

Innate Immunosensors, the Toll like receptors explored in Yak and Mithun

‘Toll like receptors’ are germline-encoded, evolutionarily conserved, innate immune receptors, which not only eliminates the infective pathogens but also strengthens the more specific host acquired immunity. Till now 13 TLRs have been identified till date, of which 10 have been fully characterized in humans, mice and few domestic animals. Binding of pathogen activates TLR family members, which ultimately lead to a wide variety of responses from different cell types ranging from chemokine and cytokine production, increases in antigen presenting capacity, initiation of cell (having immunological properties) proliferation and antimicrobial factor production.



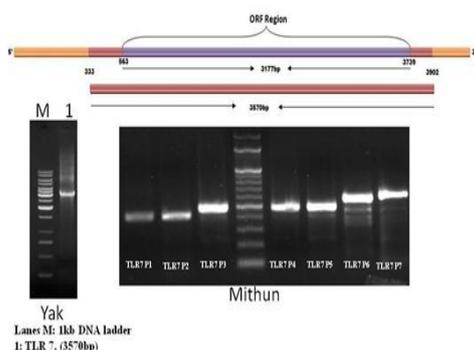
At Indian Veterinary Research Institute (IVRI), under the NAIP project, the TLR genes playing important role in the identification and processing of viral and bacterial agents have been recognized in Yak and Mithun. These animals sometime suffer from the common diseases of other animal species. However, information on immune receptors (TLRs) of these animal species is not available which are known to play important role in the species resistance or susceptibility to diseases.

Mithun (*Bos frontalis*) is a unique ruminant found in the hill regions of north-east India, Myanmar, Bhutan, Bangladesh, China and Malaysia. It is well adapted to steep jungles at an elevation that ranges from 300 m to 3,000 m above sea level (masl) and plays an important role in the economic, social, cultural and religious life of the tribal people inhabiting the region. The mithun is a semiwild animal and its breeding selection is not controlled by humans. This is an under-utilised animal and it has great potential for human sustenance. We characterized the innate immune repertoire of these animals. Yak (*Bos grunniens*) is a long-haired bovid found throughout the Himalayan region of south Central

Asia, the Tibetan Plateau and as far north as Mongolia and Russia. Most yaks are domesticated.

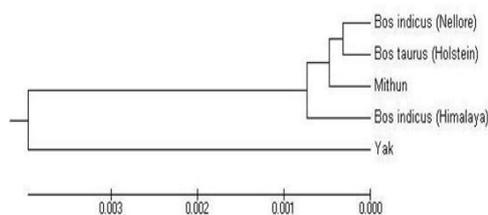
In India, Yak and Mithun, both play important role in the life of high altitude living farmers mostly in North East of India and Himalayan foot hills. The farmers depend on these animals for hair, meat, milk and transportation. TLR7 genes, which recognize ssRNA viruses, and initiates signal transduction of genes involved in innate and adaptive immunity with production of pro-inflammatory cytokines were explored for the first time. Nucleotide and amino acid sequence analysis of TLR7 gene revealed point mutations at 25 nucleotide positions with corresponding 15 amino acid changes in Yak, while changes at 6 nucleotide positions with no changes in corresponding amino acid positions in Mithun. SMART analysis of Yak and Mithun protein domain architecture revealed Toll-Interleukin I receptor (TIR), Leucine rich repeats (LRR) and signal peptide region. The variations in Yak mainly lie in the LRR region. The findings shows existence of genetic variability in TLR7 gene of Yak, in particular the LRR region, which may plays important role in the pathogen recognition. Homology modelling revealed horse shoe shaped structure with an additional alpha helix in Yak, which was not detected in *Bos indicus*. The results would improve our knowledge about genetics and immune system of these species of high altitude.

Analysis of TLR 7 gene of Mithun and Yak

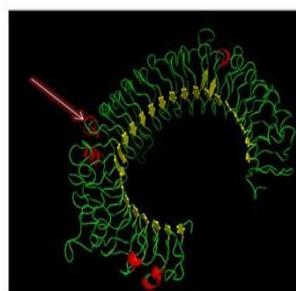


	Yak	Mithun	<i>Bos indicus</i> (Himalayan)	<i>Bos indicus</i> (Nellore)	<i>Bos taurus</i> (Holstein)	Ovine
Yak		99.2	99.2	99.2	99.3	97.8
Mithun	98.5		99.8	99.9	99.9	98.5
<i>Bos indicus</i> (Himalayan)	98.2	99.7		99.8	99.9	98.4
<i>Bos indicus</i> (Nellore)	98.4	99.9	99.6		99.9	98.6
<i>Bos taurus</i> (Holstein)	98.5	100.0	99.7	99.9		98.5
Ovine	96.8	98.3	98	98.4	98.3	

Percent of identities of nucleotides (upper right) and deduced amino acids from ORF portions (lower left) between TLR7 genes of Yak



Phylogenetic Tree of TLR 7 gene of Yak and Mithun



3 Dimensional tertiary structure of TLR 7 (136-810aa) predicted using Swiss-Model Workspace by Homology Modeling

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