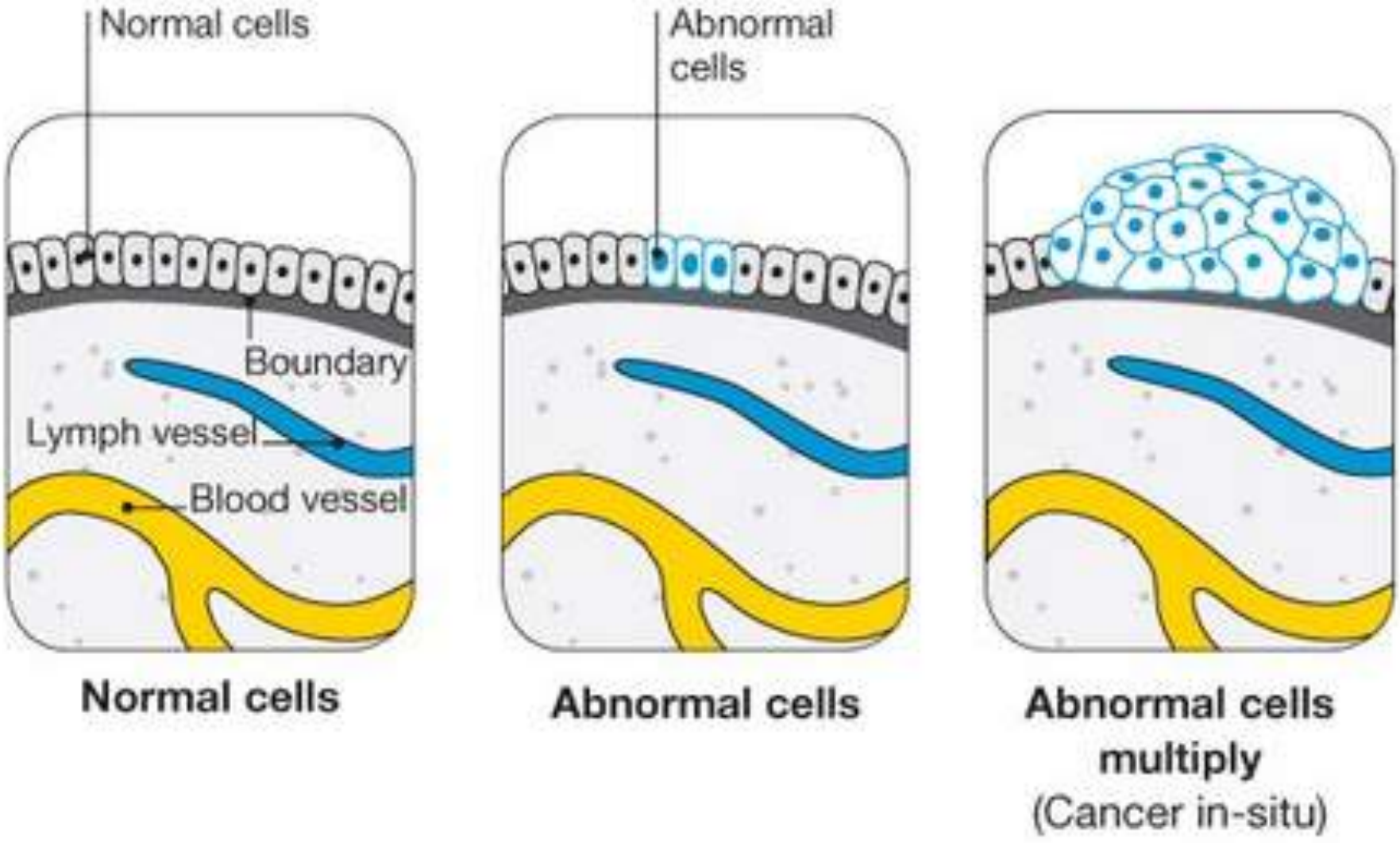

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Abnormal cells

Abnormal cells multiply
(Cancer in-situ)

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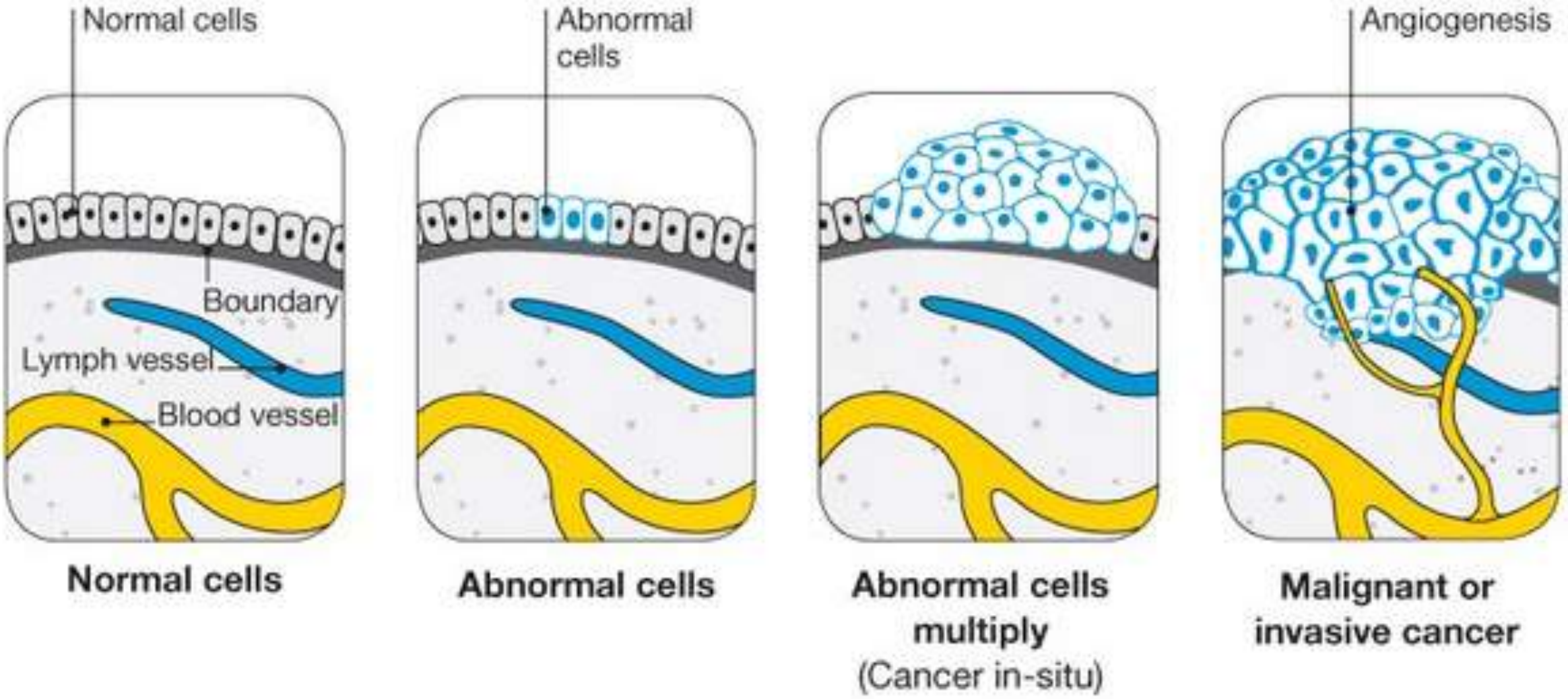

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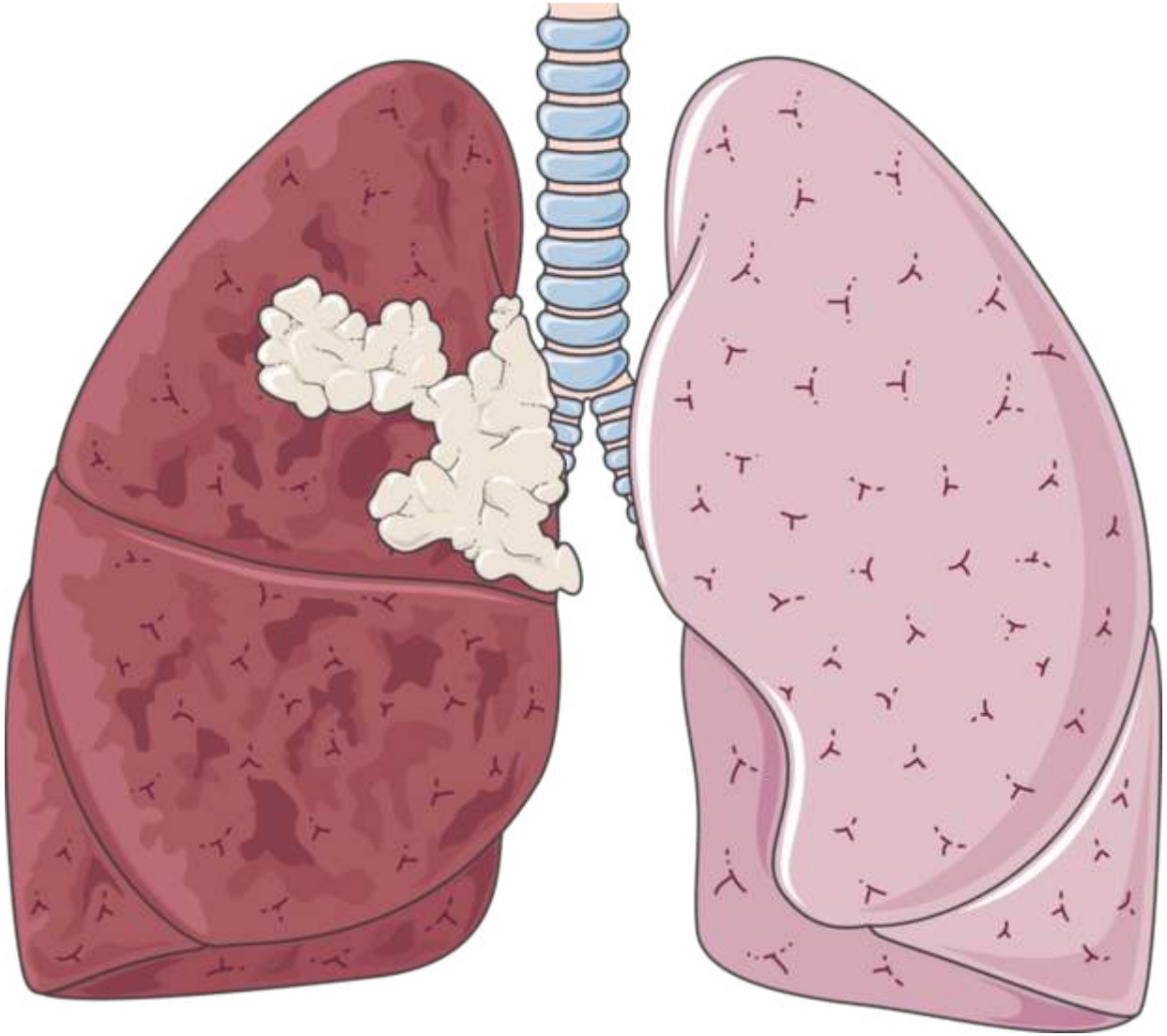
Malignant or invasive cancer

What is Lung Cancer?



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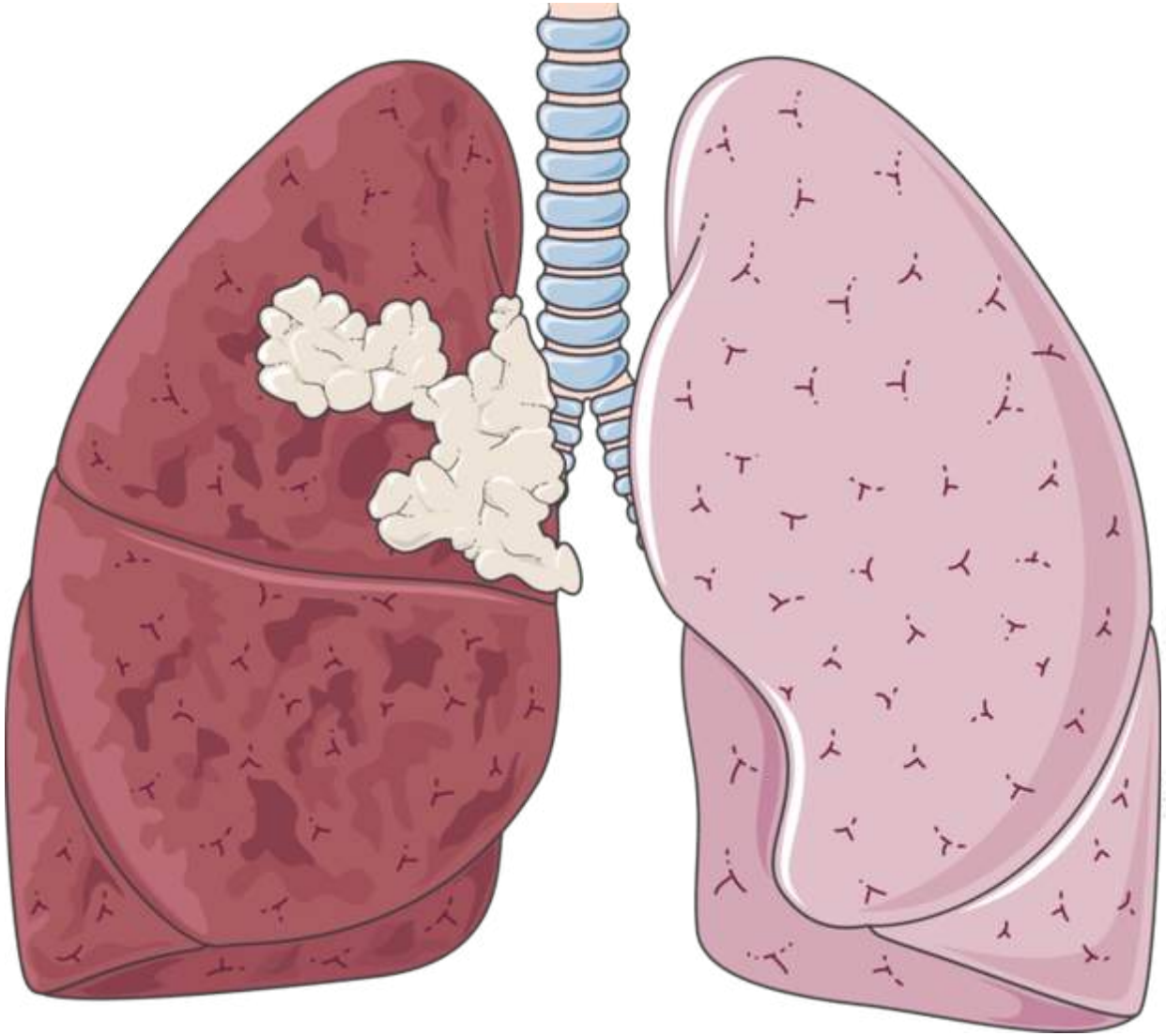
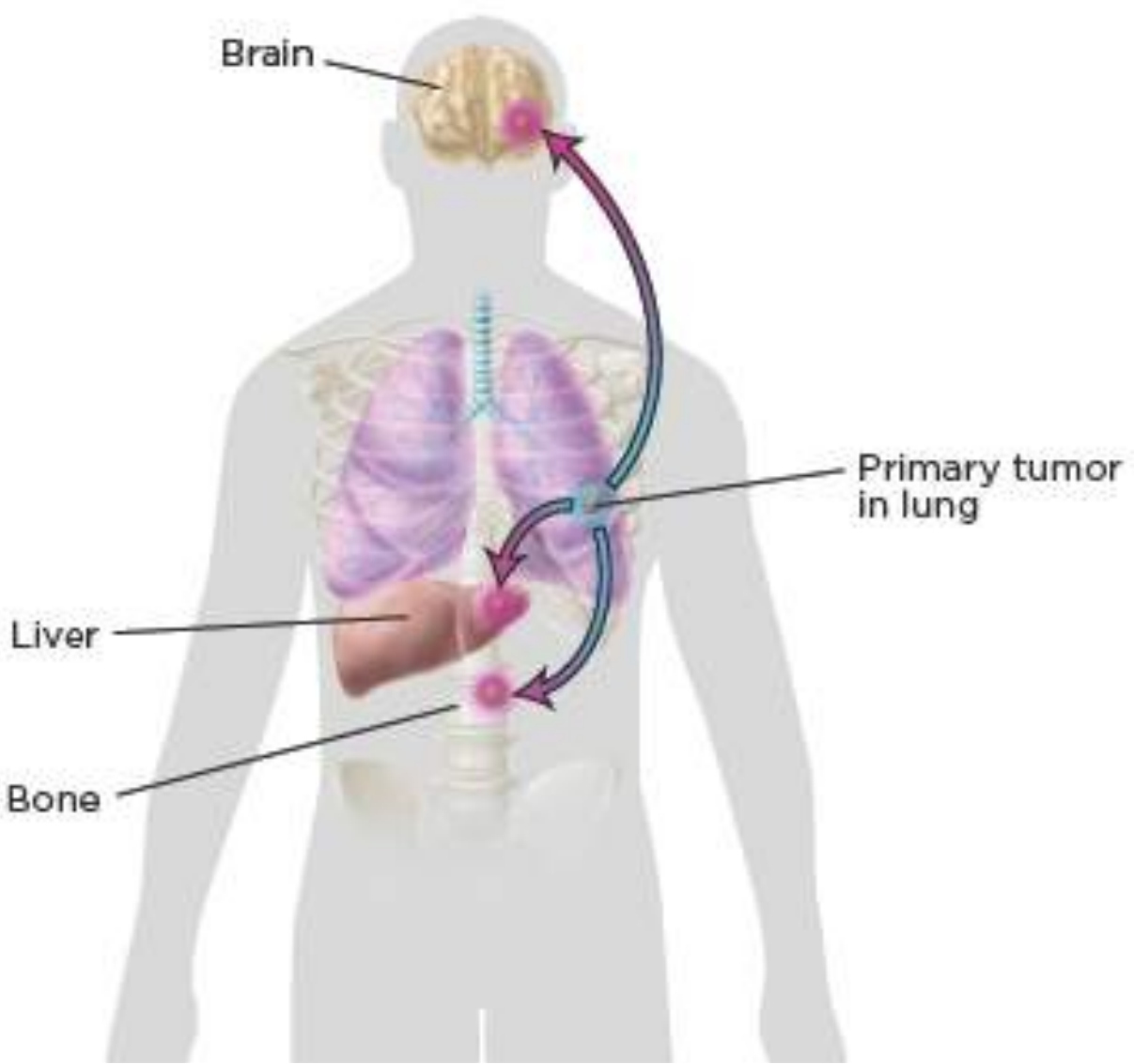
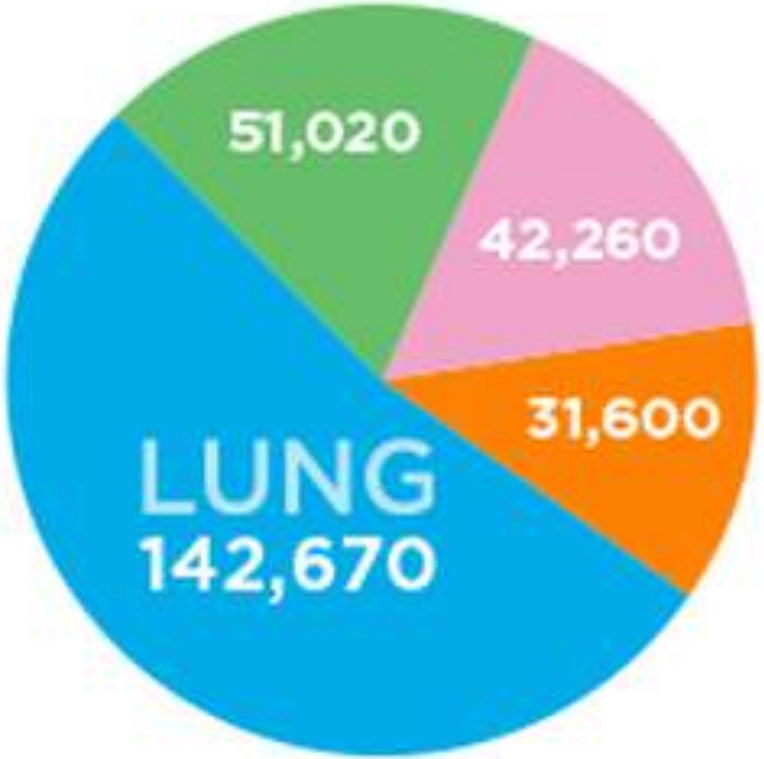


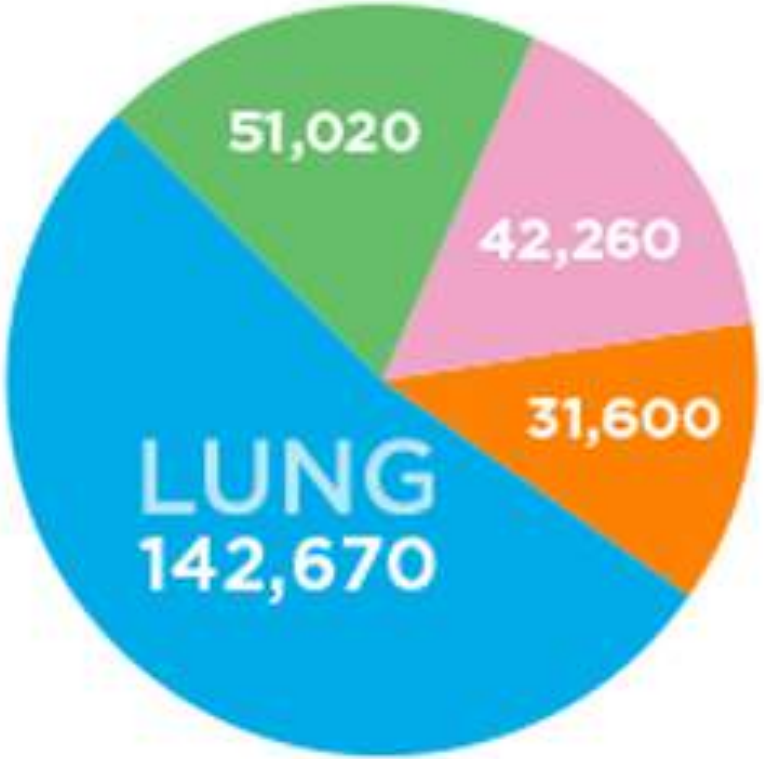


How deadly is lung cancer?



Lung cancer takes more lives annually in the U.S. than the next three most common cancers combined

How deadly is lung cancer?



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Lung cancer kills about 2.5 times as many men as prostate cancer

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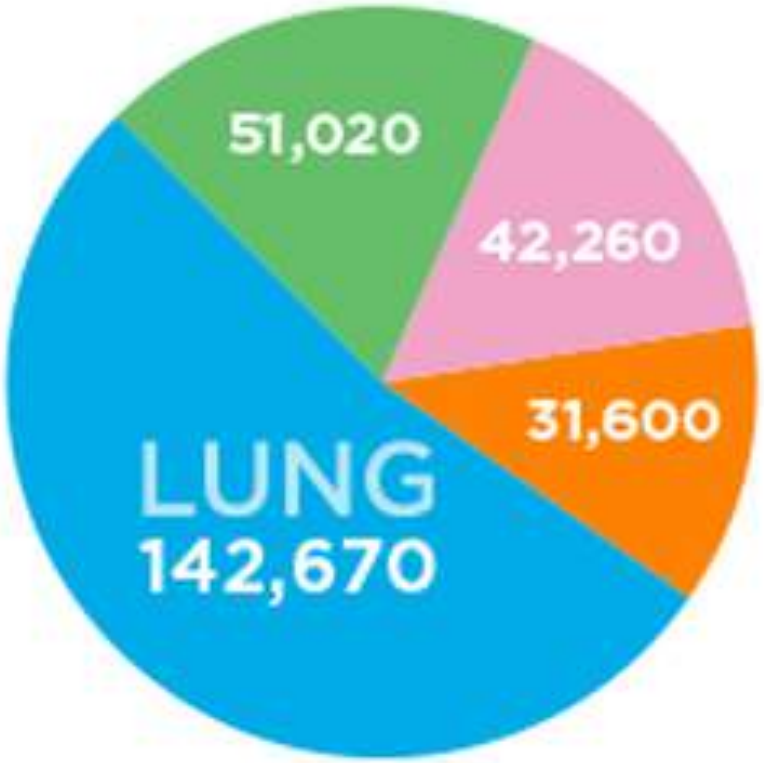

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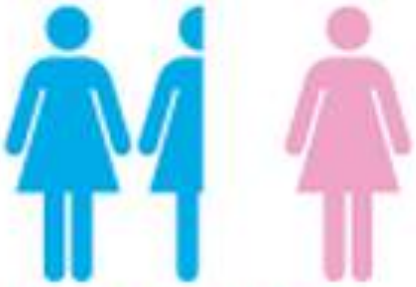

Lung cancer kills about 1.5 times as many women as breast cancer

What are genes are involved in lung cancer?

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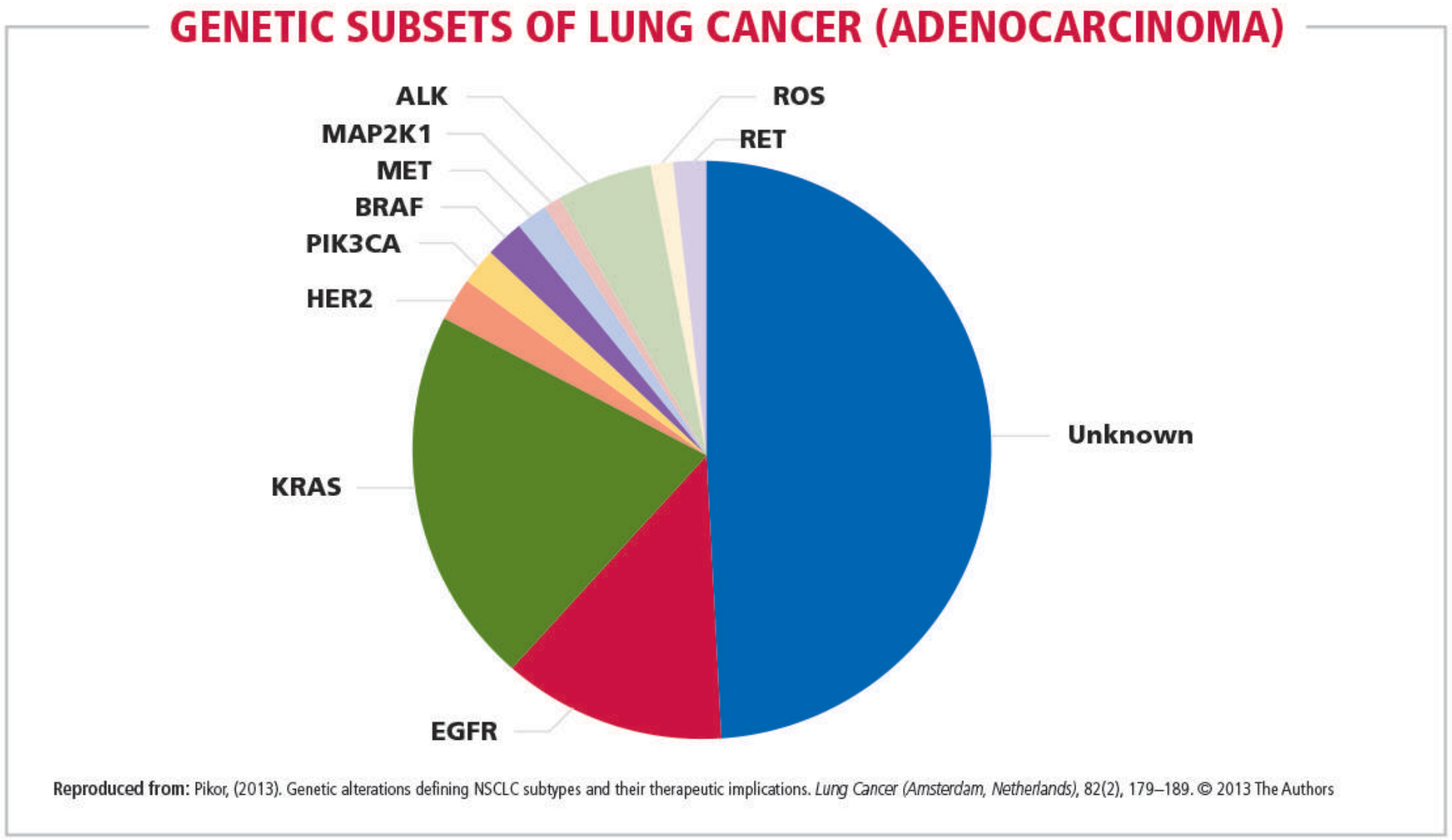

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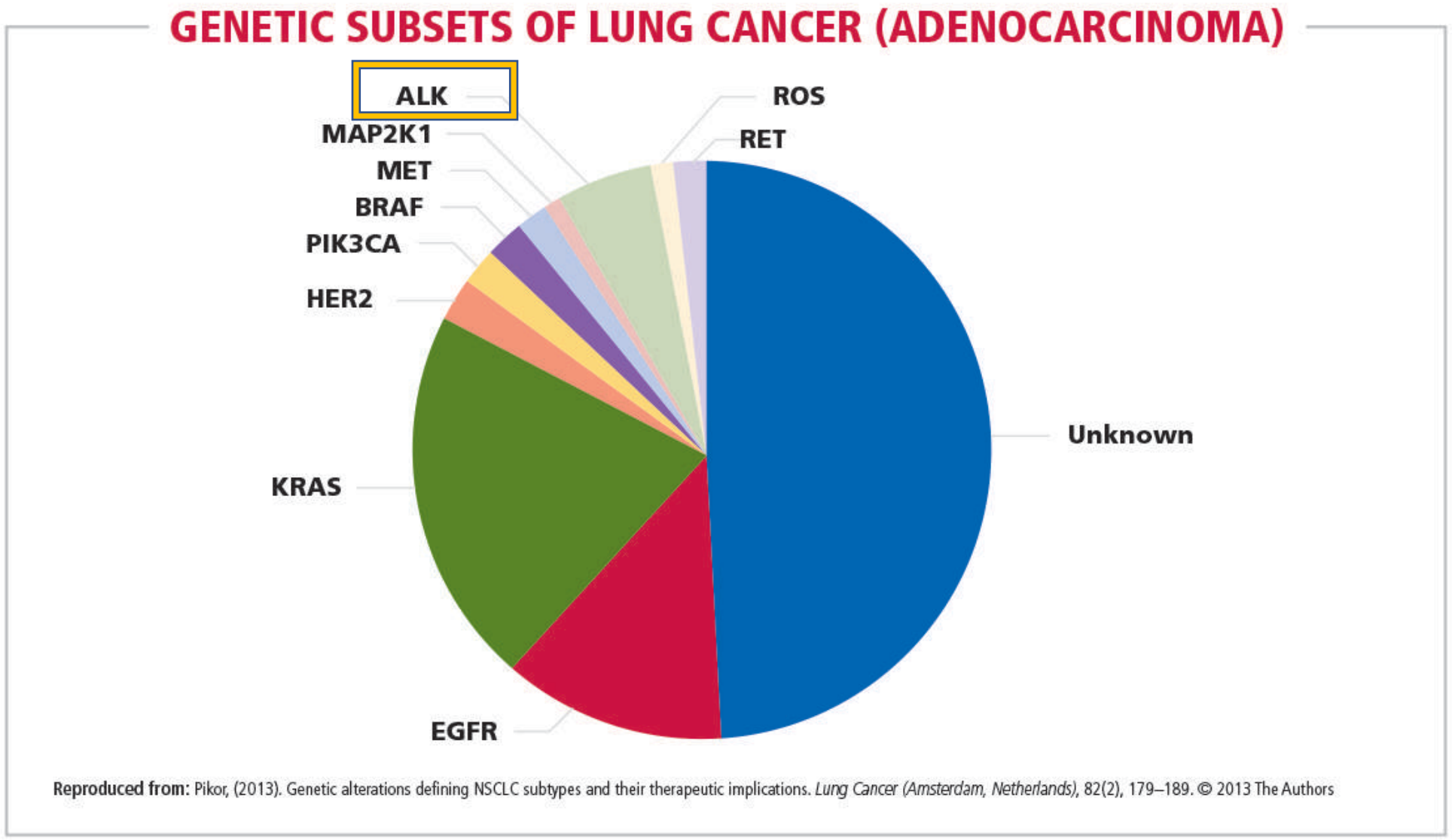
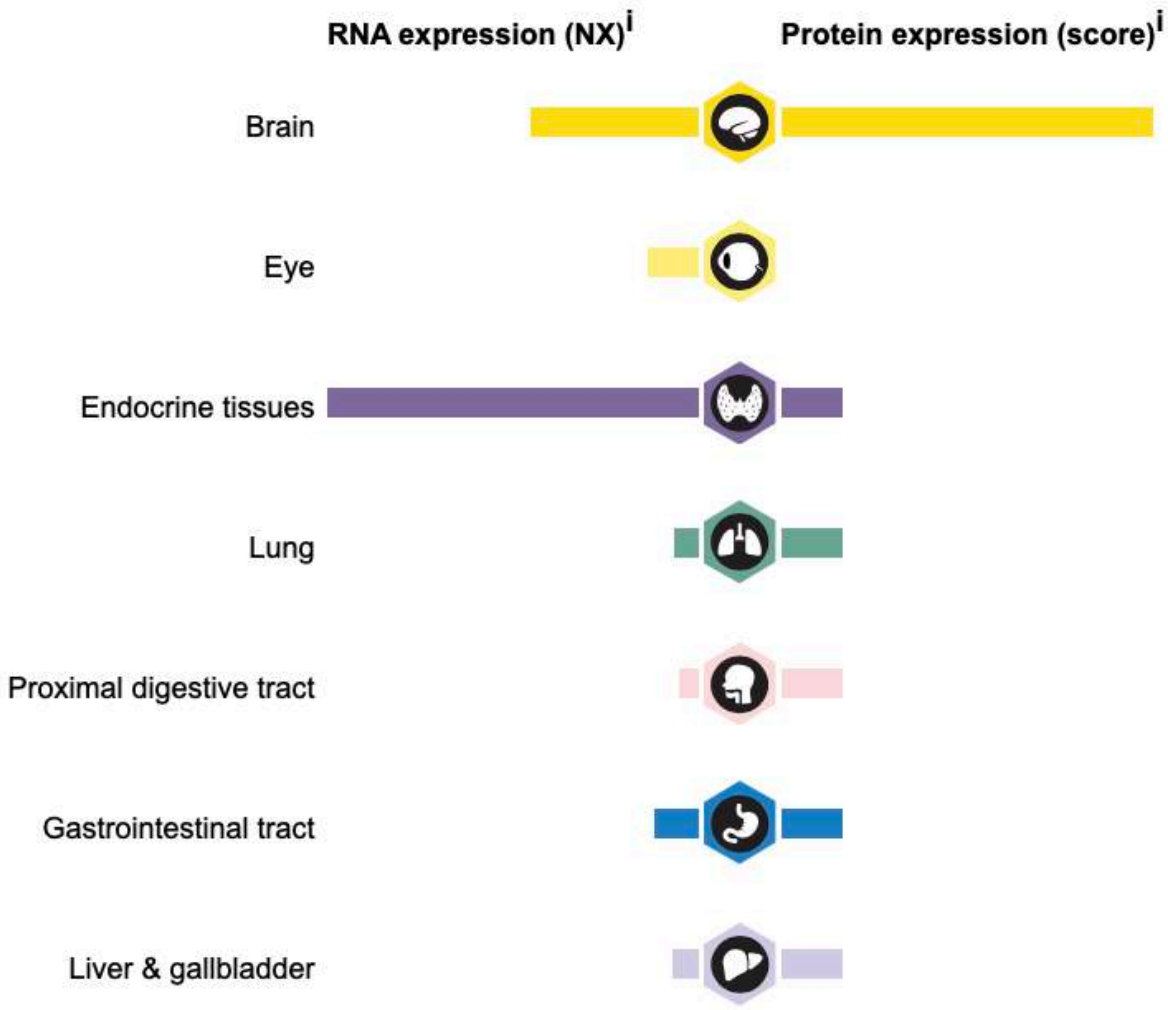


What is anaplastic lymphoma kinase (ALK)?



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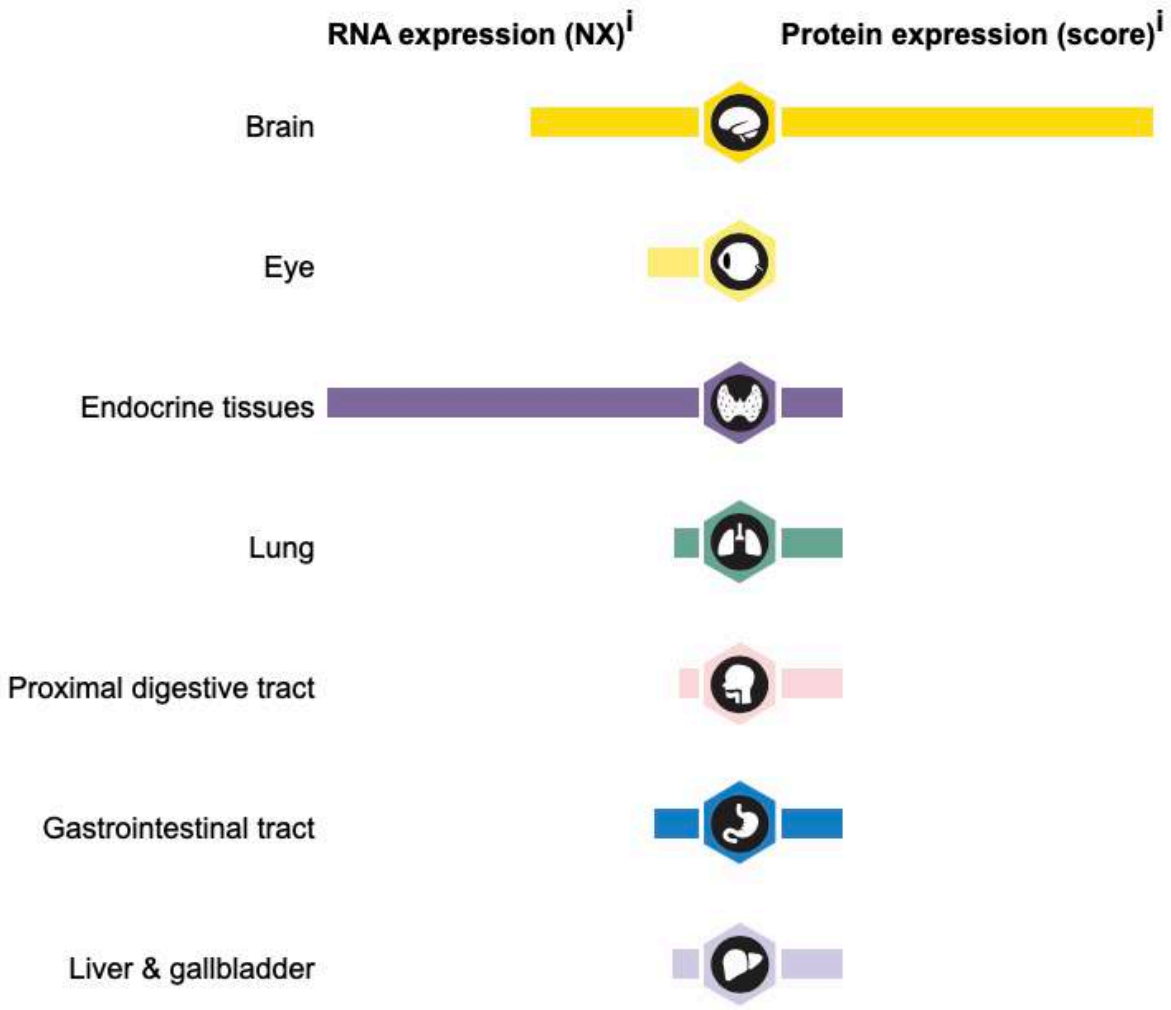
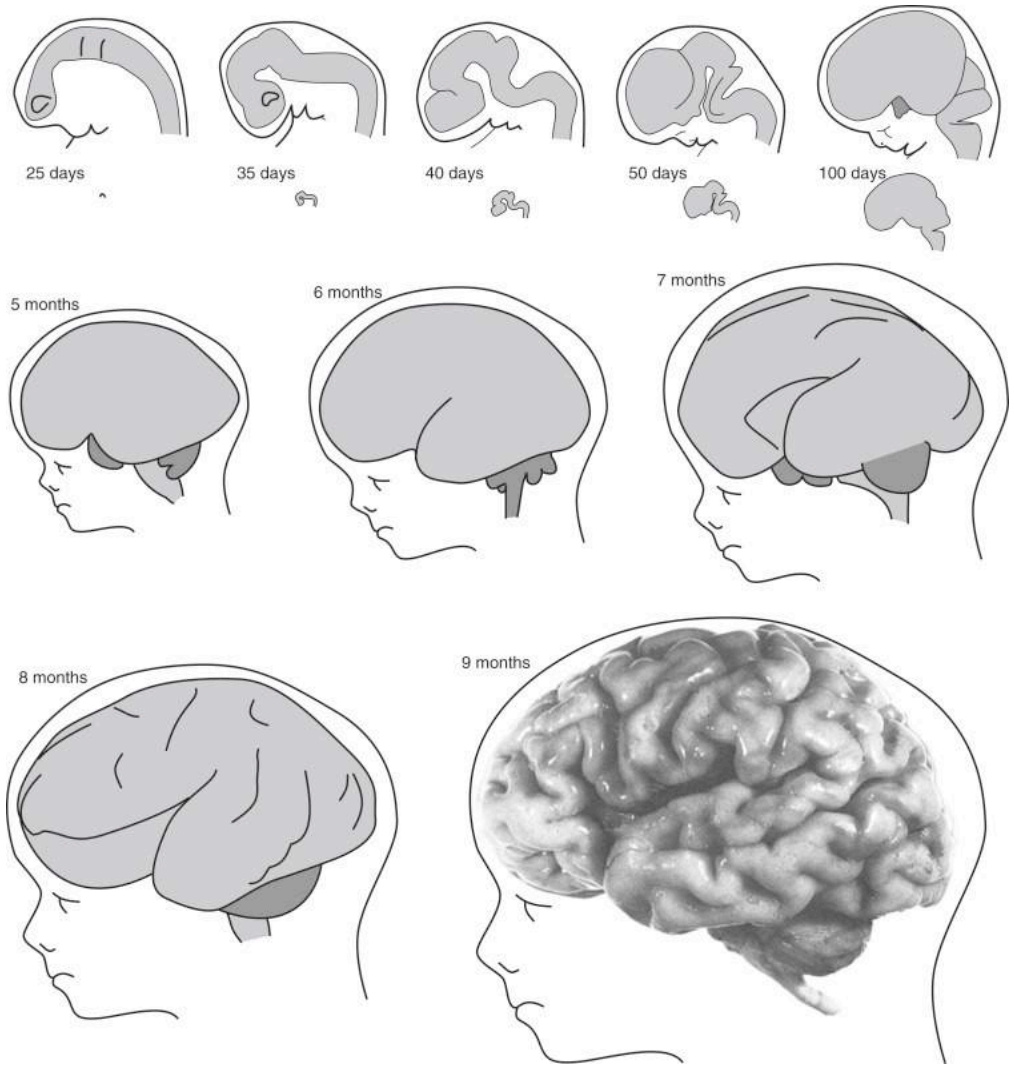
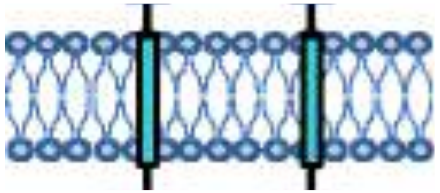




What is Gene Ontology of ALK?

Cellular Function



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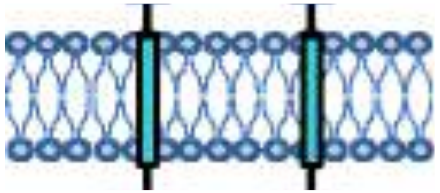

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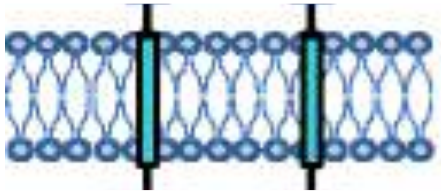

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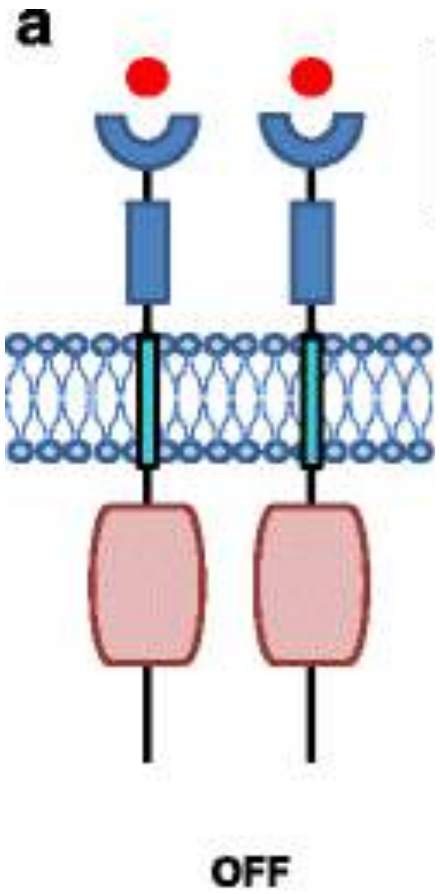

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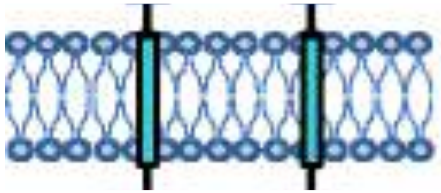

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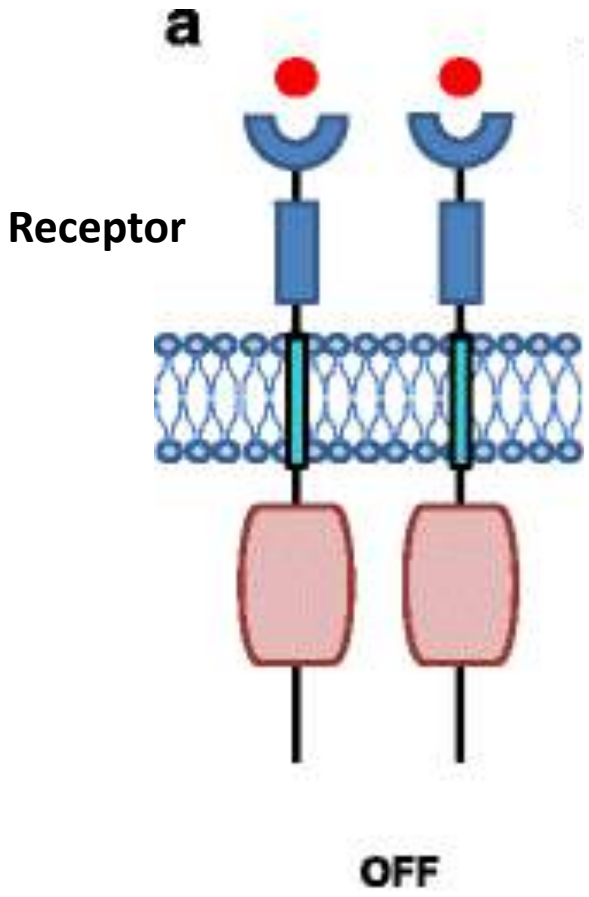

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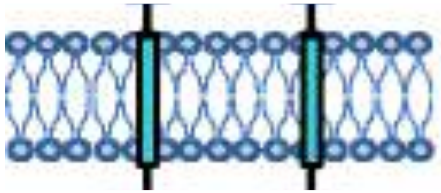

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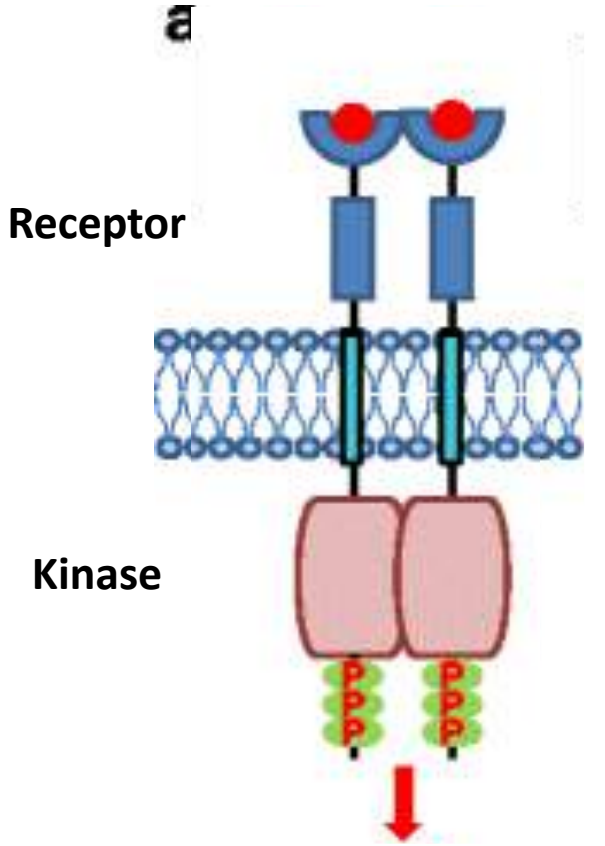

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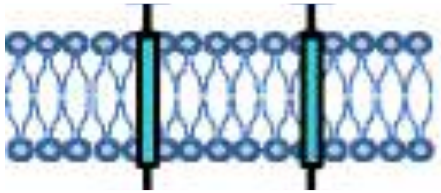

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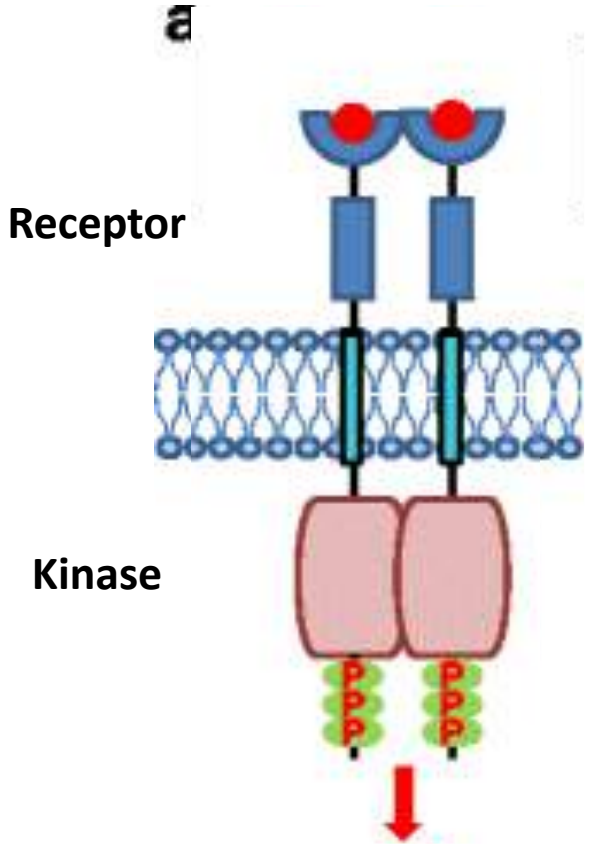

Biological Function

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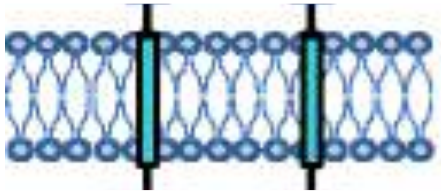

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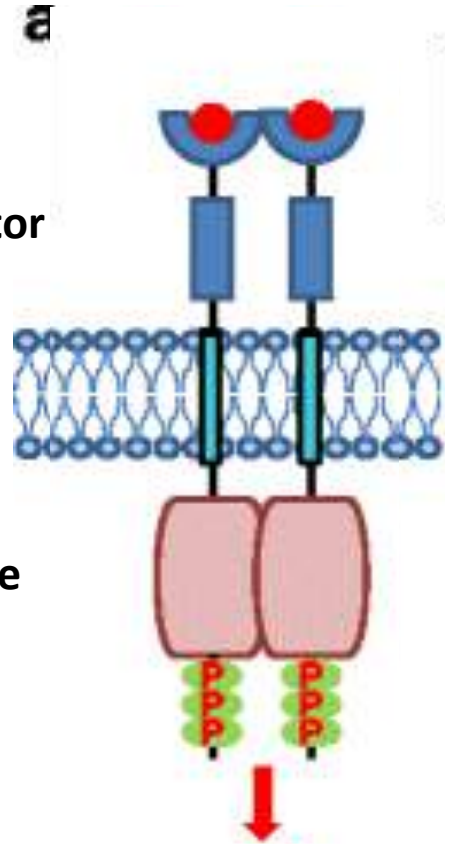

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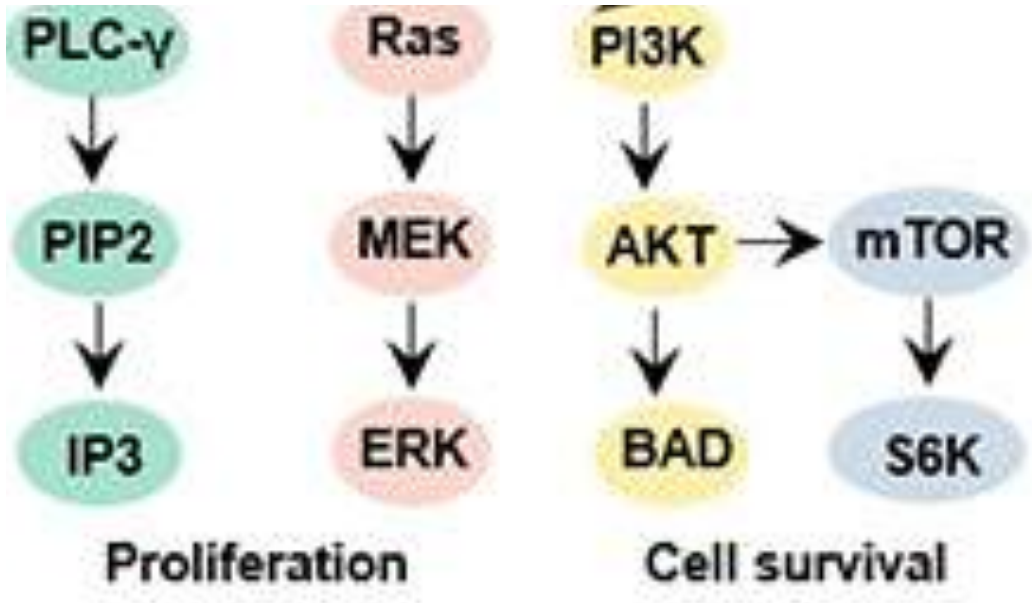
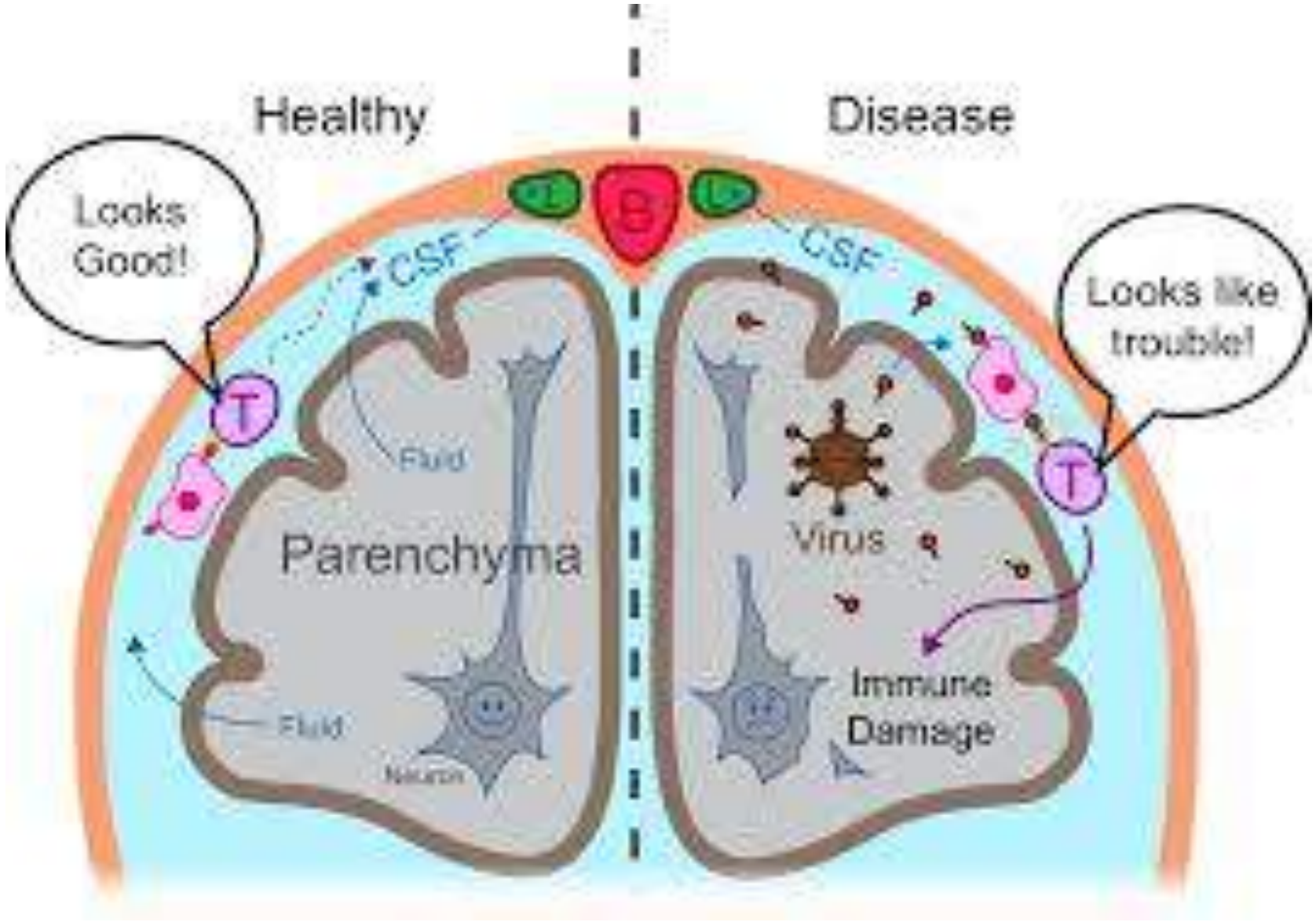
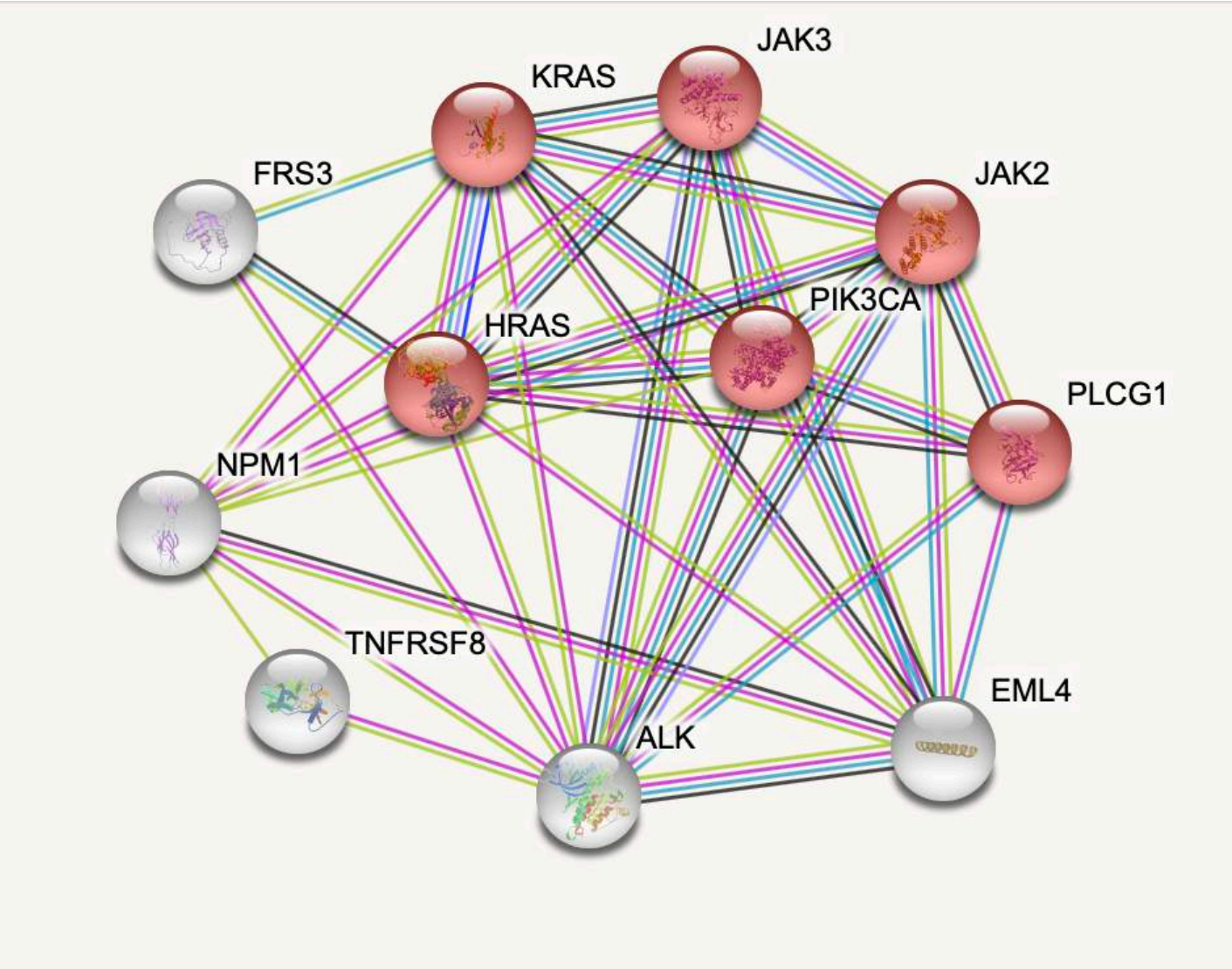


Immune Evasion

What is immune evasion?

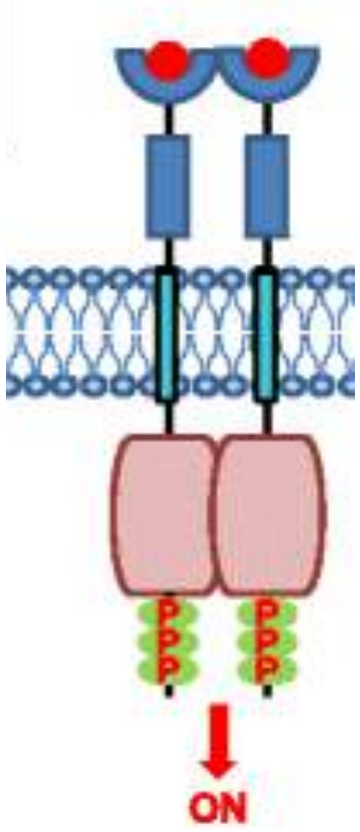


ALK gene major driver of lung cancer



Immune Function

What is the current gap in knowledge?



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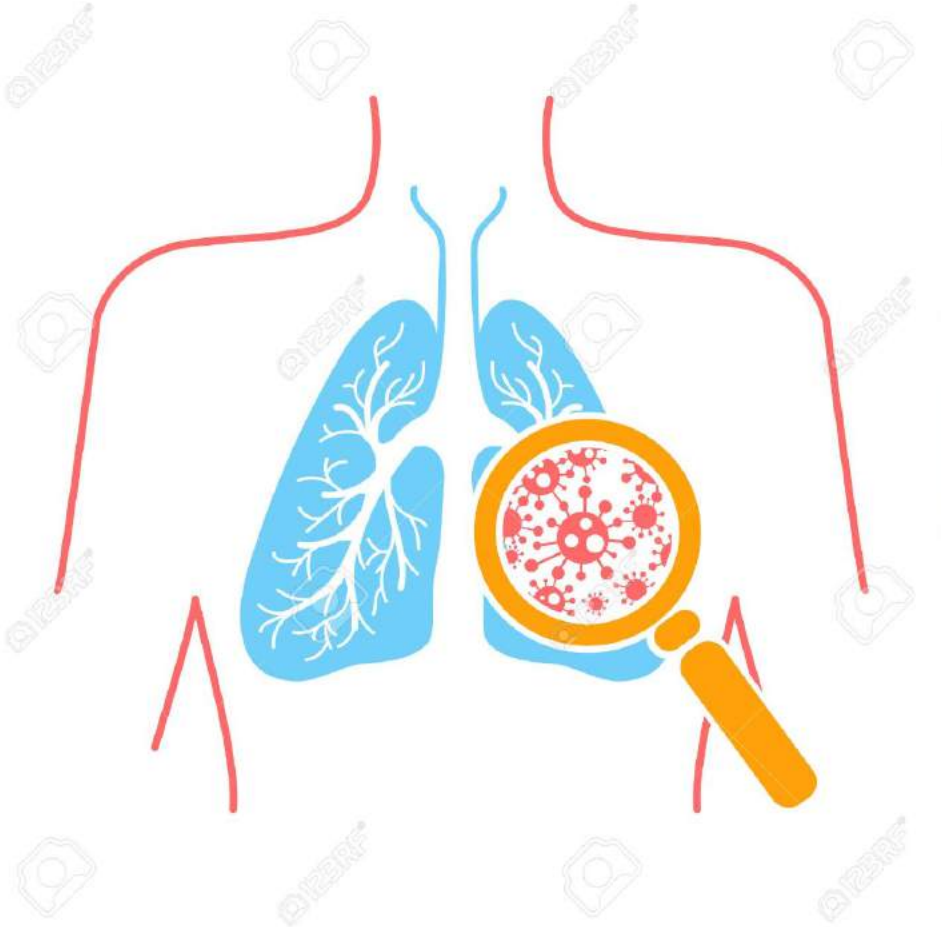
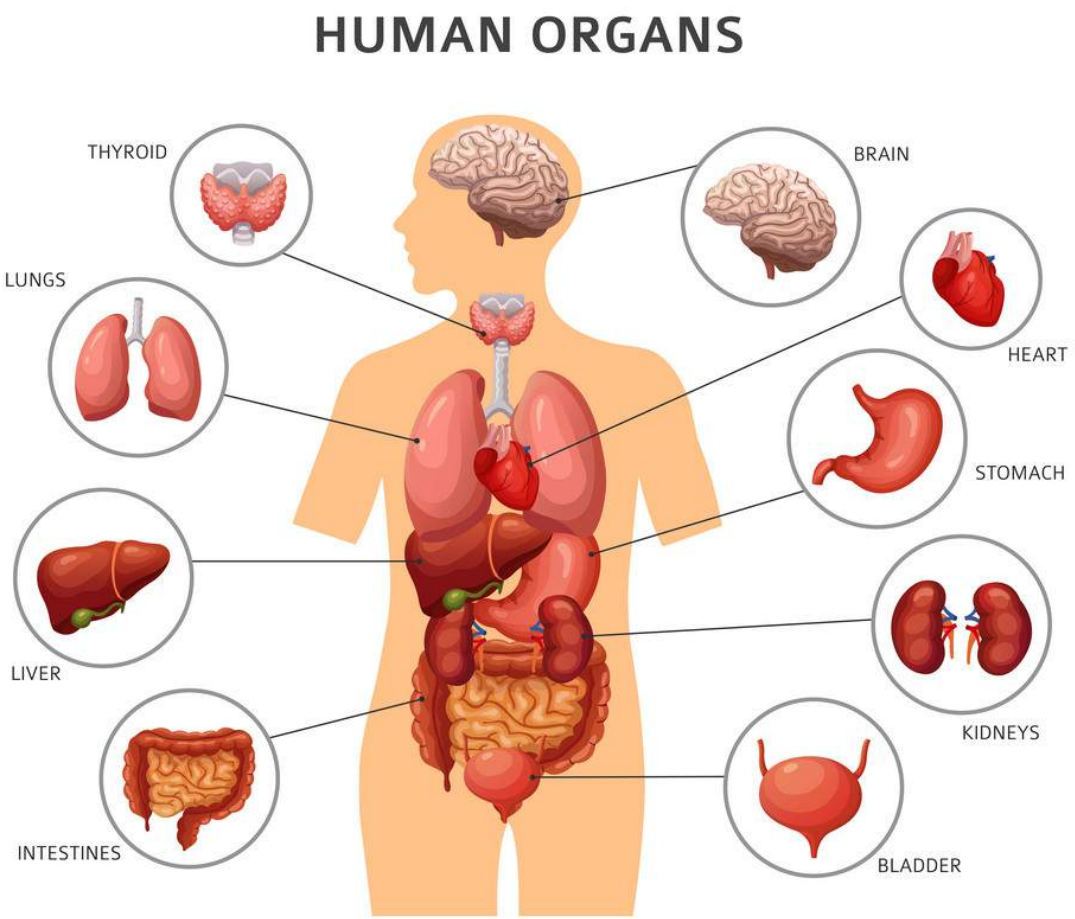


ALK

Lung Immune Response

What model organism to study ALK?



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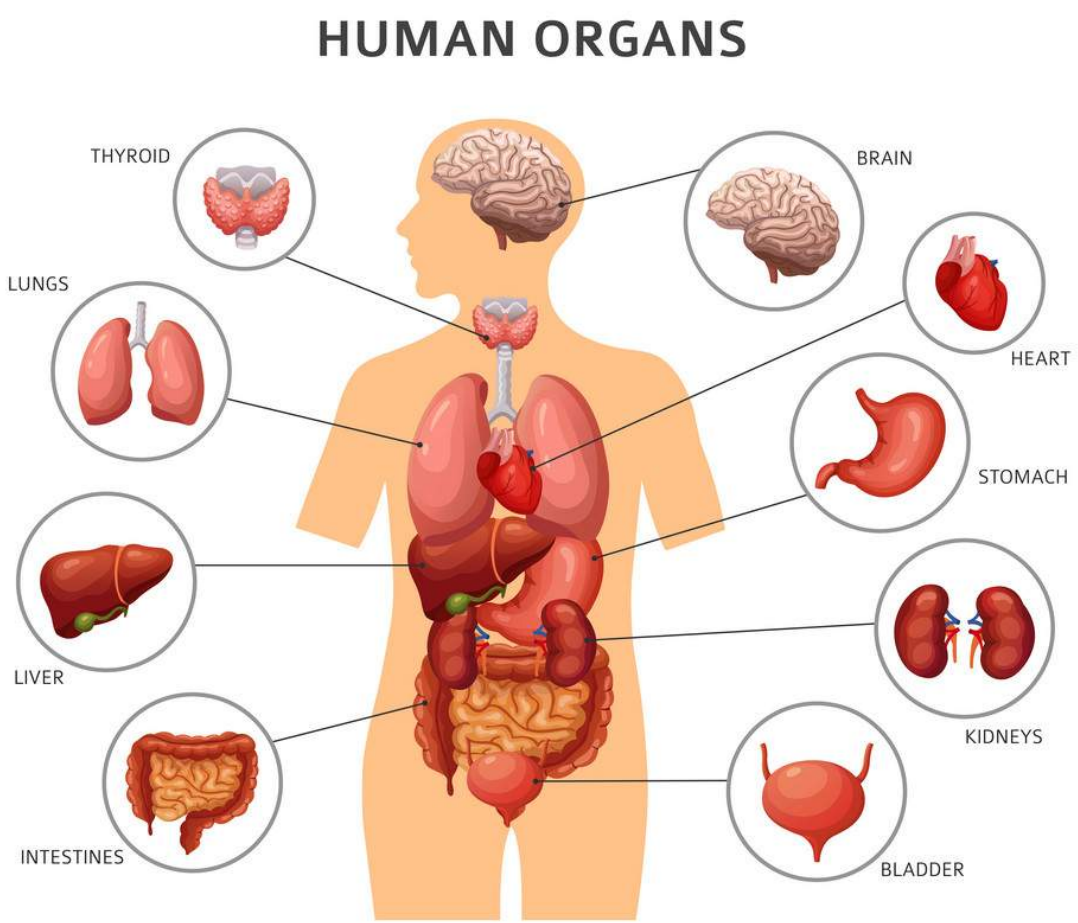
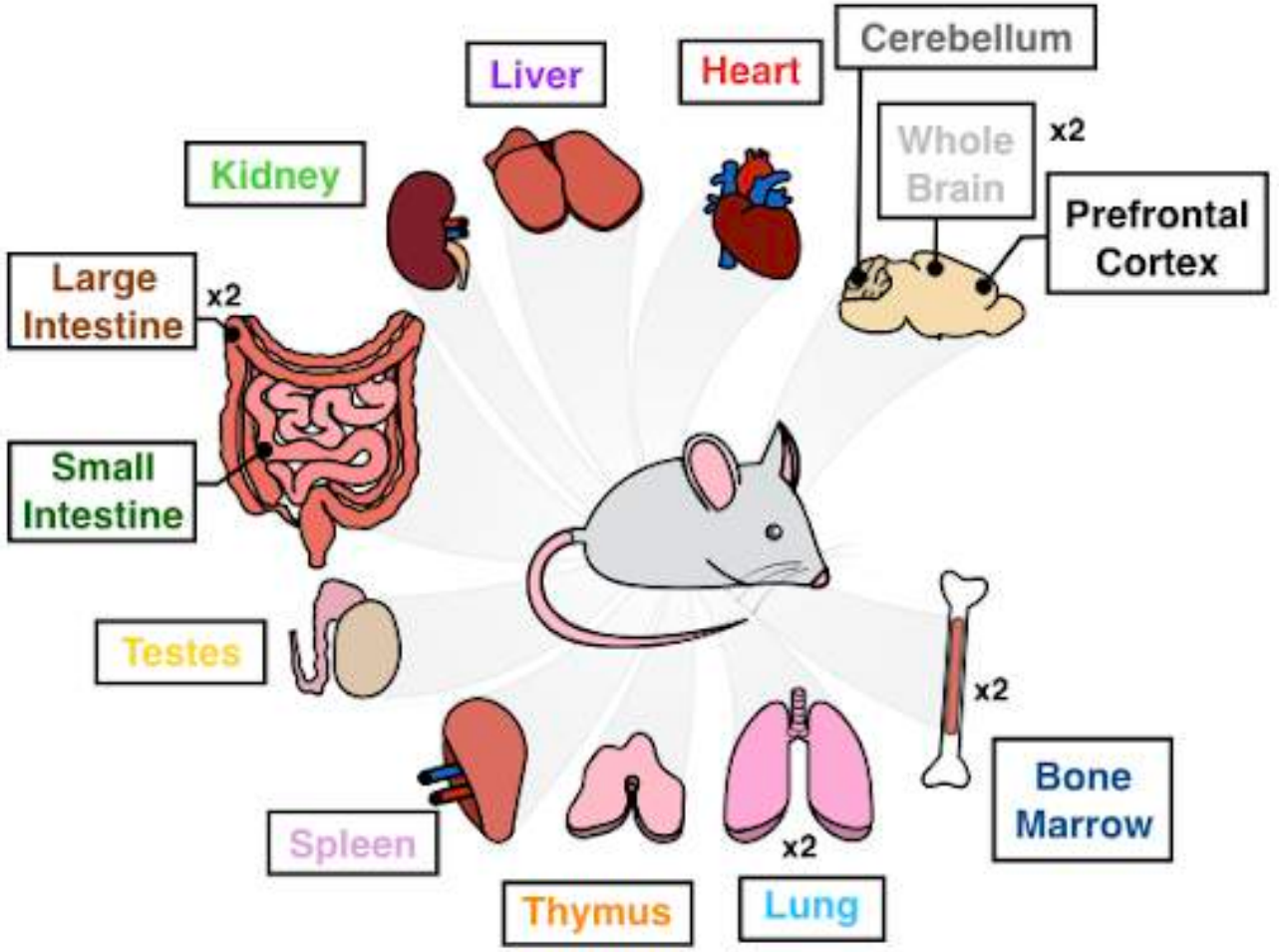
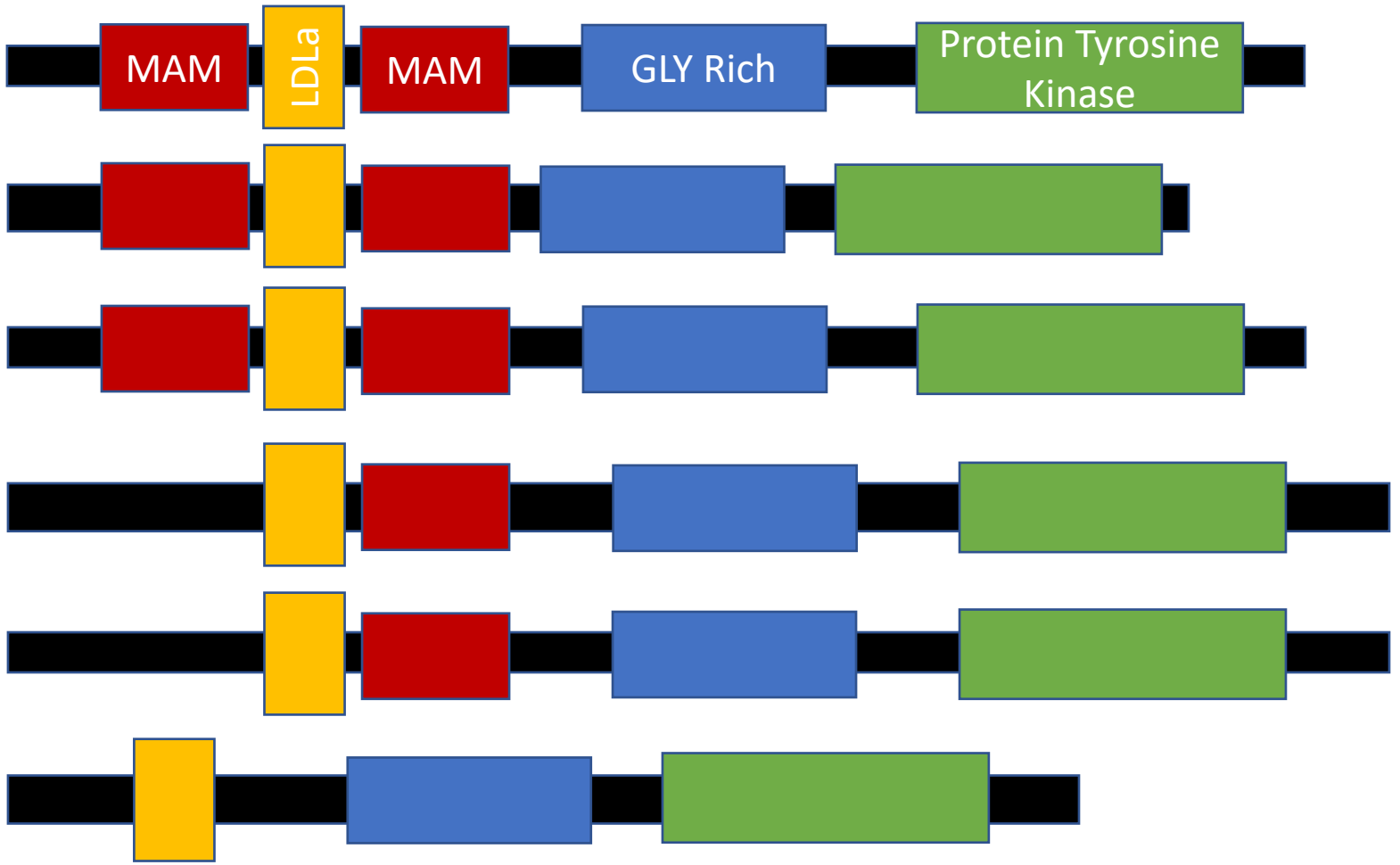




Conservation of ALK across model organisms



Species	AA Length	Percent Identity
Human	1620	100%
Chimpanzee	1419	95%
Mouse	1621	84%
Fly	1701	50%
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Nematode	1351	44%

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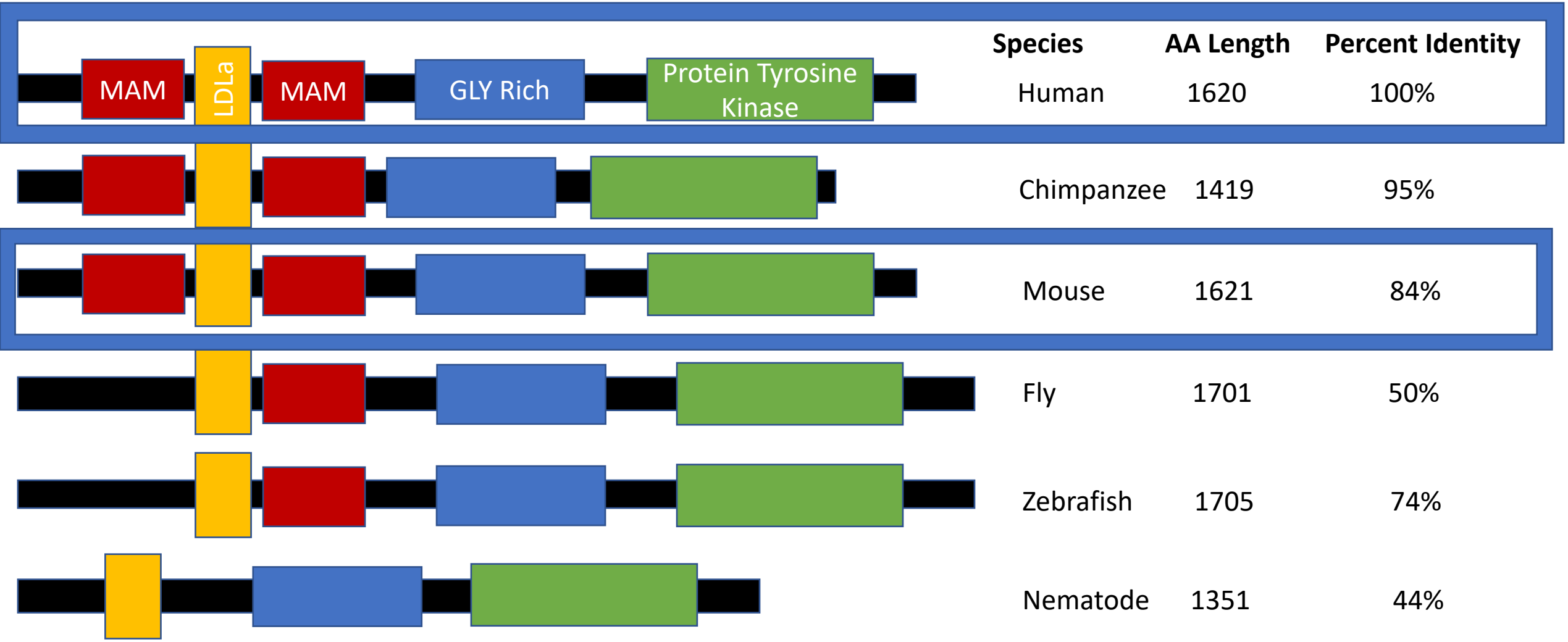

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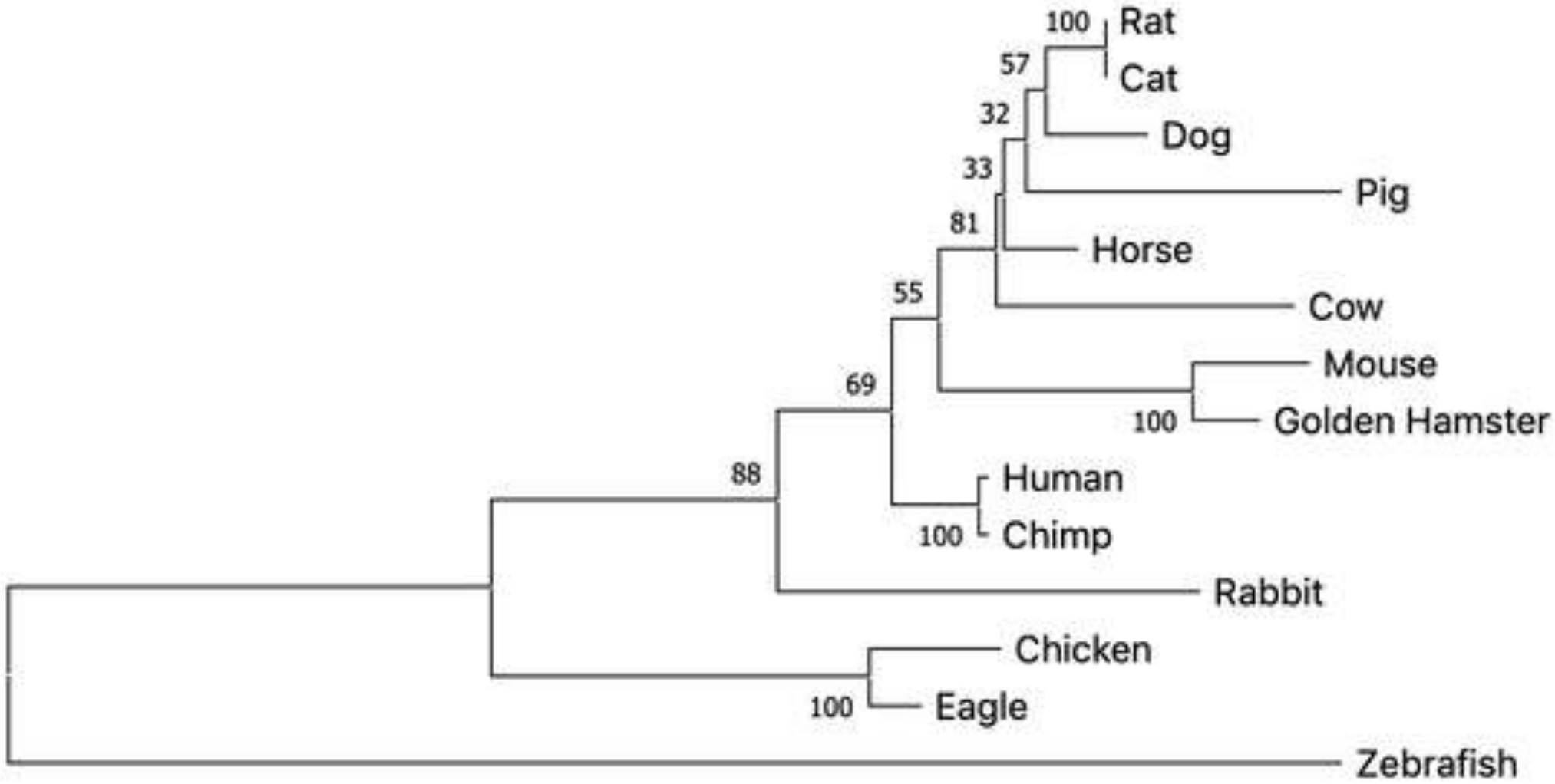
ALK homologs relationships



What is the primary goal?

To better characterize ALK’s role in cancer immune envision.

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AIM 1

Characterize specific ALK mutations in lung cancer.

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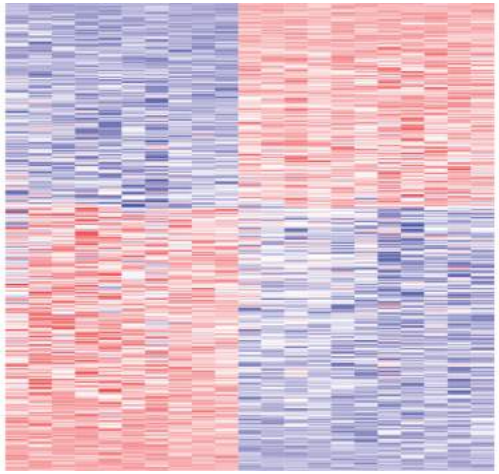
AIM 2

Identify expression of Immune genes in ALK driven lung cancer



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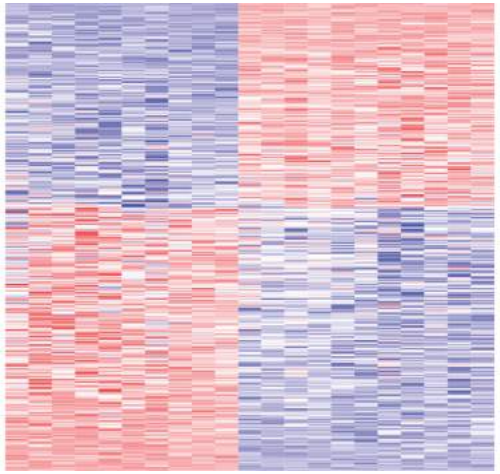
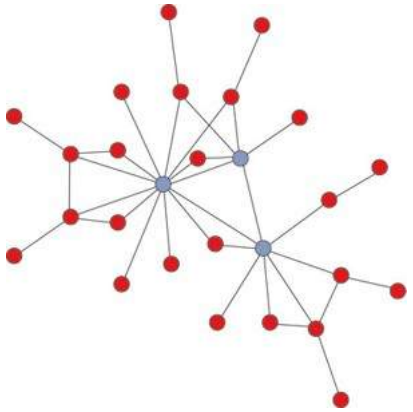
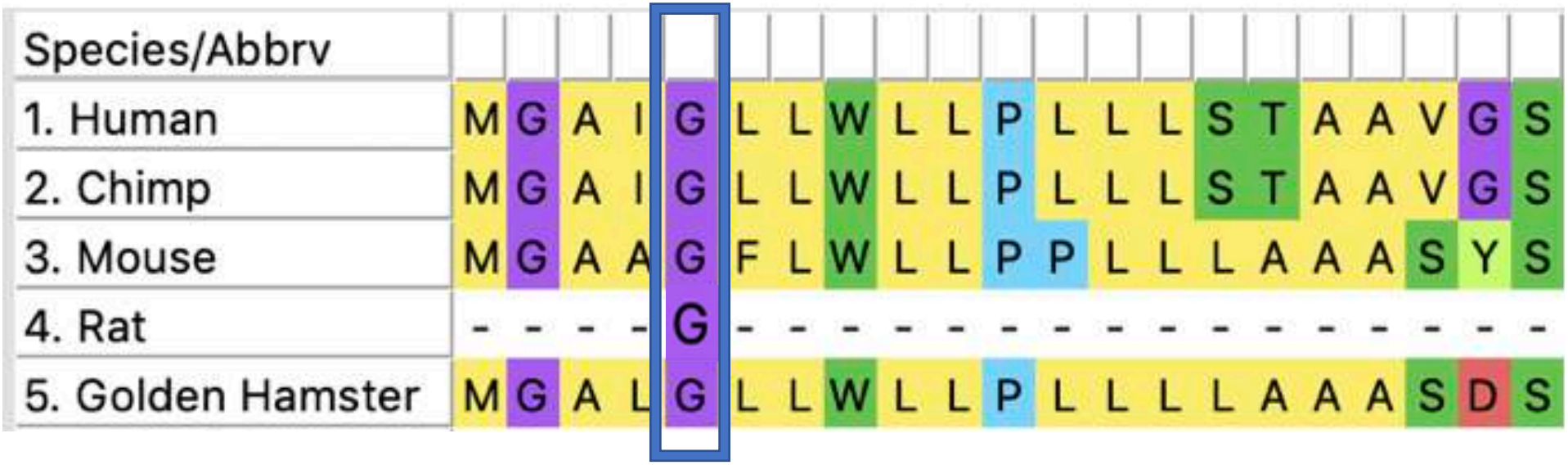


AIM 3

Identify immune evasion proteins that interact with ALK.



AIM 1: Characterize ALK mutations in NSCLC



ClustalOmega → CRISPR-Cas9 → Screen

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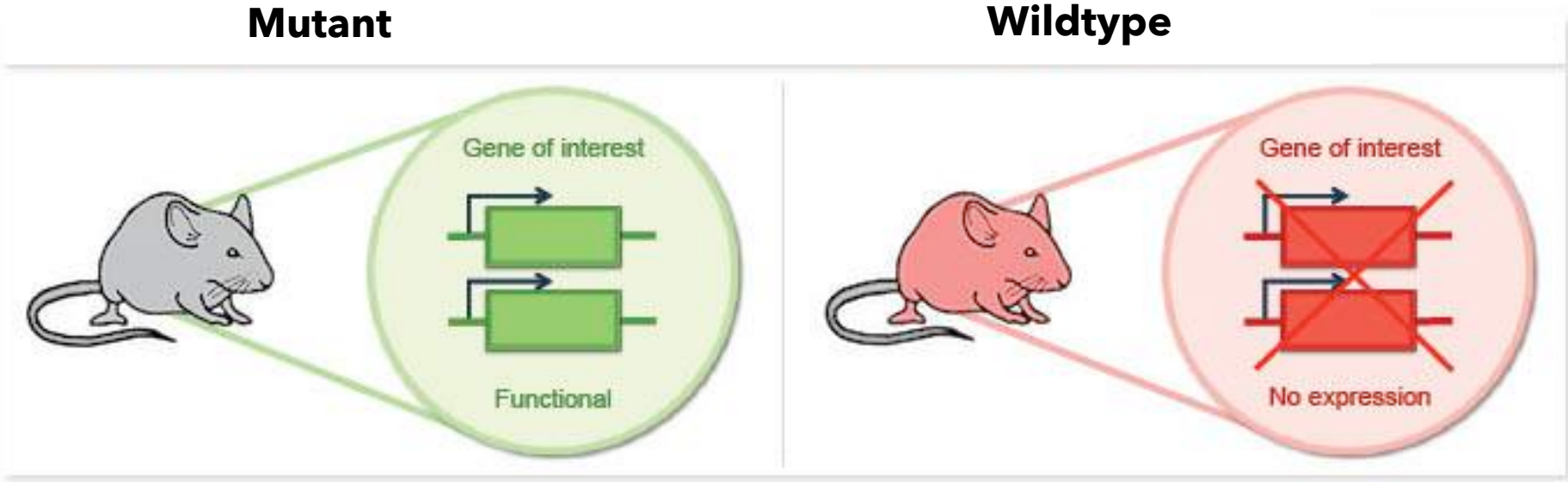

ClustalOmega → CRISPR-Cas9 → Screen

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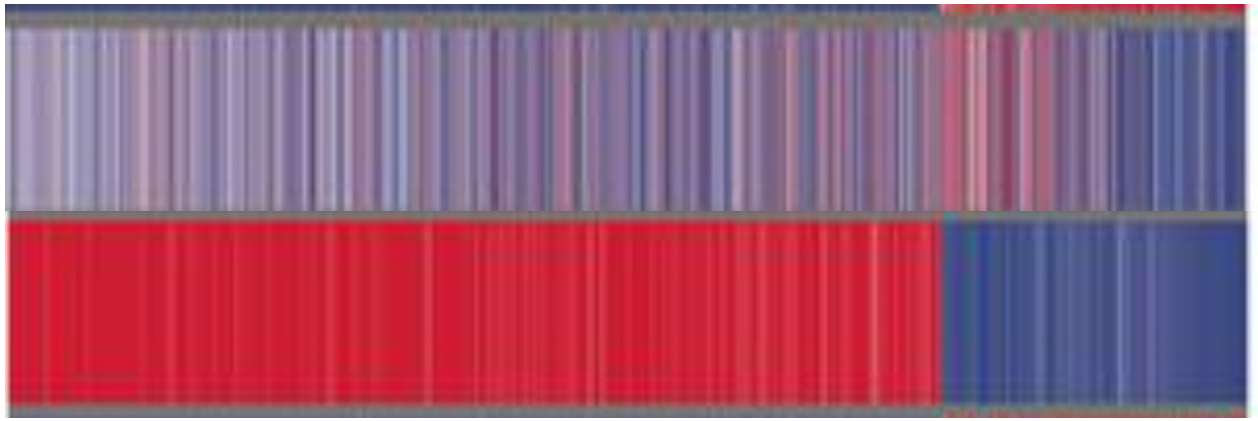
(A)

ClustalOmega → CRISPR-Cas9 → Screen

AIM 2: Identify differentially expressed genes

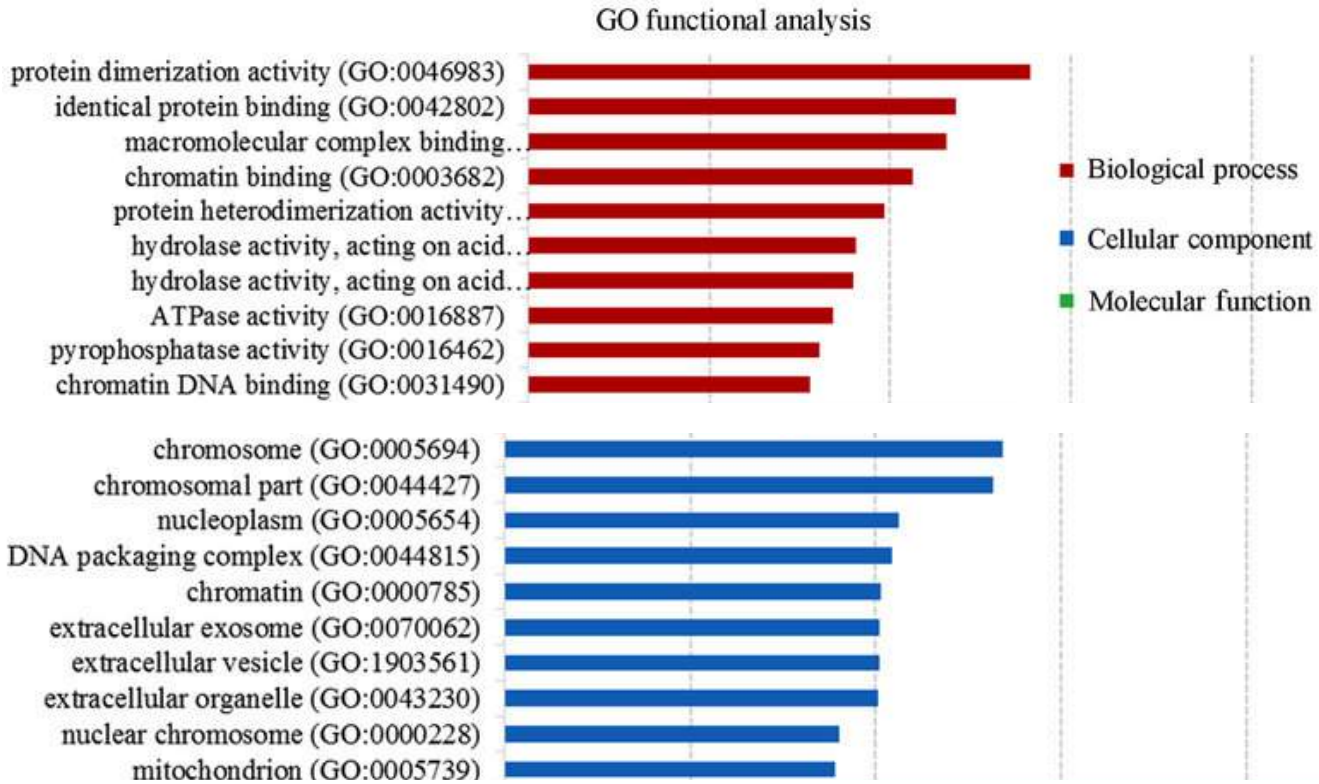


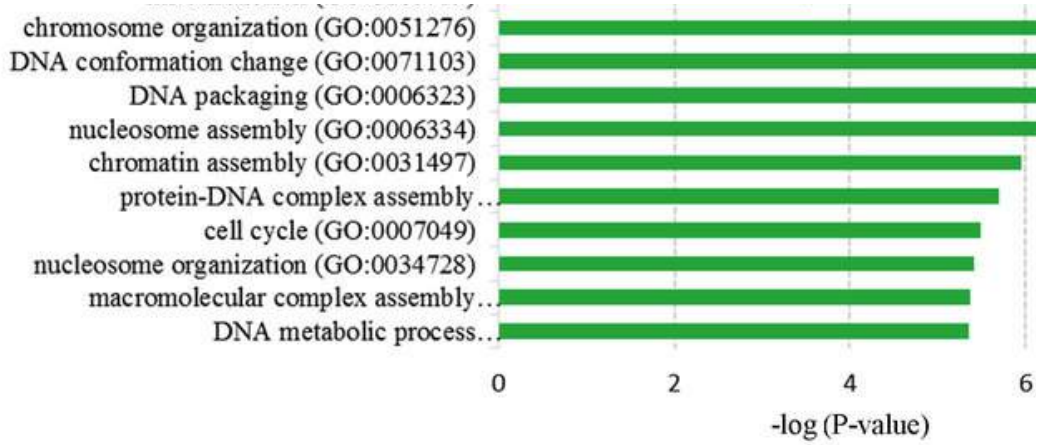
Wild Type

ALK Mutant

RNA-Seq → GO → Pathway Analysis

AIM 2: Identify differentially expressed genes





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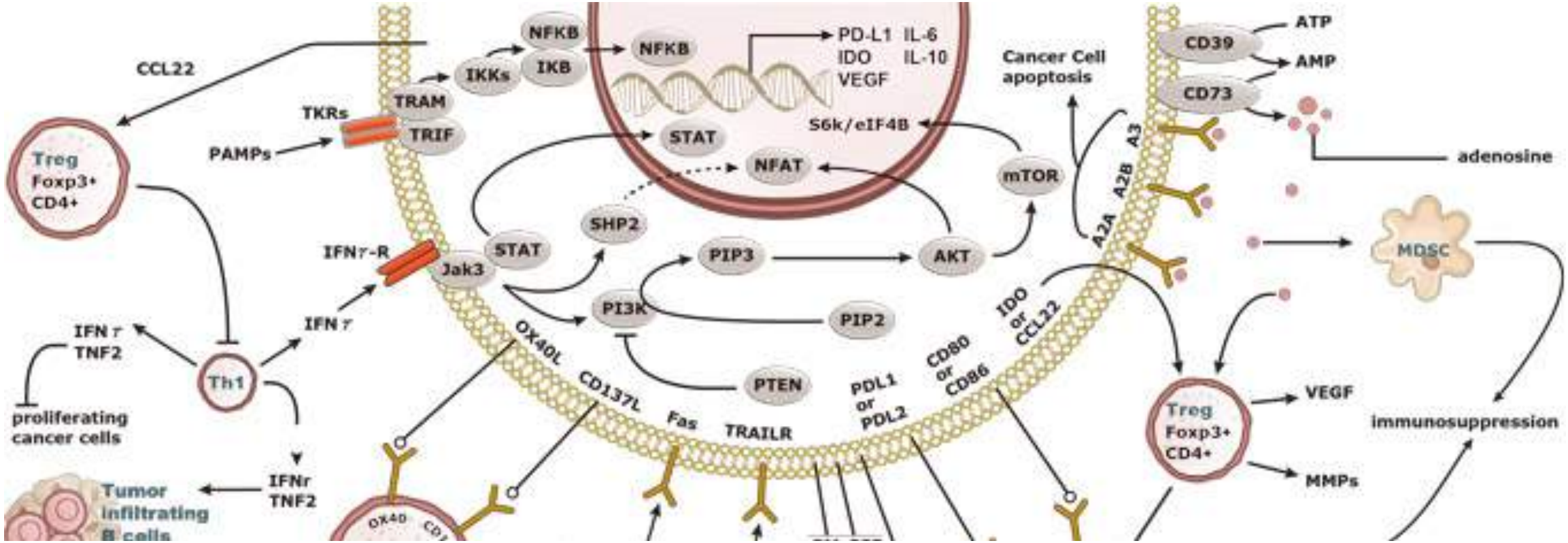
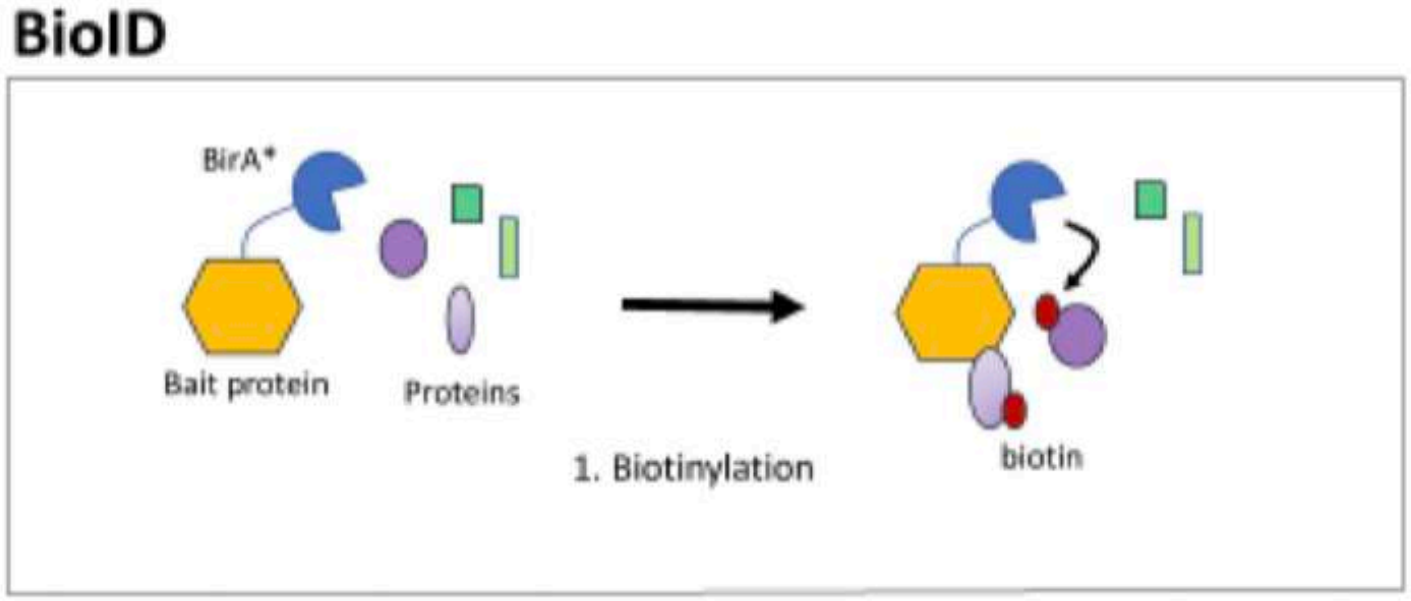


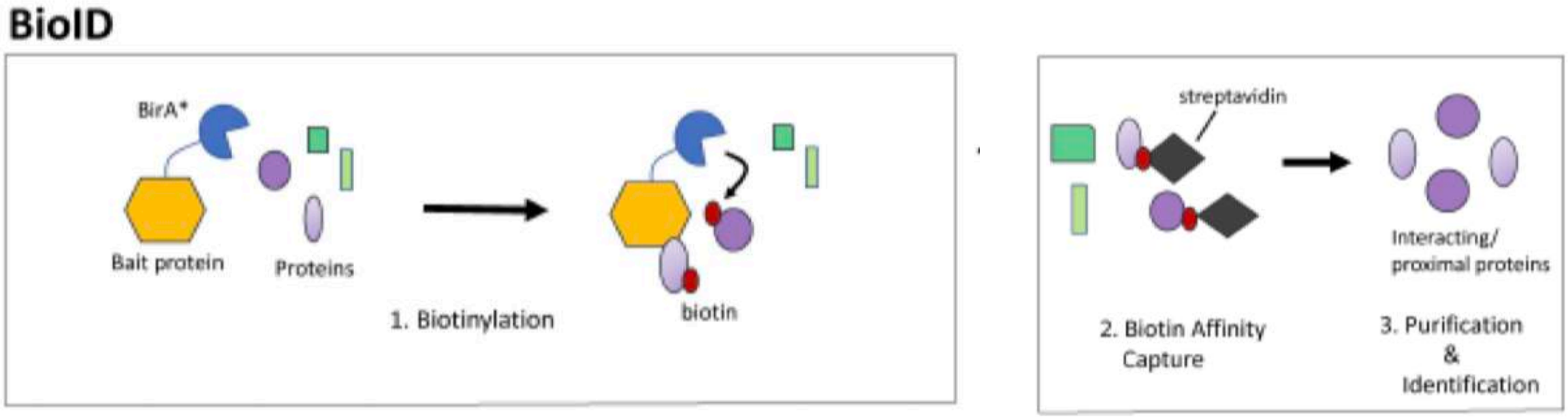
RNA-Seq → GO → Pathway Analysis

AIM 3: Identify immune envision proteins



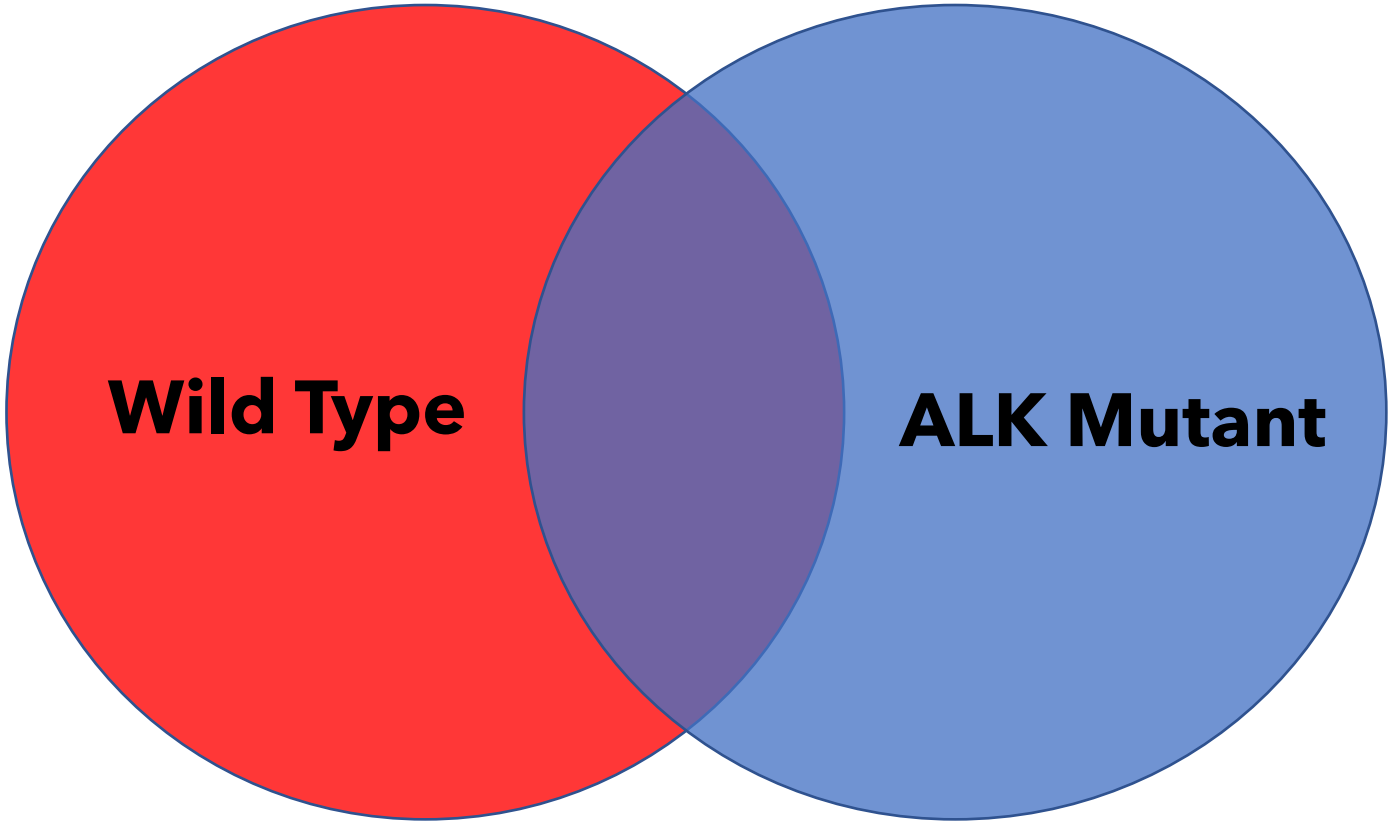
BioID → Mass Spec → Compare

AIM 3: Identify immune envision proteins



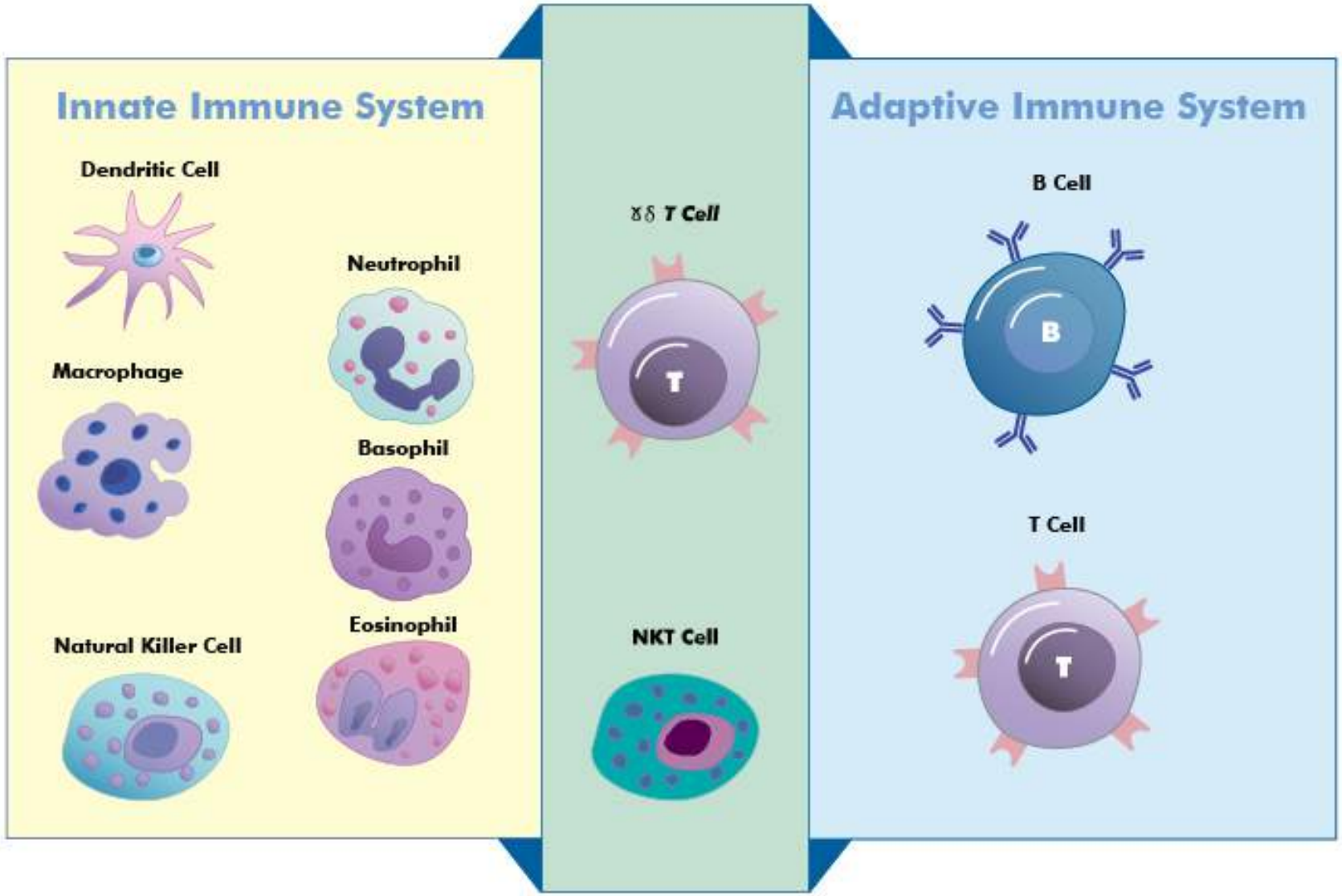
BioID → Mass Spec → Compare

AIM 3: Identify immune envision proteins



BioID → Mass Spec → Compare

Conclusions

- **ALK is a gain of function mutation that is involved in many cancers.**
- **ALK may have a function related to immune system and cancer immune invasion.**
- **By learning more about ALK and its role with the immune system, it can be better understood the role ALK plays in promoting lung cancer.**

Future Directions