

INTRODUCTION

Inflammasomes are multiproteic cytosolic complexes involved in regulating inflammation pathways in response to Damage Associated Molecular Patterns (DAMPs) and Pathogen Associated Molecular Patterns (PAMPs) [1].

Although many different protein families can assemble inflammasomes, as pyrin or Interferon-inducible protein absent in melanoma 2 (AIM2), nucleotide binding oligomerization domain leucine-rich-repeat-containing proteins (NLRs) are the best studied molecular components of inflammasomes in mammalian innate immune system. [1] [2]. Furthermore, some NLR genes are involved in regulation of embryogenesis, hematopoiesis, fertilization; and can also control many immune-related components (MHCs) and regulatory pathways such as NF- κ B, or MAPK. [2].

Classically, it has been established the phylogenetic relationships of NLR genes based on their biochemical composition and structure, defining three main subfamilies: NOD, NAIP/IPAF and NLRP. [3]

In human NLR repertoire, these families have suffered significant expansions.

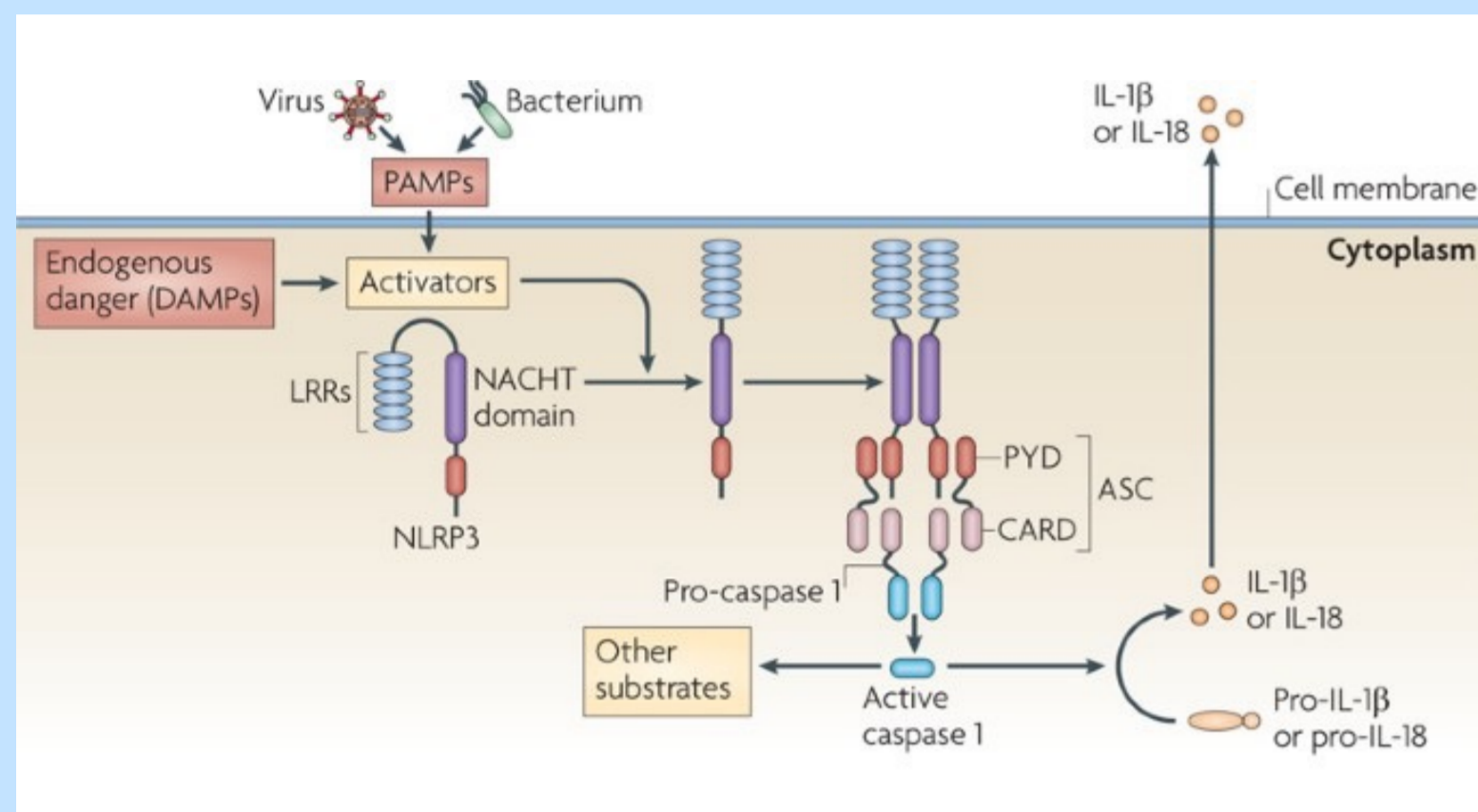


Figure 1: Simplified structure of NLRP inflammasome. Extracted from Tschopp, J., Schroder, K. (2010). NLRP3 inflammasome activation: the convergence of multiple signalling pathways on ROS production?. *Nature Reviews Immunology* 10, 210–215.

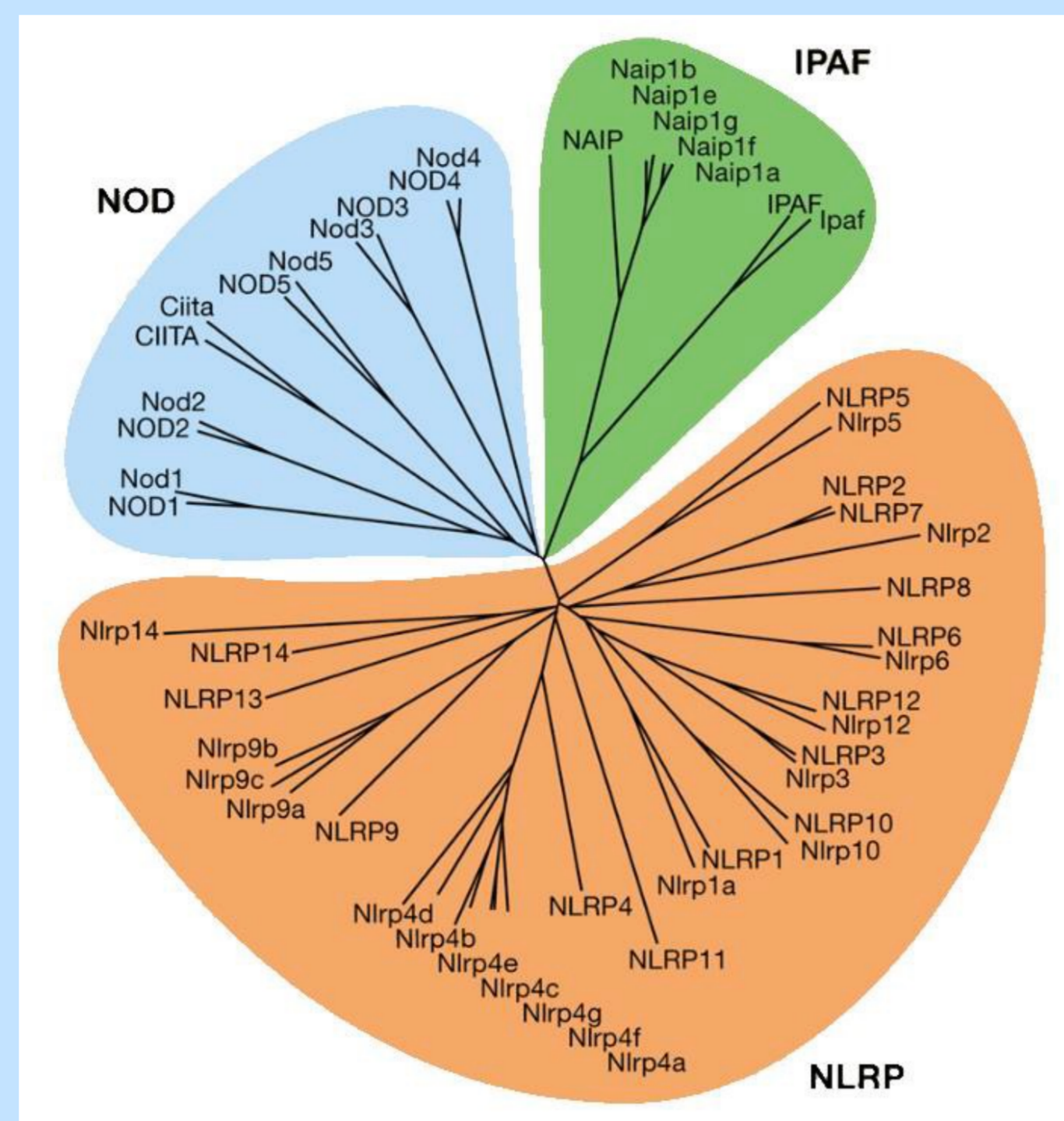


Figure 2: Classical Phylogeny of NLR genes. Extracted from Schroder K, Tschopp J. (2010). The NLR gene family: from discovery to present day. *Nature Reviews Immunology*, 23 (10), 635-654.

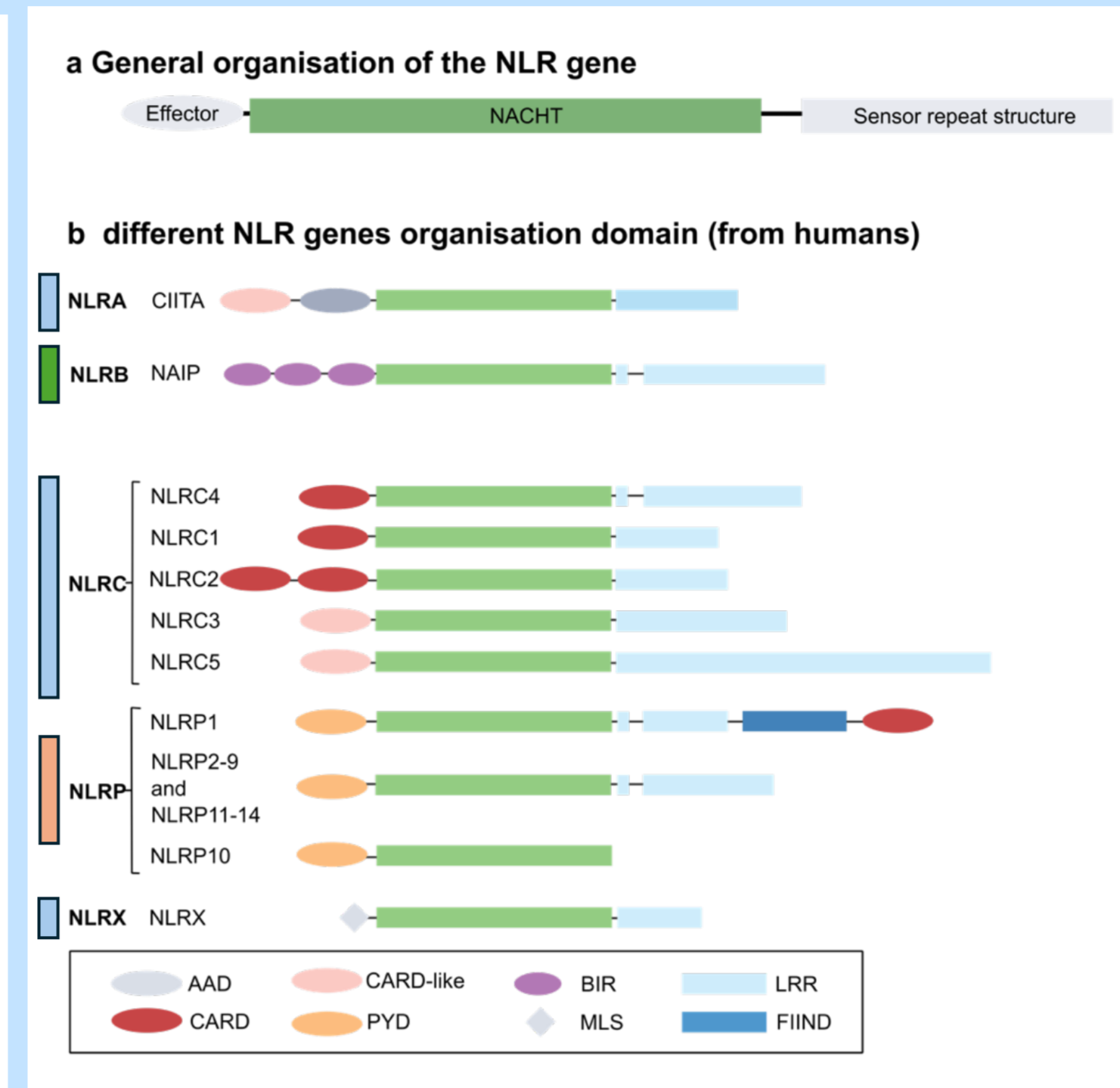


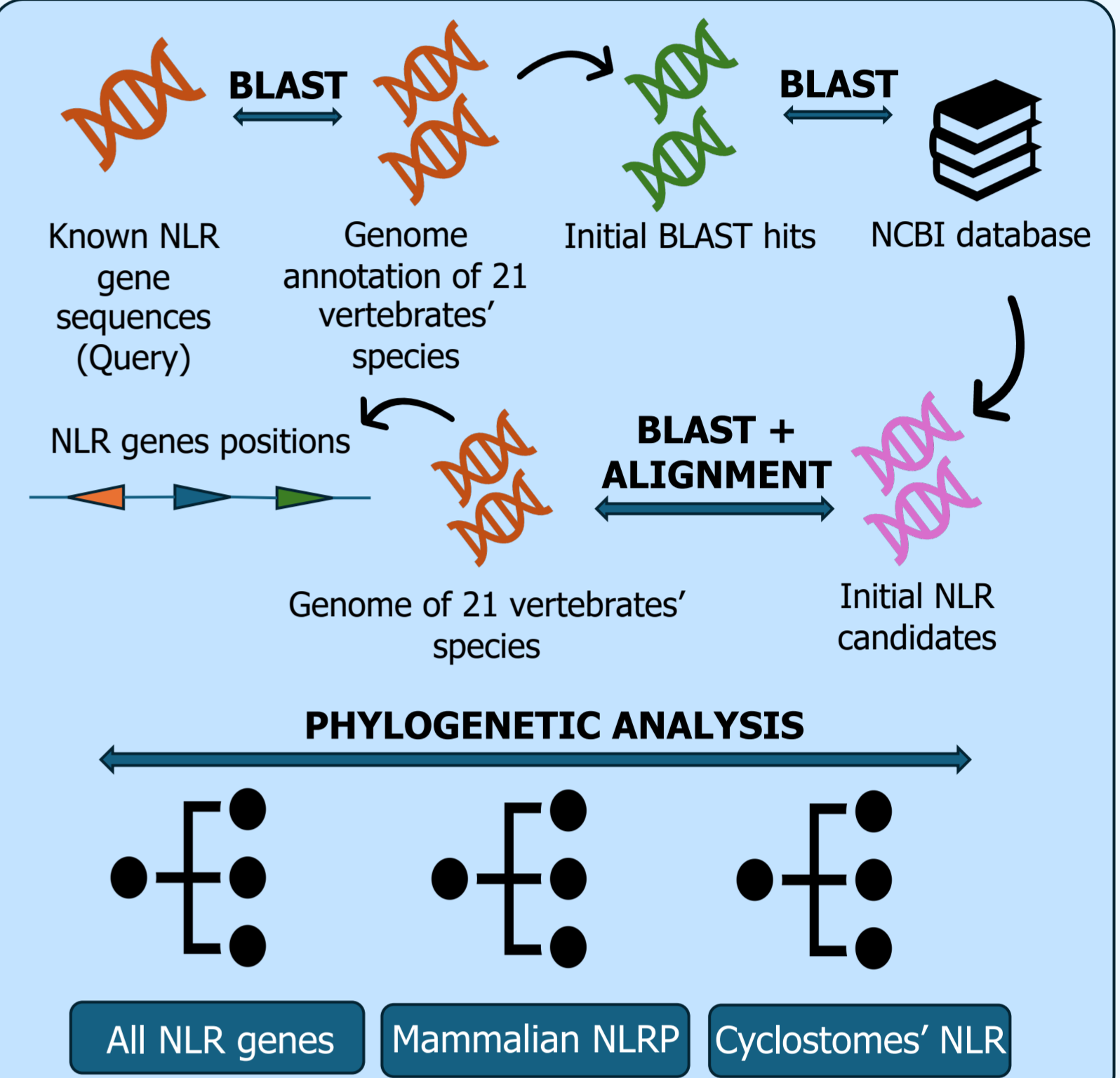
Figure 3: General structure of NLR genes. Extracted from Chou, W. C., Jha, S., Linhoff, M. W., & Ting, J. P. (2023). The NLR gene family: from discovery to present day. *Nature Reviews Immunology*, 23 (10), 635-654.

OBJETIVE

Gene members of the NLR family are present across all metazoan tree of life, however the NLR repertoires in most non-model organisms are poorly studied. [4].

In this work we pretend to establish a comprehensive comparative analysis of NLR gene repertoires in vertebrates to know the evolution and diversification of this important gene family.

MATERIALS AND METHODS



RESULTS

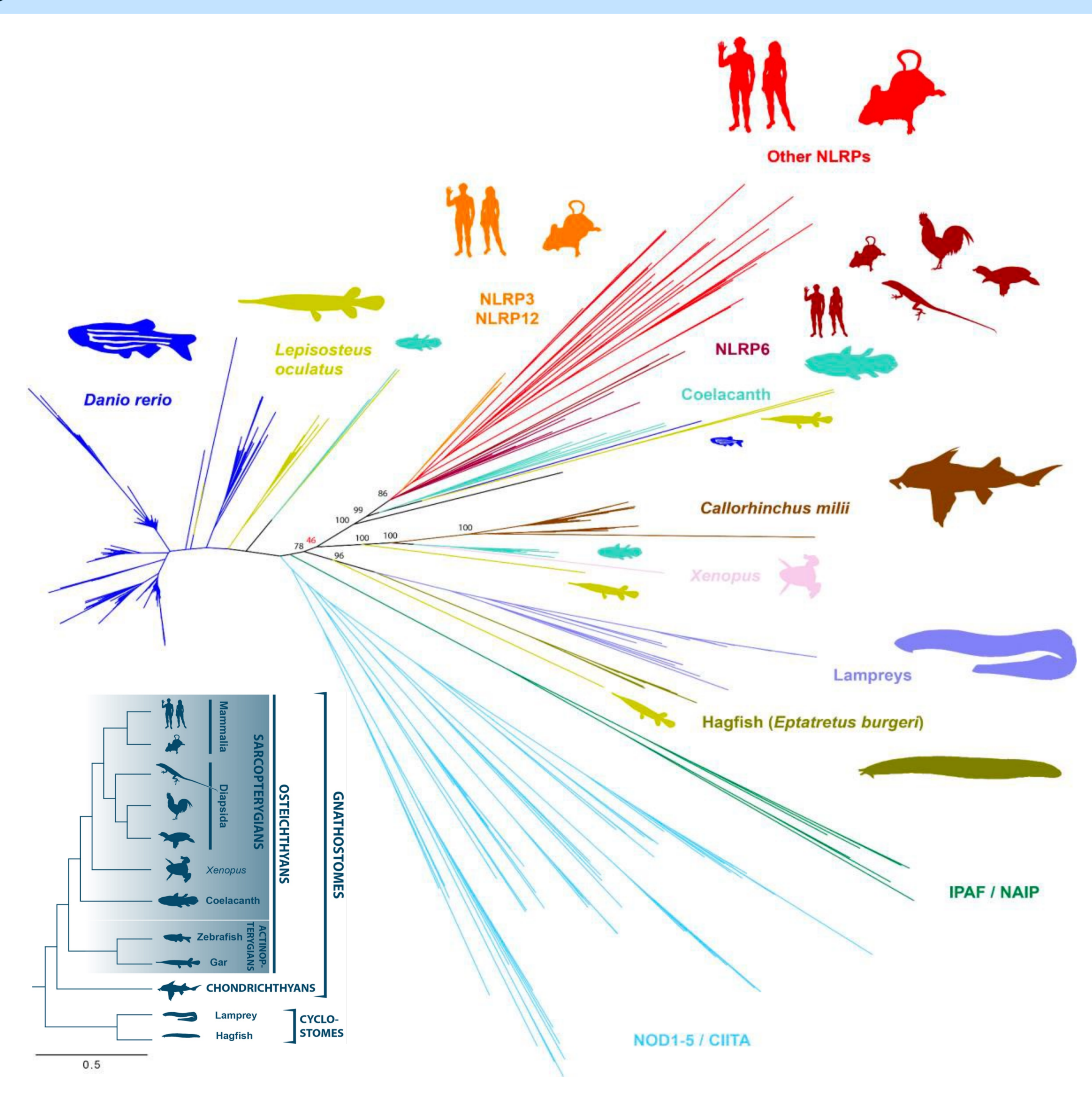


Figure 5: Rooted maximum likelihood phylogenetic tree depicting relationships between NLRs from the subfamilies NLRB, NLRC, NLRA and NLRX, and the sequences that grouped close to them. The numbers on the nodes correspond to the ultrafast nod support bootstrap value and the line below the tree marks the number of substitutions per site. All of groups were recovered with the apparition of a new potential subfamily close to the NLRC3 subgroup.

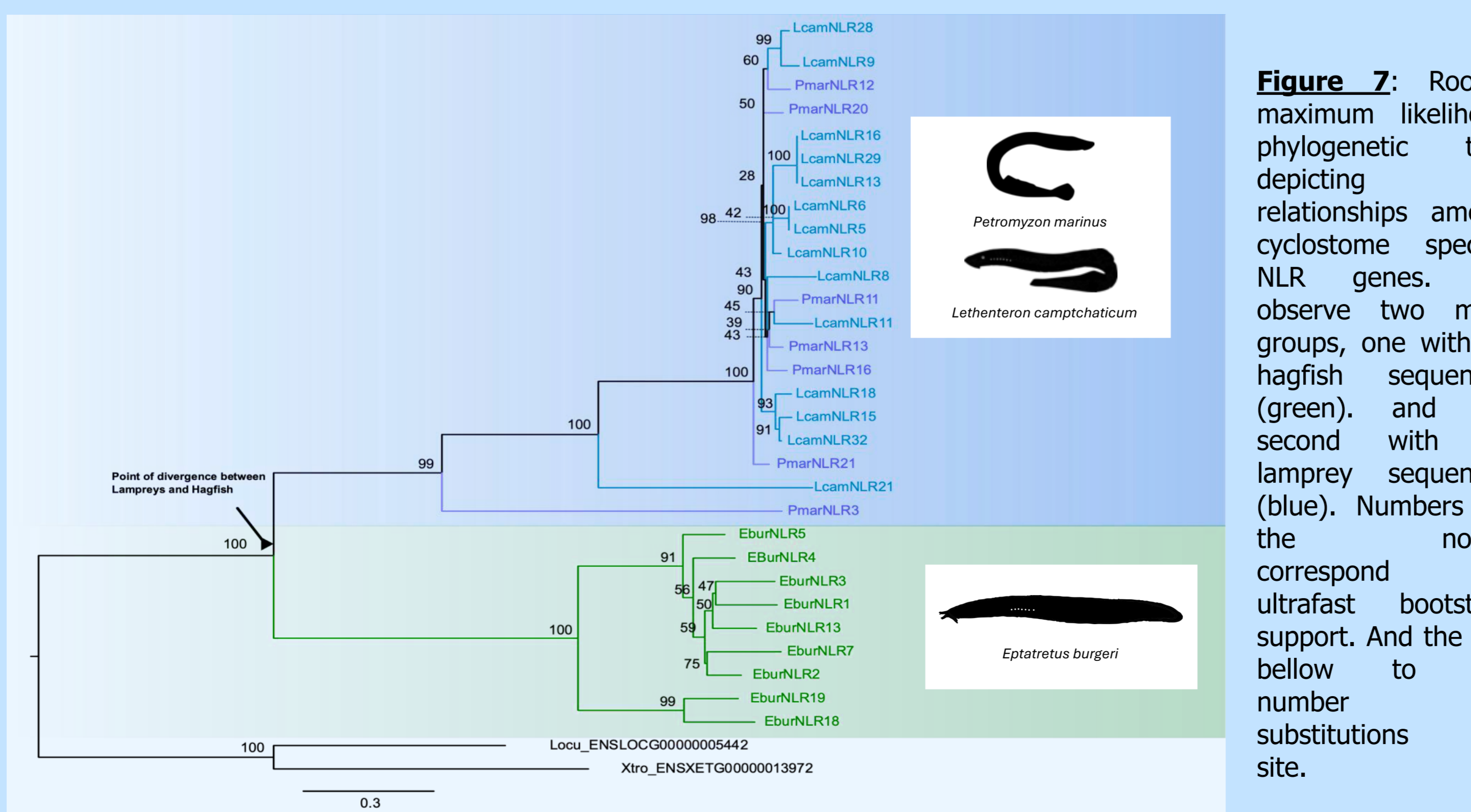


Figure 7: Rooted maximum likelihood phylogenetic tree depicting relationships among cyclostome specific NLR genes. we observe two main groups, one with all hagfish sequences (green), and the second with all lamprey sequences (blue). Numbers on the nodes correspond to ultrafast bootstrap support. And the like below to the number of substitutions per site.

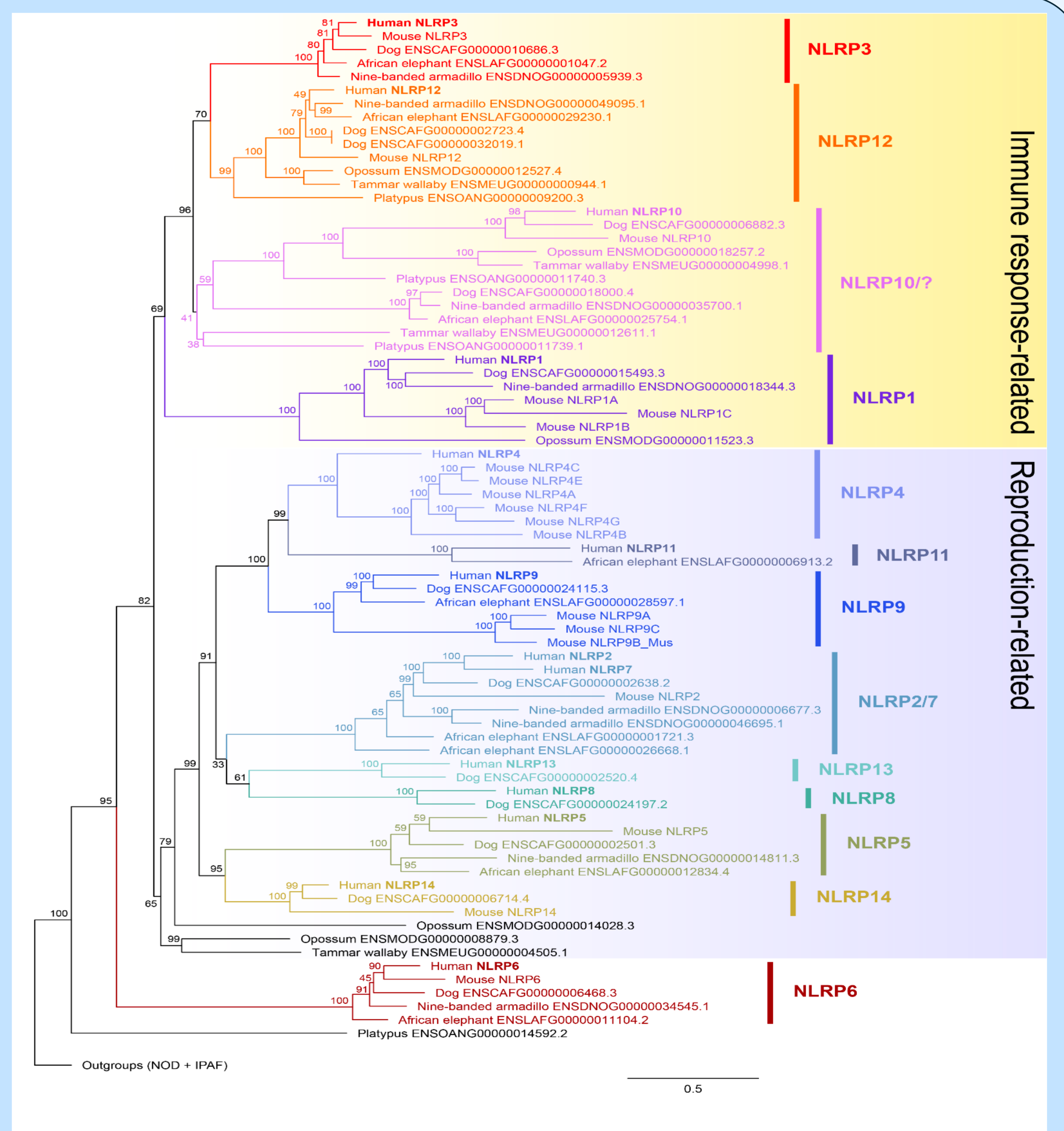


Figure 6: Rooted Maximum likelihood phylogenetic tree depicting relationships among mammalian NLRP genes. We observe three main groups composed of NLRP1, 3, 10 and 12 (innate immune response role); NLRP2, 4, 5, 7, 8, 9, 11, 13 and 14 (Reproduction related role); and NLRP6. Numbers on the nodes correspond to maximum-likelihood ultrafast bootstrap support. The bar represents the number of amino acid substitutions per site.

CONCLUSIONS

- 1) Four NLR clades in vertebrates (one novel NLR subfamily)
- 2) Specific lineage expansions of NLR genes and convergent evolution of inflammasomes
- 3) NLRP inflammasomes only in mammals, associated to an expansion and divergence of NLRP genes
- 4) Novel functions of NLR genes acquired due to these expansions

BIBLIOGRAPHY

- [1] Broz, P., & Dixit, V. M. (2016). Inflammasomes: Mechanism of assembly, regulation and signalling. *Nature Reviews Immunology*, 16 (7), 407-420.
- [2] Chou, W. C., Jha, S., Linhoff, M. W., & Ting, J. P. (2023). The NLR gene family: from discovery to present day. *Nature Reviews Immunology*, 23 (10), 635-654.
- [3] Chou, W. C., Jha, S., Linhoff, M. W., & Ting, J. P. (2023). The NLR gene family: from discovery to present day. *Nature Reviews Immunology*, 23 (10), 635-654.
- [4] Ting, J. P.-Y., Lovering, R. C., Alnemri, E. S., Bertin, J., Boss, J. M., Davis, B. K., Flavell, R. A., Girardin, S. E., Godzik, A., Harton, J. A., Hoffman, H. M., Hugot, J.-P., Inohara, N., Mackenzie, A., Maltais, L. J., Nunez, G., Ogura, Y., Otten, L. A., Philpott, D., ... Ward, P. A. (2008). The NLR Gene Family: A Standard Nomenclature. *Immunity*, 28 (3), 285-287.