



Nicholas Moehn

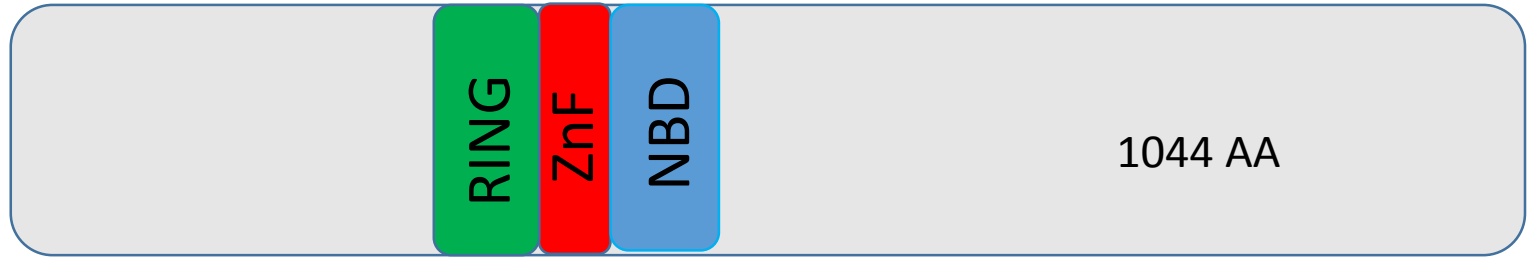
# Omenn Syndrome and RAG1

# What is Omenn Syndrome?

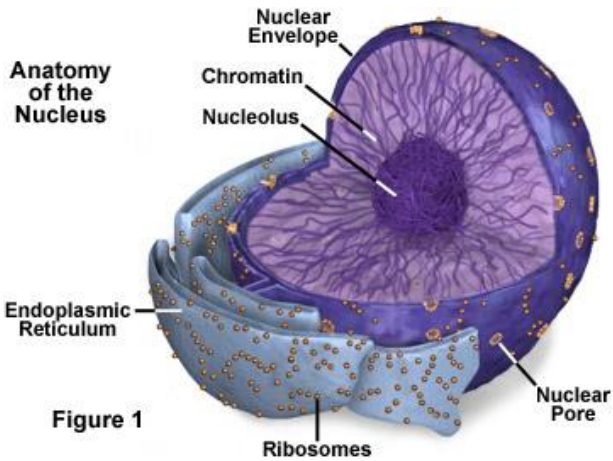


# Mutations in RAG1 causes Omenn Syndrome

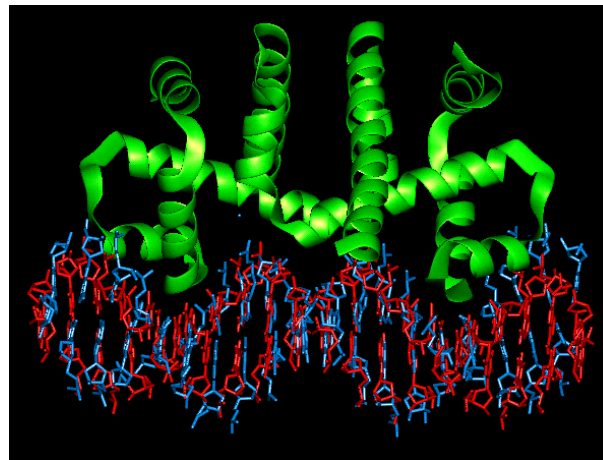
RAG1



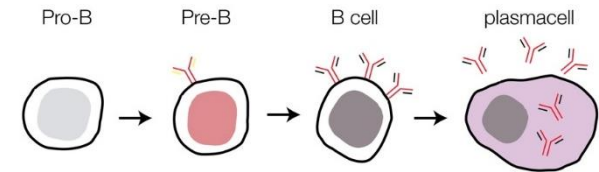
Cellular Compartment



Molecular Function

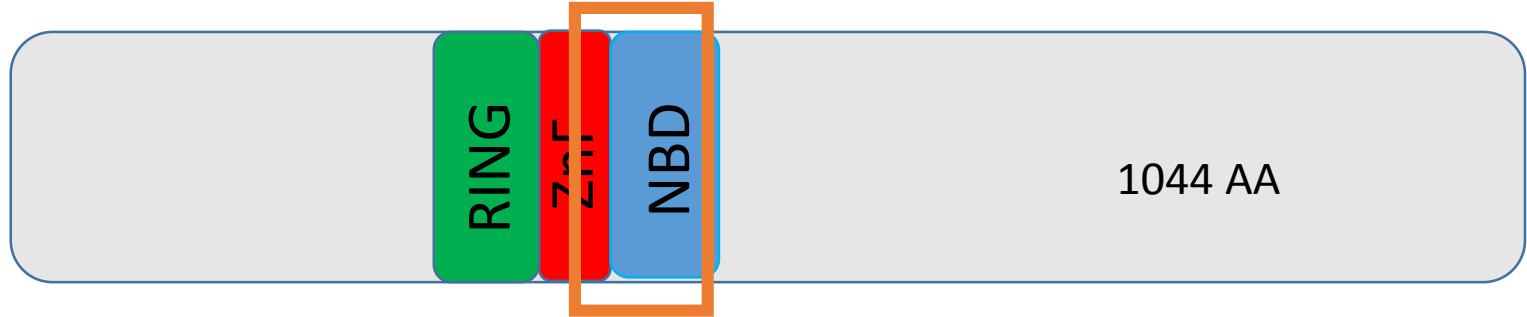


Biological Process

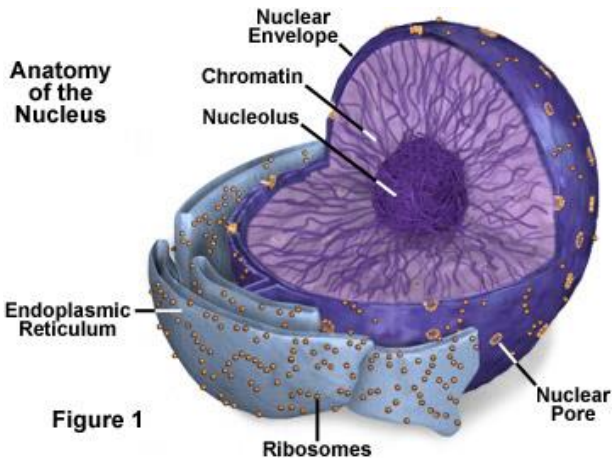


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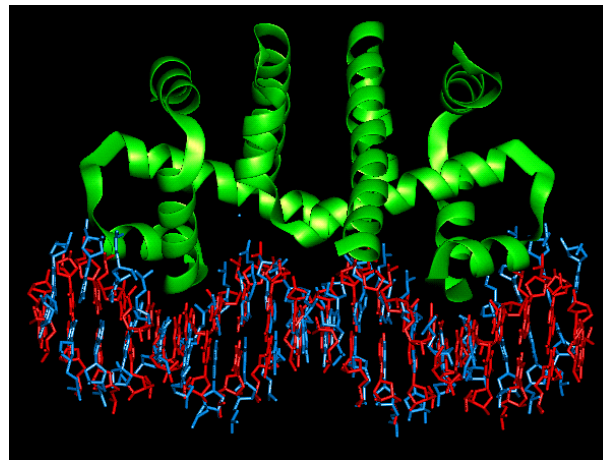
RAG1



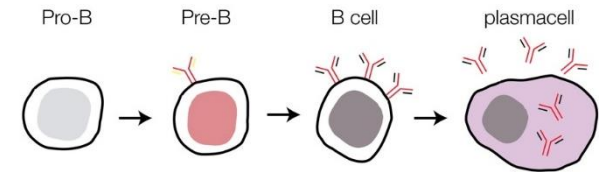
Cellular Compartment



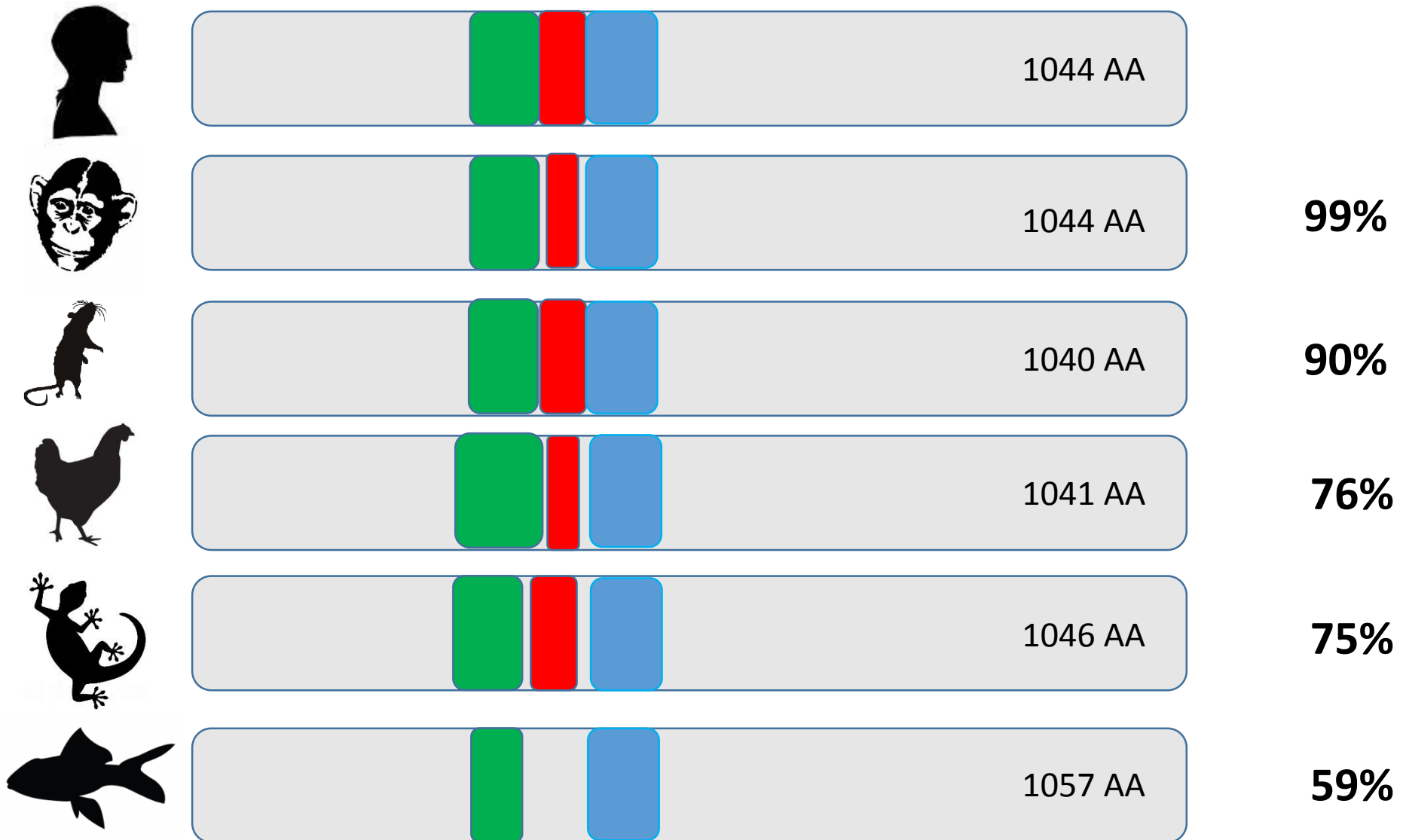
Molecular Function



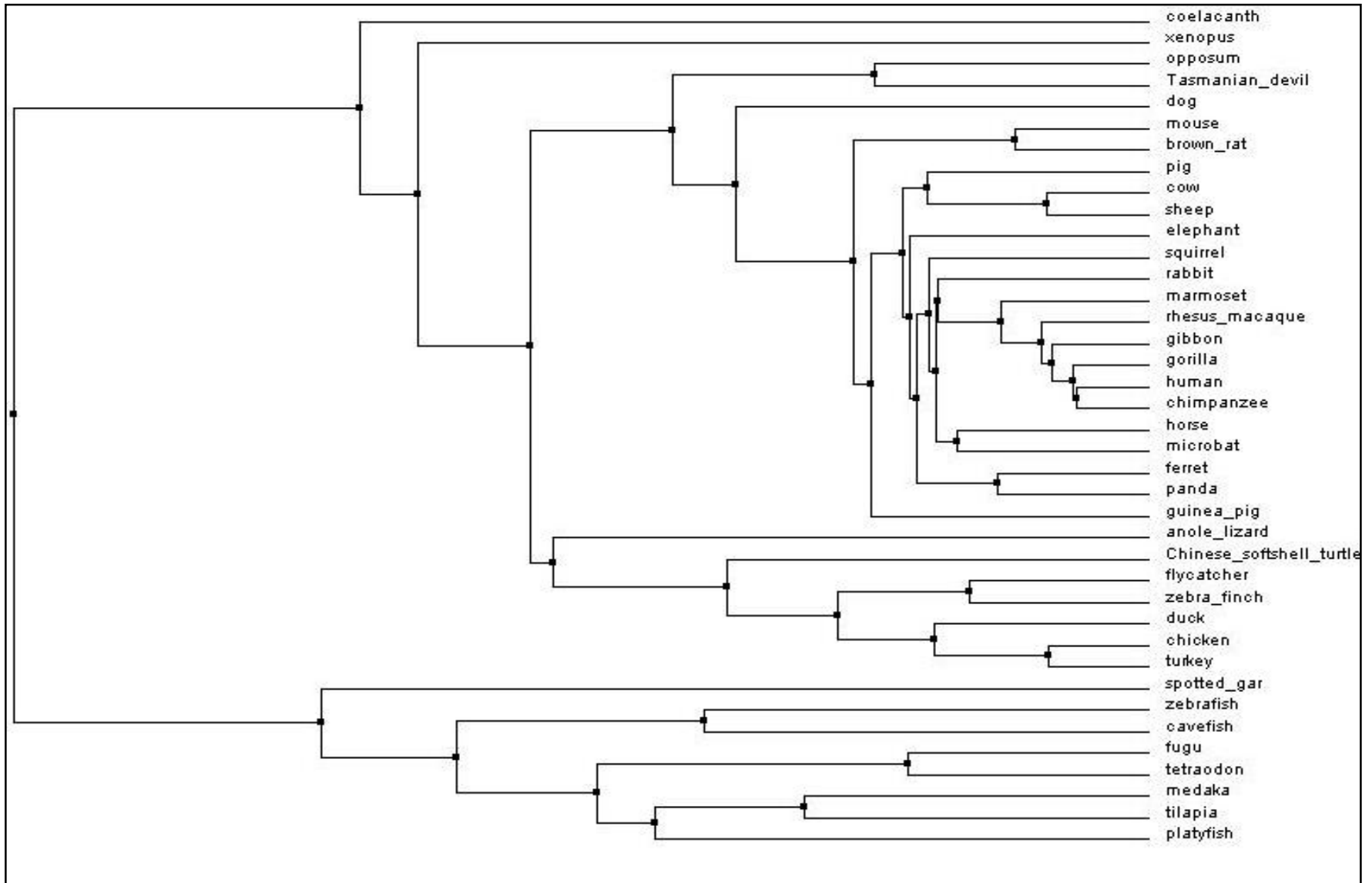
Biological Process



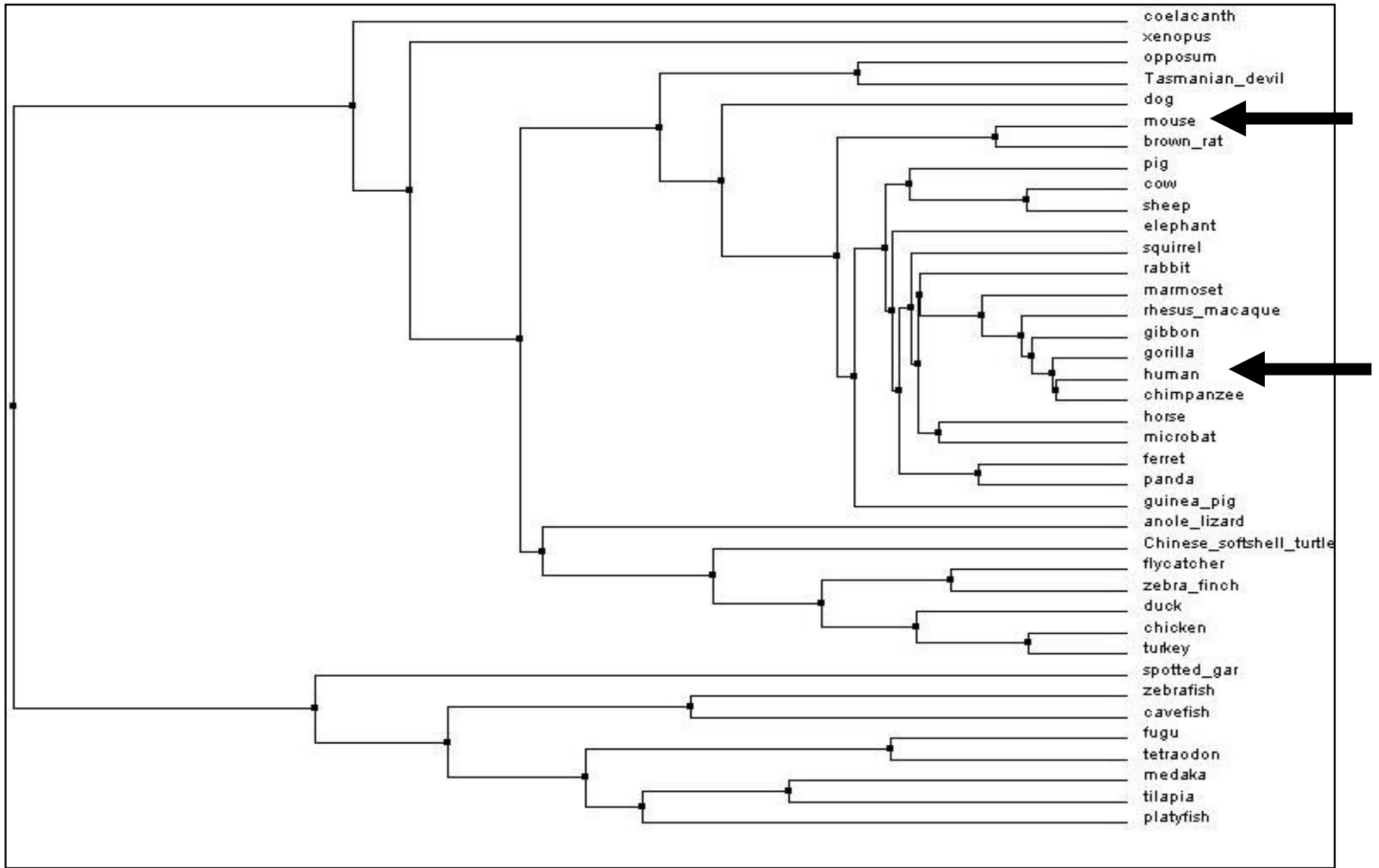
# How well conserved is RAG1?



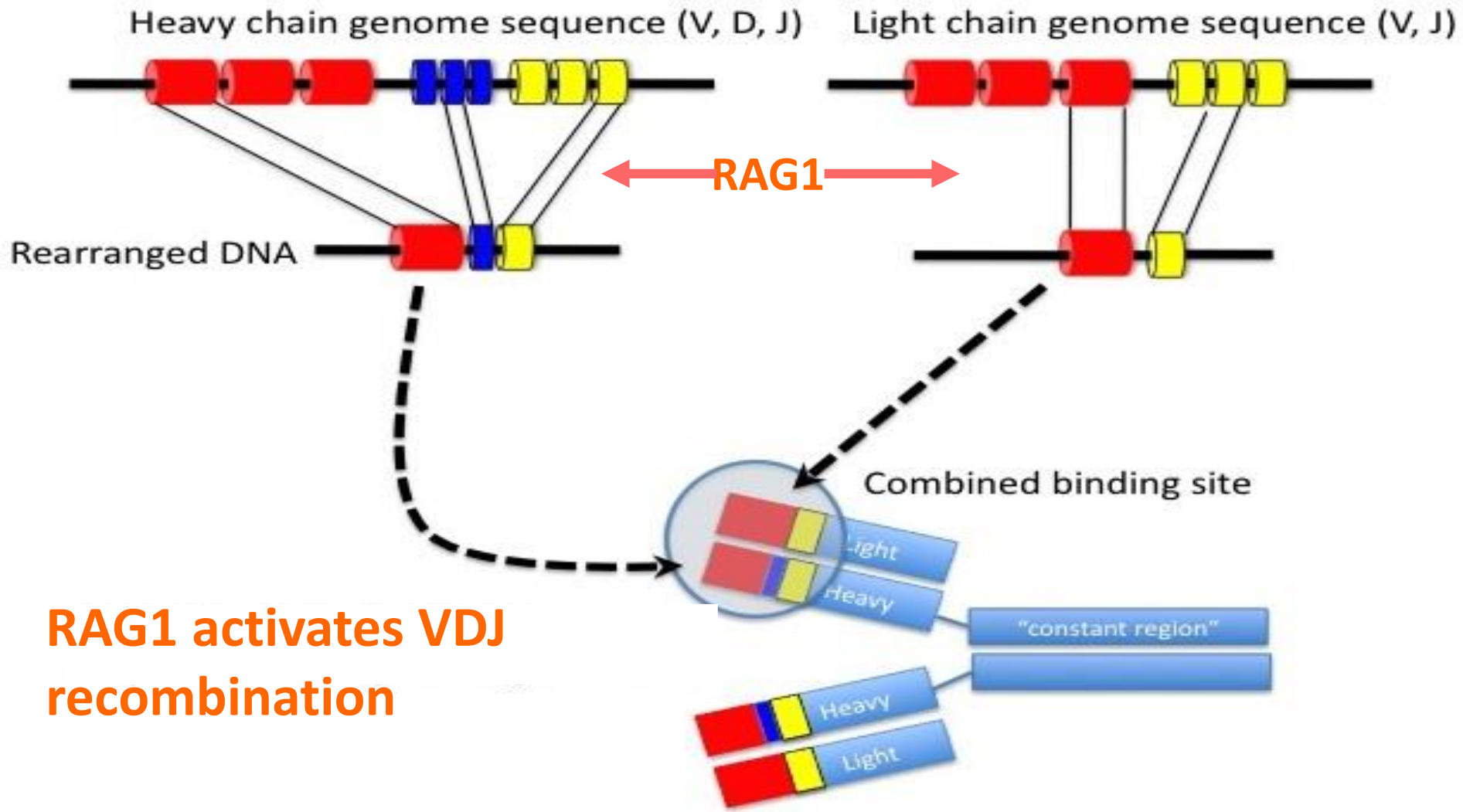
# RAG1 across species



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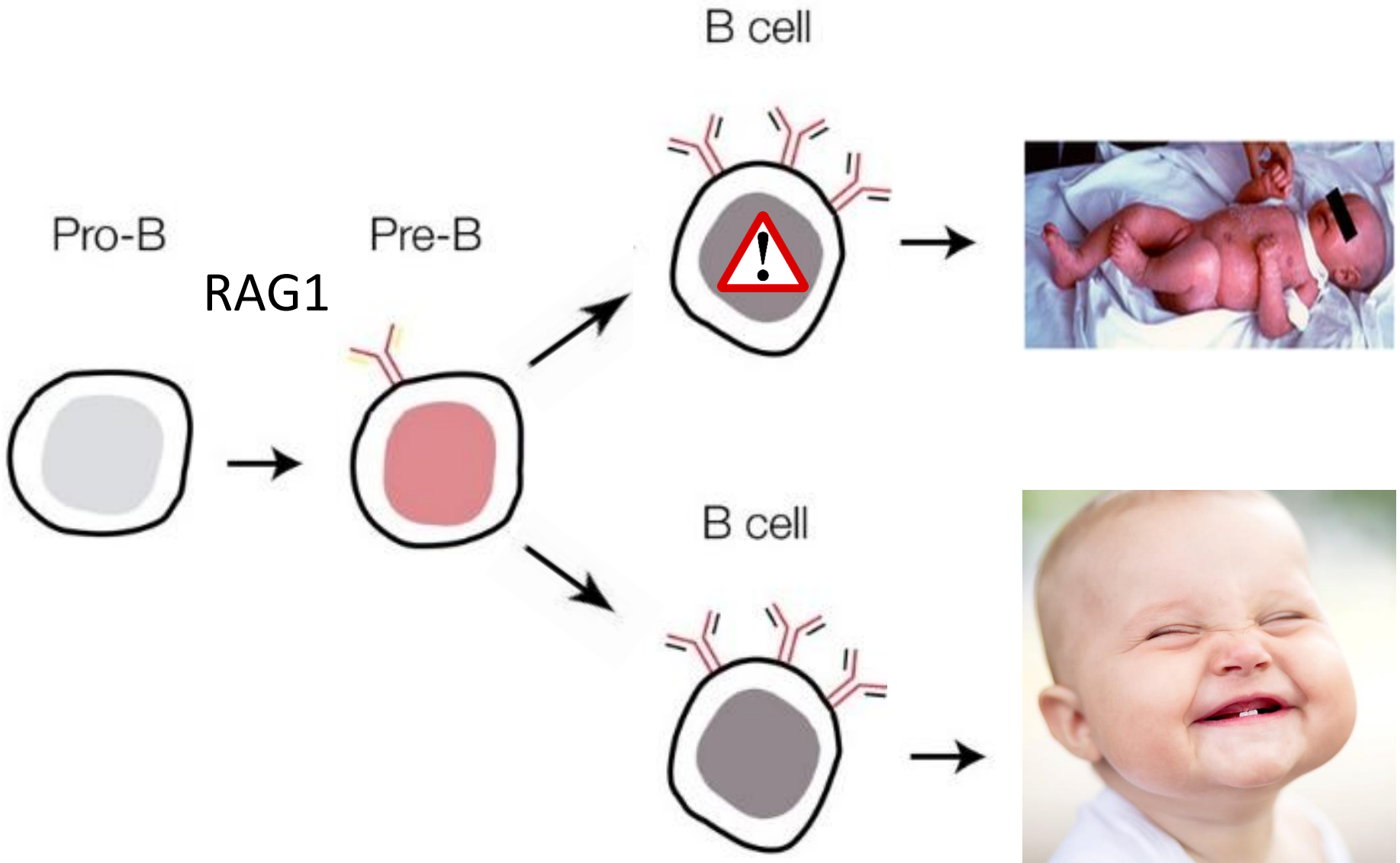


# RAG1 functions in DNA recombination

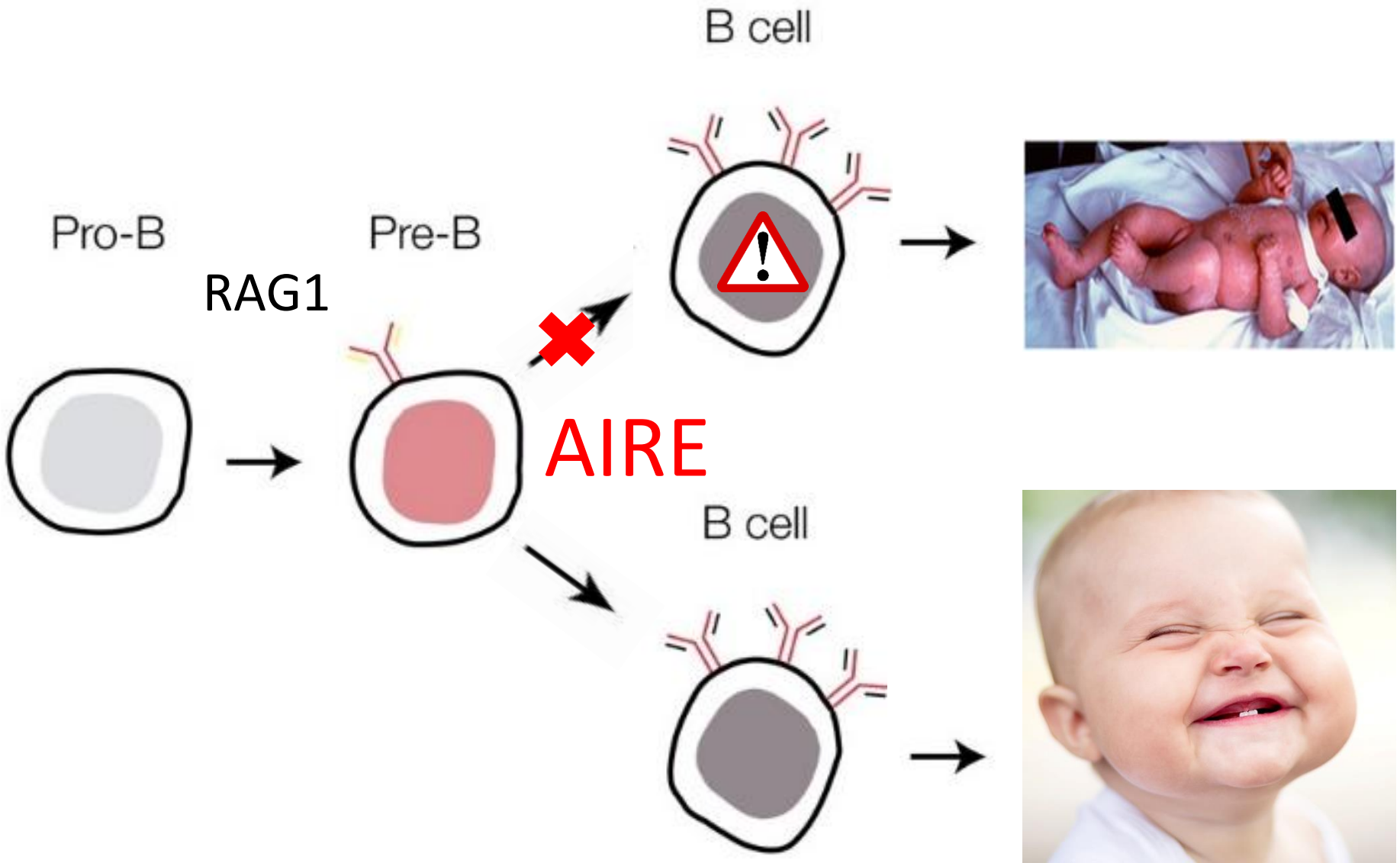




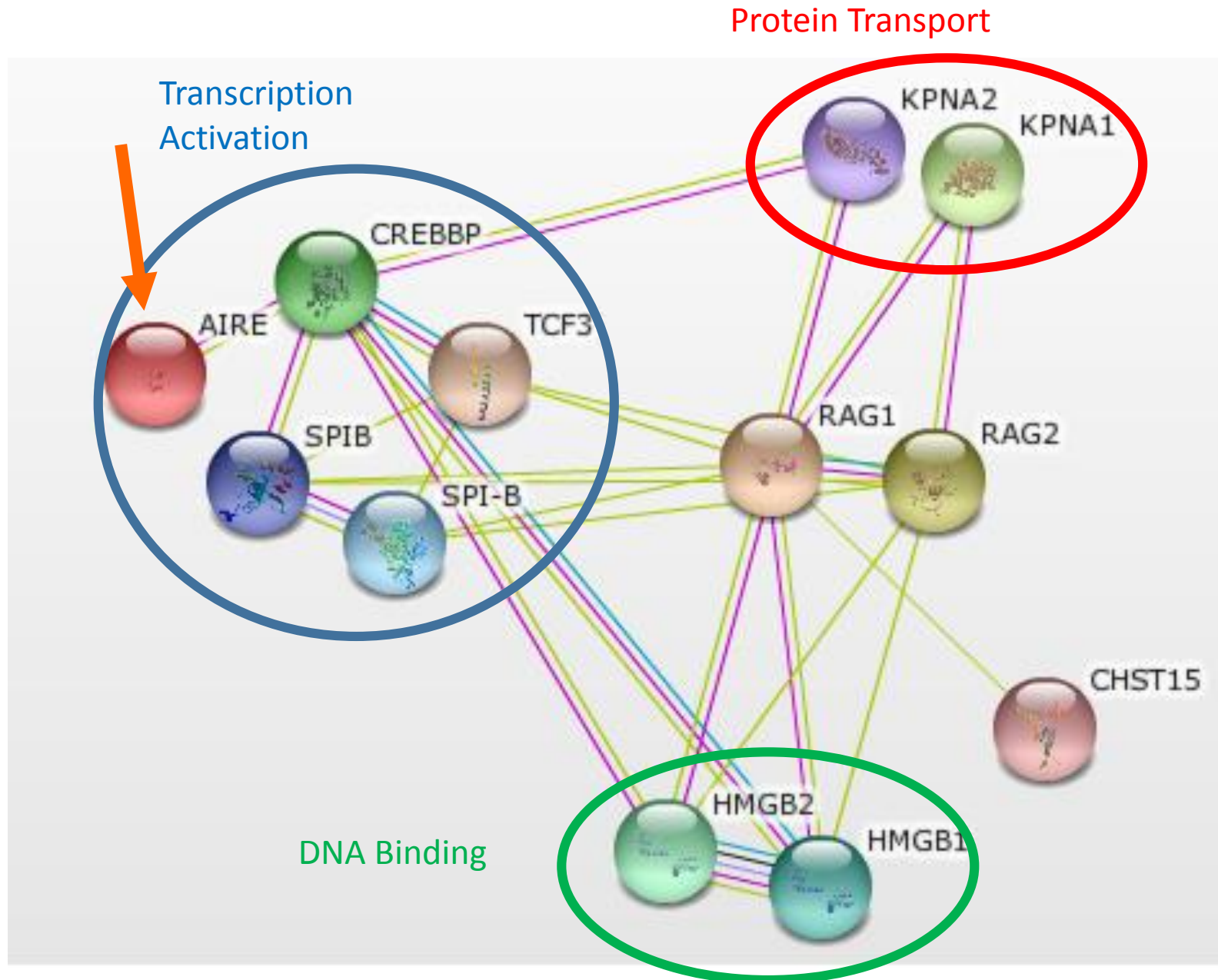
# How do organisms regulate autoimmunity?



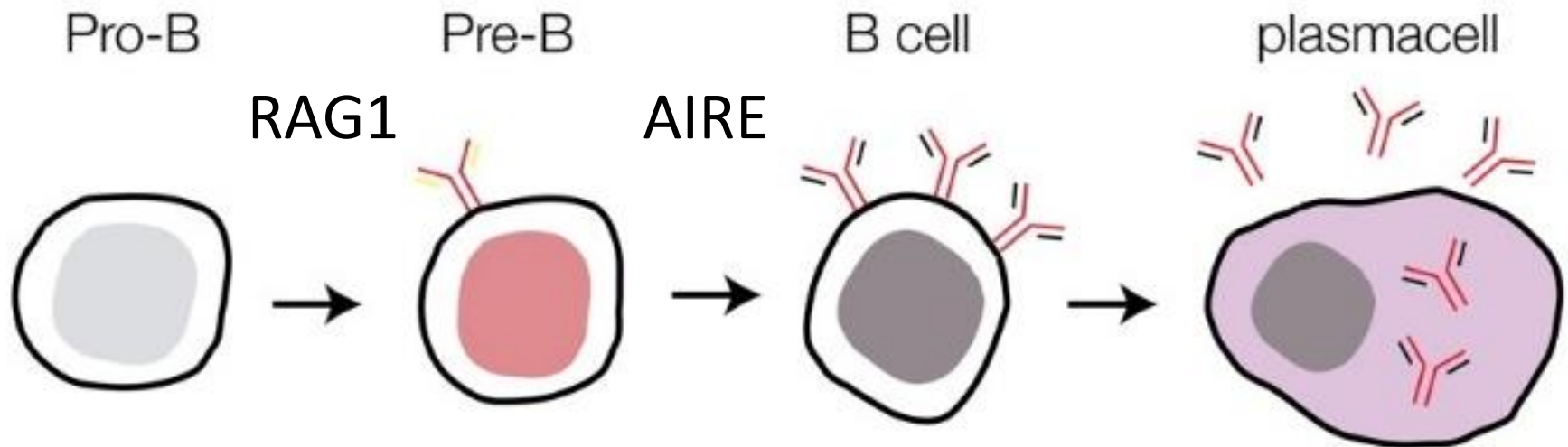
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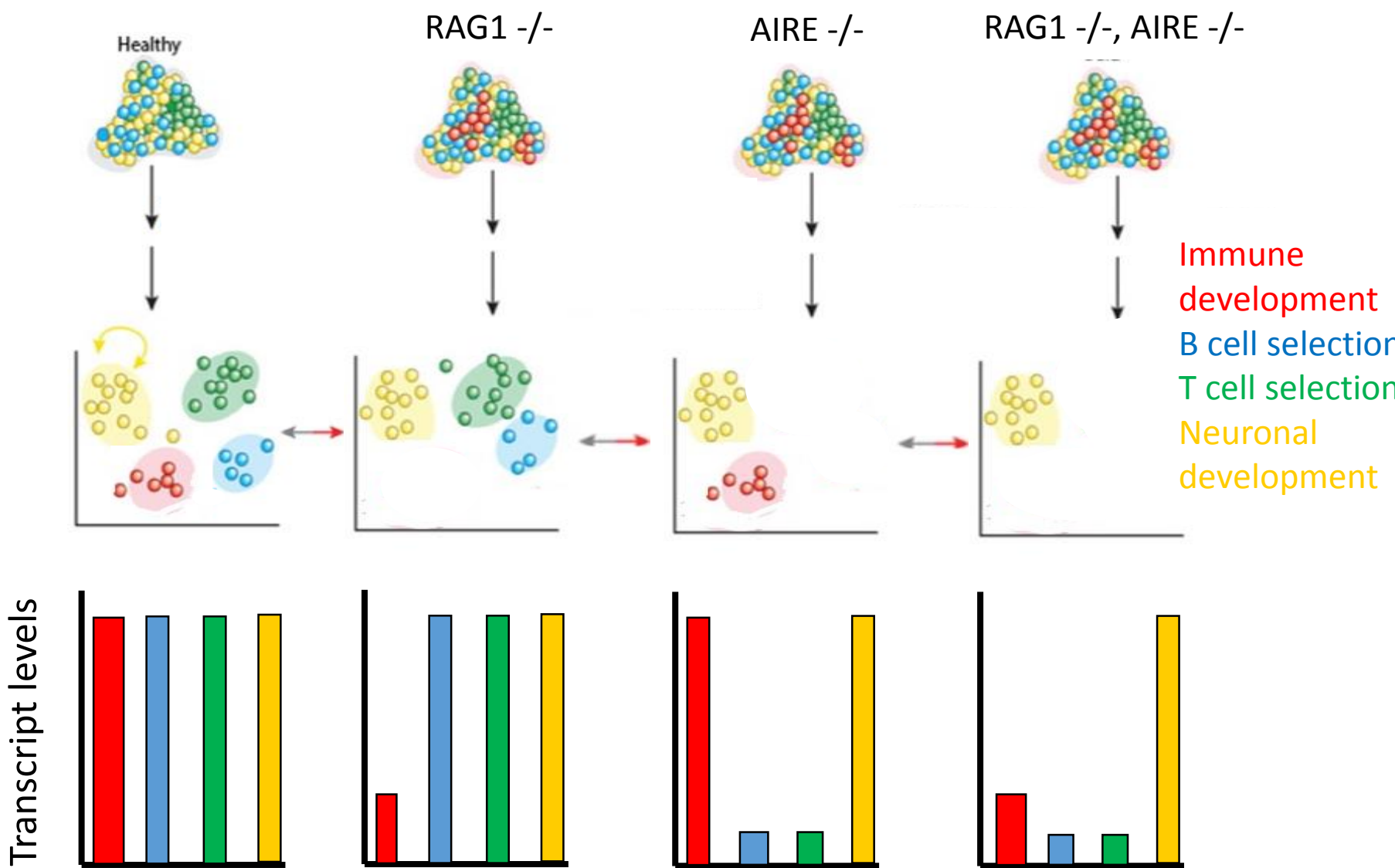
# RAG1 interacts with AIRE in immune cell development



Goal: To explore how AIRE and RAG1 contribute to immune cell development

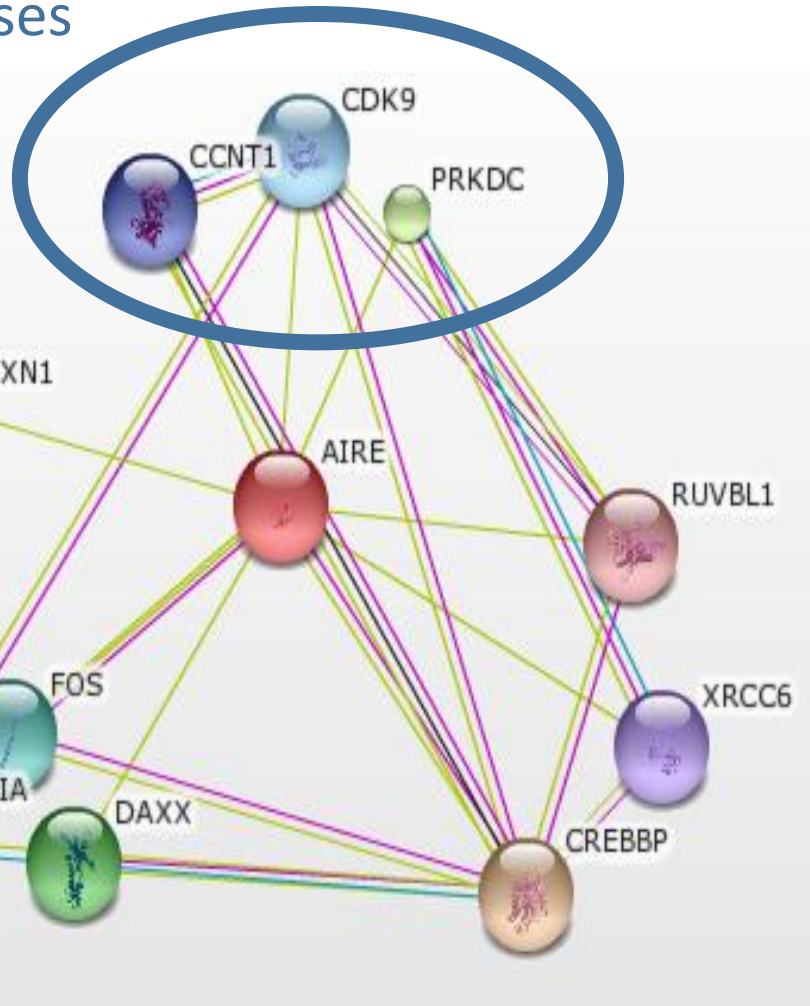


# Aim 1: Determine changes in gene expression in RAG1 and AIRE double mutants



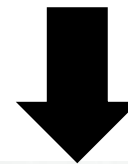
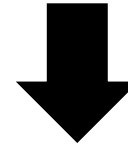
# Aim 2: Identify phosphorylation sites in AIRE that function in immune cell development

## Kinases



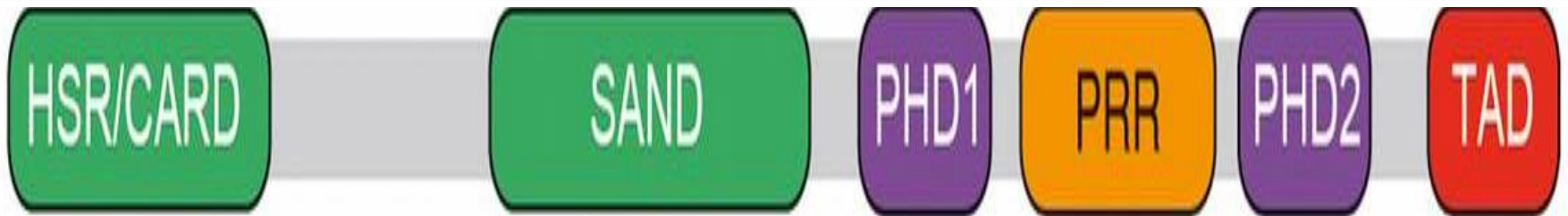
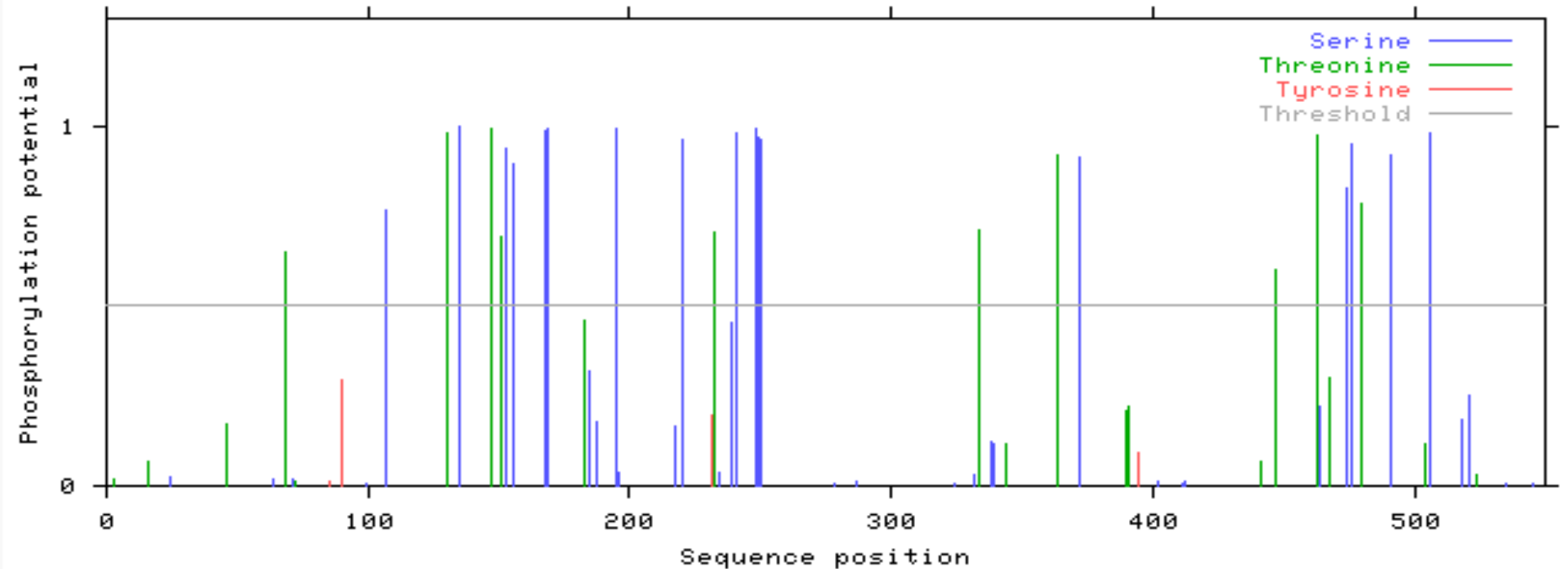
NetPhos 2.0 Server - prediction results

Technical University of Denmark



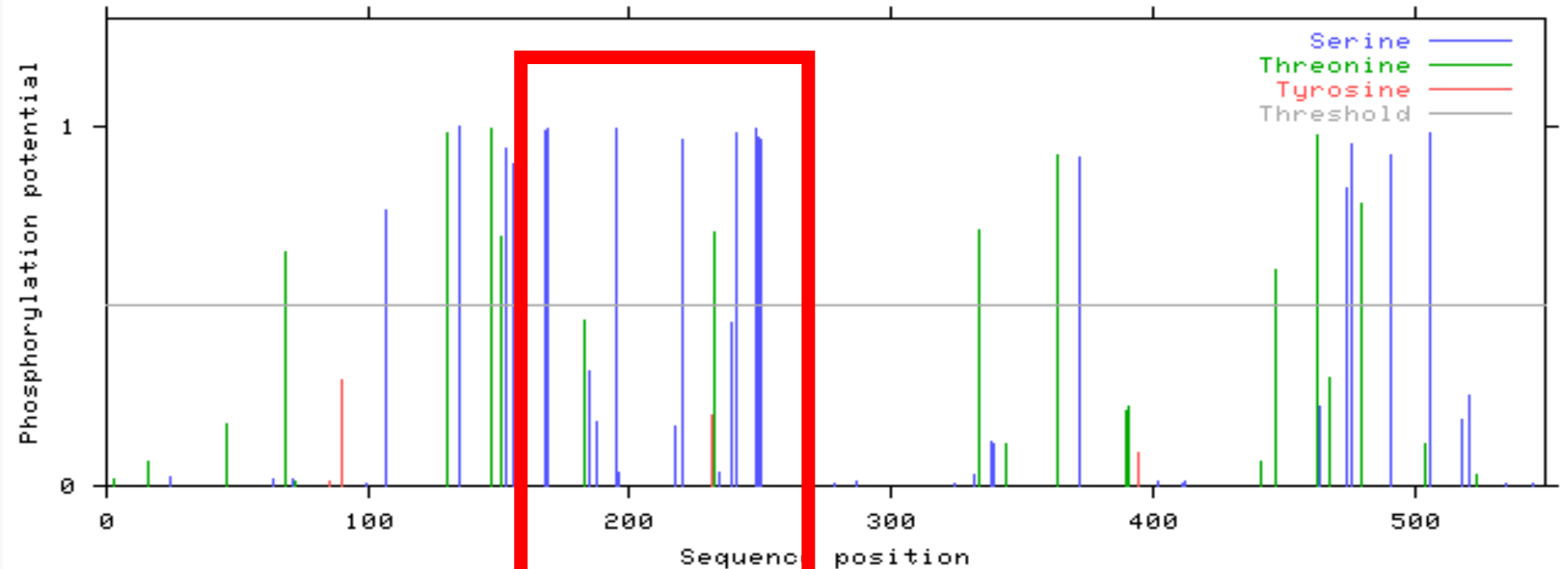
# Aim 2: Identify conserved phosphorylation sites in AIRE

NetPhos 2.0: predicted phosphorylation sites in Sequence



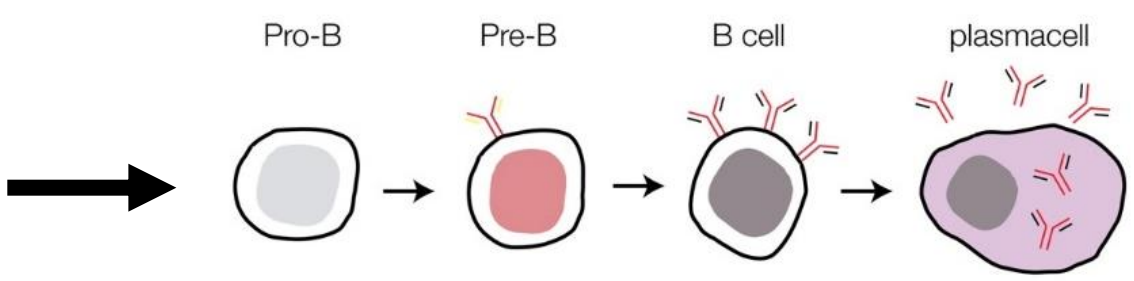
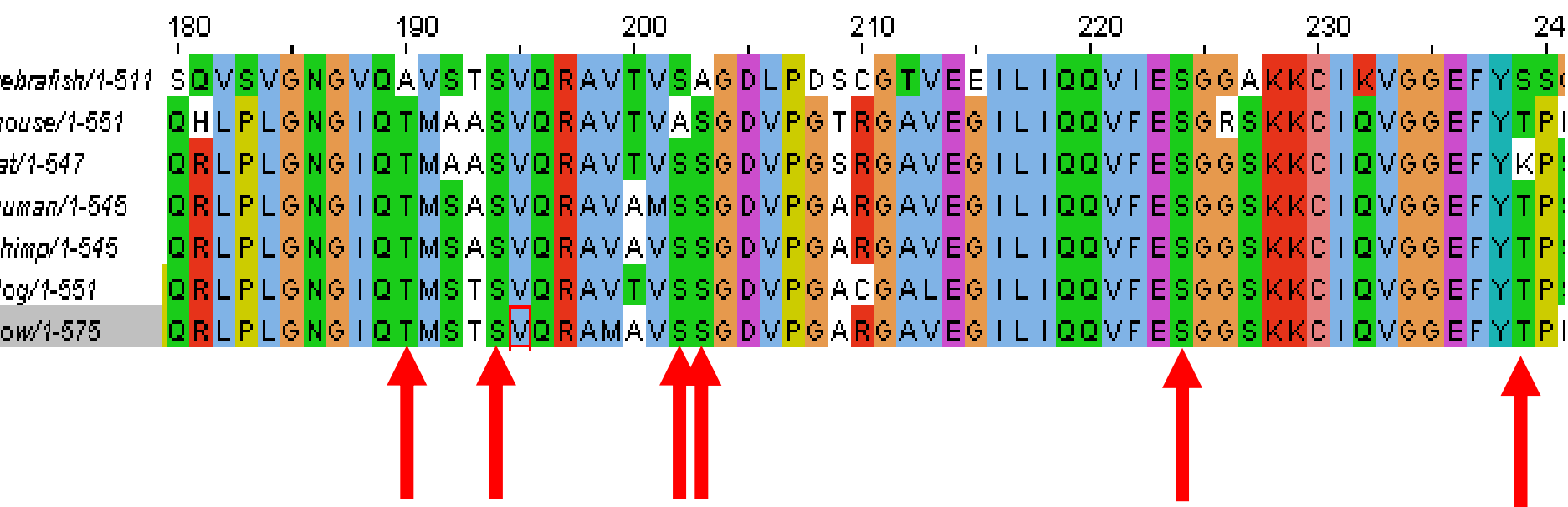
# Aim 2: Identify conserved phosphorylation sites in AIRE

NetPhos 2.0: predicted phosphorylation sites in Sequence

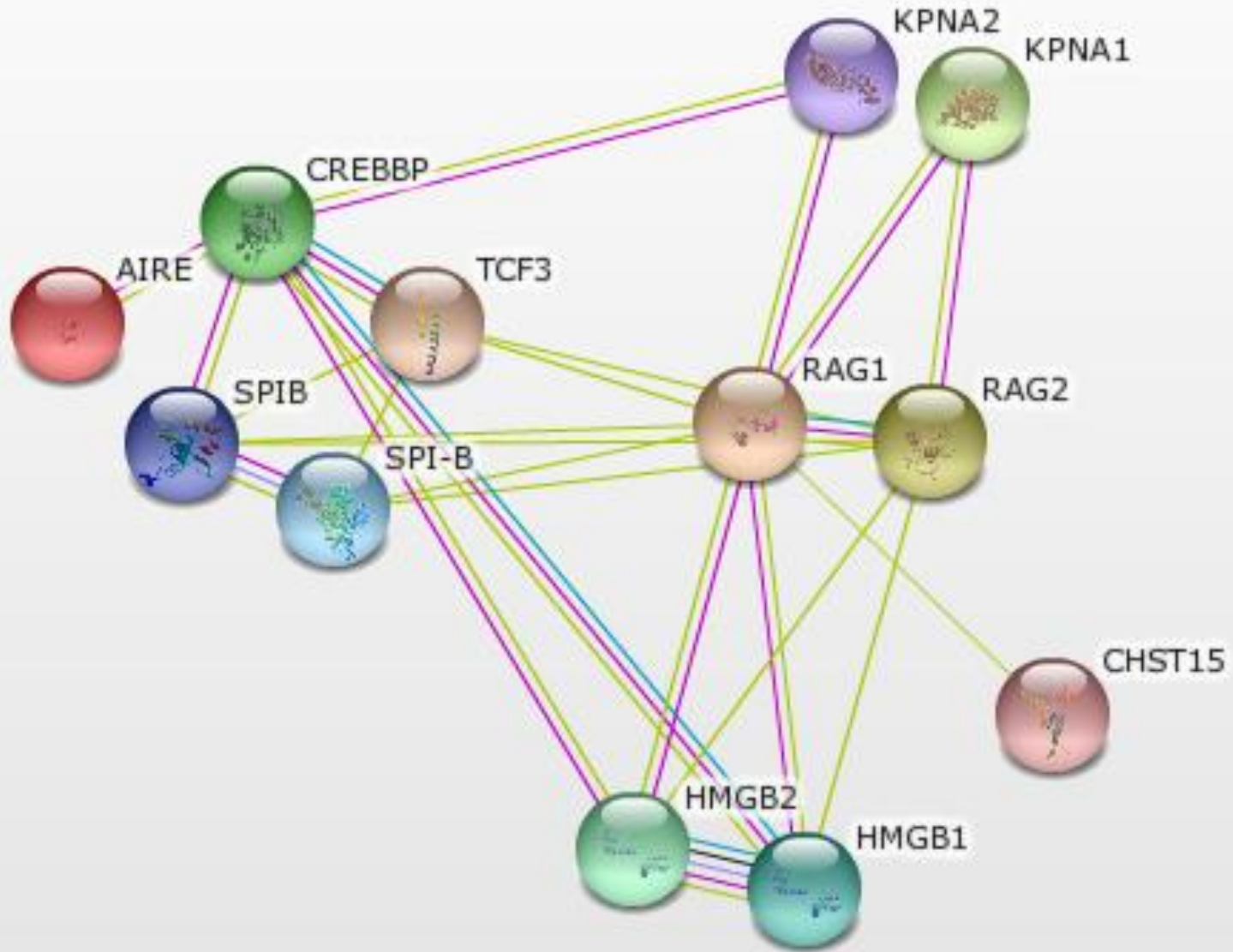




# Aim 2: AIRE has multiple conserved phosphorylation sites in its DNA binding domain

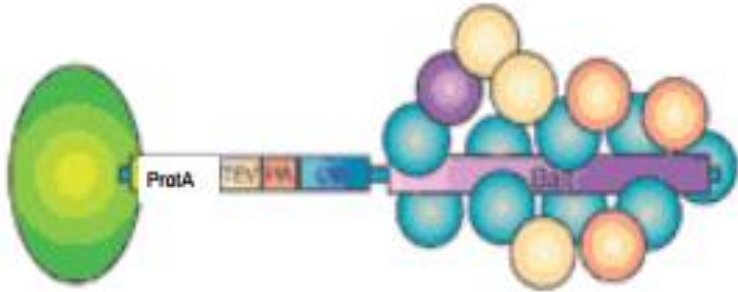


Aim 3: ID shared interacting proteins between AIRE and RAG1 important to immune cell development

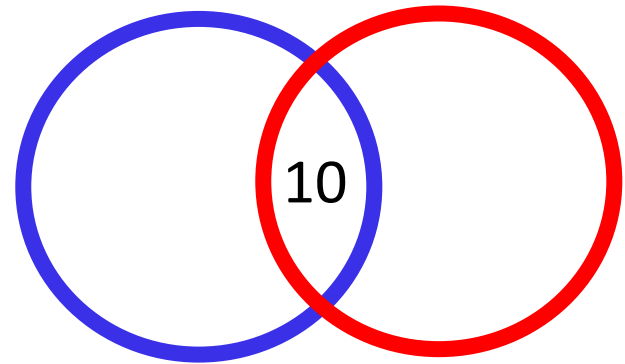


# Aim 3: ID shared interacting proteins between AIRE and RAG1 important to immune cell development

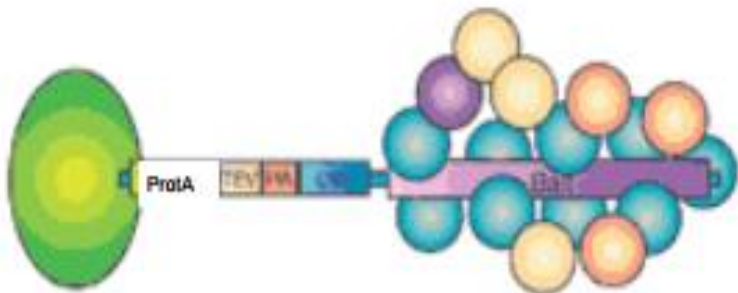
## RAG1



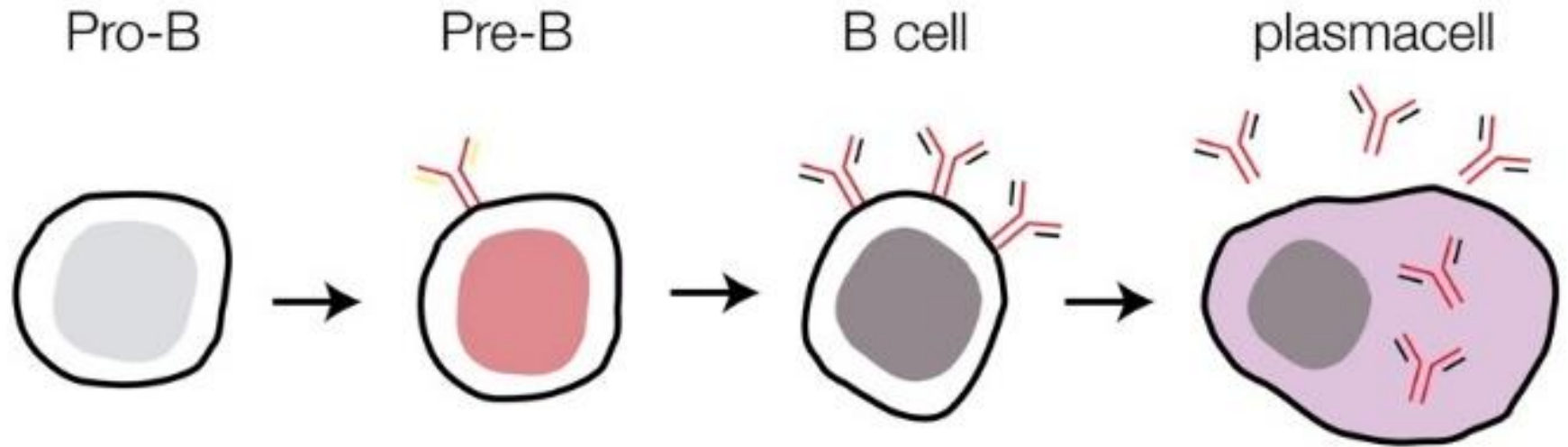
## Interacting Proteins



## AIRE



# Future Directions



# References

- 1) Marrella, V., Poliani, P.L., Sobacchi, C., Grassi, F., Villa, A. (2008). Of Omenn and mice. *Trends in Immunology* 29:133-140
- 2) Niehues, T., Perez-Becker, R., Schuetz, C. (2010). More than just SCID—The phenotypic range of combined immunodeficiencies associated with mutations in the recombinase activating genes (RAG) 1 and 2. *Clinical Immunology*. 135:183-192
- 3) Villa, A. (2011). Omenn Syndrome: inflammation and autoimmunity. *J Transl med*. 9(suppl2): 15
- 4) Owen, J., Punt, J., Stranford, S., Jones, P., Kuby, J. (2013). *Kuby Immunology* (7th ed). New York : W.H. Freeman and Company
- 5) Online Mendelian Inheritance in Man, OMIM (TM). Johns Hopkins University, Baltimore, MD. RAG1: {179615}. Last updated: {11/8/2014}.
- 6) Geha, Raif; Notarangelo, Luigi (2012). *Case Studies in Immunology: A Clinical Companion* (6th ed.). Garland Science.
- 7) Gomez, L., Le Deist, F., Blanche, S., Cavazzana-Calvo, M., Griscelli, C., Fischer, A. (1995) Treatment of Omenn Syndrome by bone marrow transplantation. *The Journal of Pediatrics*. 1:76-81
- 8) van Til NP, Sarwari R, Visser TP, Hauer J, Lagresle-Peyrou C, van der Velden G, et al. Recombination-activating gene 1 (Rag1)-deficient mice with severe combined immunodeficiency treated with lentiviral gene therapy demonstrate autoimmune Omenn-like syndrome. *J Allergy Clin Immunol* 2014;133: 1116-23.
- 9) Schwartz, R.A. (2014, Nov 7). Omenn Syndrome. *Medscape*. Retrieved 2/18/15 from <http://emedicine.medscape.com/article/887687-overview#a0101>

## Image References

- 1) <http://beyondessential.com/healthy-immune-system/>
- 2) [http://en.wikipedia.org/wiki/Omenn\\_syndrome#mediaviewer/File:Omenn\\_syndrome.png](http://en.wikipedia.org/wiki/Omenn_syndrome#mediaviewer/File:Omenn_syndrome.png)
- 3) <http://showyourhope.com/2012/11/04/>
- 4) <http://micro.magnet.fsu.edu/cells/nucleus/nucleus.html>
- 5) [http://www.cryst.bbk.ac.uk/PPS2/projects/jennings/pps\\_diss.htm](http://www.cryst.bbk.ac.uk/PPS2/projects/jennings/pps_diss.htm)
- 6) [http://nfs.unipv.it/nfs/minf/dispense/immunology/lectures/files/bcell\\_tcell\\_development.html](http://nfs.unipv.it/nfs/minf/dispense/immunology/lectures/files/bcell_tcell_development.html)
- 7) <https://ittakes30.wordpress.com/2011/08/11/sequencing-the-immune-response/>
- 8) <http://fcsanahuac.com/category/temas-selectos-de-ciencias-de-la-salud/>
- 9) <http://pixshark.com/bone-marrow-transplant-needle.htm>
- 10) <http://medicareunder65.com/esrd-and-medicare/medicare-for-kidney-transplant-recipients/immunosuppressive-drug-therapy/>

QUESTIONS??