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Original Article

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Identification of Avian Toll-Like Receptor 3 and 7 and Analysis of Gene Variation Sites

ABSTRACT

Toll-like receptors 3 and 7 (TLR3 and 7) mediate immune responses through the recognition of viral single-stranded RNA and doublestranded RNA and therefore play important roles in host defense. Differences in TLR3 or 7 may affect host resistance to RNA viral infection. To illuminate these differences, the partial coding sequence (CDS) of TLR3 and 7 genes were cloned and amplified from the Phasianus colchicus and Numida meleagris, total 64 avian species of TLR3 and 7 sequences were later analyzed. Based on the results, 315 nonsynonymous mutation sites and 202 synonymous mutation sites were also observed in the avian TLR3, and 227 non-synonymous mutation sites and 174 synonymous mutation sites were observed in the avian TLR7. Among these sites, 44 and 45 sites were observed in functional regions of TLR3 and 7, used common variation of amino acids in most avian species. A number of these different sites appeared to affect the recognition and were also visualized. H59Y, E60K, G64R, E93K, L112S, K117E, N118K, R120H, V123M, L163F, R443Q, R459K, E460D, C485H, and F511L for TLR3, and I432V, M437V, and T732S for TLR7 were considered. It is possible that these sites bind to ligands and play crucial roles in viral recognition. These data indicated that the positive selection has occurred in the avian TLR3 and 7 genes.

INTRODUCTION

Toll-like receptors (TLRs) are the most-characterized receptors among the pattern recognition receptors (PRRs). PRRs are recognized as a diverse range of pathogen associated molecular patterns (PAMPs) and play a critical role in antimicrobial host defense (Medzhitov, 2001). Tolllike receptors are critical proteins linking innate and acquired immunity (Akira, 2001). TLRs are evolutionarily conserved with homologs present in insects, fish, mammals, and birds (Kimbrell & Beutler, 2001; Roach et al., 2005; Satake & Sasaki, 2010; Valanne et al., 2011). Ranges of TLR genes have been identified in avian species (Boyd et al., 2001; Fukui et al., 2001; Iqbal et al., 2005; Philbin et al., 2005; Yilmaz et al., 2005; Brownlie & Allan, 2011; Keestra et al., 2013). All avian TLR family have 10 members that include TLR1 type 1 and type 2, TLR2 type 1 and type 2, TLR3, TLR4, TLR5, TLR7, TLR15, and TLR21. However, not all birds have exact 10 TLRs. Several species have duplicated TLR7, others not functional TLR5 (Brownlie & Allan, 2011; Velova et al., 2018). TLR1, TLR2, TLR4, and TLR5 have recognized bacterial components, such as peptidoglycans (PGN), lipopolysaccharides (LPS), cell wall lipids, and flagellum (Brownlie & Allan, 2011). TLR15 has recognized yeast-derived components (Boyd et al., 2012). TLR21 has recognized microbial DNA and is homologous with fish (Keestra et al., 2010). The recognition of viral RNA depends on TLR3 and TLR7, which recognize viral double-



stranded RNA and single-stranded RNA (Alexopoulou *et al.*, 2001; Heil *et al.*, 2004).

Due to the important roles in resistance to pathogen invasion, TLR genes have been conserved throughout evolution. Mutations in TLRs may have a profound influence on the host's response to pathogens and are also associated with resistance to and susceptibility to diseases (Chen et al., 2009; Hawn et al., 2009; Al-Qahtani et al., 2012; Goyal et al., 2012; O'Dwyer et al., 2013). There are many studies researching mutations in human TLRs (Misch & Hawn, 2008; Mukherjee et al., 2019). Several studies have focused on avian TLR gene mutations and polymorphisms (Alcaide & Edwards, 2011; Ruan et al., 2012; Ruan et al., 2015; Swiderska et al., 2018; Velova et al., 2018). In the present study, we explored different genetic patterns of TLR3 and 7 in the Phasianus colchicus, Numida meleagris, and other 62 avian species. The results were helpful to understand the genetic evolution of avian TLR3 and 7.

MATERIALS AND METHODS

Sources of avian breeds

The Numida meleagris and the Phasianus colchicus used in this study were obtained from Beijing Shahe breeder. We arranged four repeats of individuals. All procedures were approved by the Animal Care and Use Committee of Beijing University of Agriculture (Beijing, China).

Molecular cloning of TLR3 and 7 and sequence accession number

The total RNA was obtained from spleens using TRIzol (Invitrogen, USA). The total RNA, a random primer, dNTPs, and M-MLV reverse transcriptase (Promega, USA) were used for cDNA synthesis. PCR was performed to amplify the target gene using three pairs of specific primers for TLR3 and four pairs of specific primers for TLR7 (Table1). PCR reactions were performed with *pfu* polymerase (Promega, USA). The 25 µl PCR reaction contained 50 pmol of each forward and reverse primers, 2 µl template cDNA, 200 µM each of deoxynucleotide triphosphate mixture and 2.5 U Pfu DNA polymerase (Promega) in 1× Pfu DNA polymerase buffer. Amplification conditions were as follows: initial denaturation at 94°C for 2 min, 35 cycles at 94°C for 30 s, annealing at 56°C for 30 s, and extension at 72°C for 3 min, followed by a final extension at 72°C for 10 min. PCR amplicons were verified by 1% agarose gel electrophoresis, then ligated into a *pEASY-Blunt* simple cloning vector (TransGen, Beijing, China). Recombinant

plasmids were characterized by PCR using gene specific and vector primer pairs. Recombinant plasmids with avian *TLR3* and *7* were sequenced from both ends by Sangon Biotech Co., Ltd. Sequences for *TLR3* and *7* for *Numida meleagris* and the *Phasianus colchicus* were deposited in the GenBank database under accession number MG604328-MG604332. Other sequences of TLR3 and 7 of 62 avian species were acquired from GenBank, the accession numbers are shown in Table 2.

Analysis of variation sites

Nucleotide sequences for avian TLR3 and TLR7 were aligned in MegAlign by the ClustalW method (DNAstar version 8.1.3). The nucleotide homology was showed in a report of MegAlign. The functional regions were detected with the analysis tools provided at the website (http://smart.embl-heidelberg.de and http://split.pmfst.hr). The relative frequency of non-synonymous (dN) and synonymous (dS) substitutions was calculated and constructed using the MEGA7 software (version 7) (Kumar, *et al.*, 2016). Crystal structures and non-synonymous sites in the avian TLR3 and 7 were visualized by PDB (Protein Data Bank, ID:1ZIW and 5GMF) models and PyMOL software (version 2.3, DeLano Scientific LLC).

RESULTS AND DISCUSSION

The full-length open reading frame (ORF) for avian *TLR3* was 3036 nucleotides that encoded 1011 amino acids. The ORF for avian *TLR7* was 3180 nucleotides and encoded 1059 amino acids. Partial nucleotide sequences were also analyzed for homology. The nucleotide sequence alignment showed that *Phasianus colchicus* and *Numida meleagris* share 93.6%-95% homology with chicken *TLR3* and *7*. The homology between *Numida meleagris* and the *Phasianus colchicus* was 92.8%-94.1% for *TLR3* and *7*.

The extracellular domain of the TLR, especially the leucine-rich repeat domain (LRR), is a region for recognizing pathogens (Jin and Lee, 2008; Werling, *et al.*, 2009). Cytoplasmic domains of the TLR, especially the Toll/interleukin-1 receptor domain (TIR), is a region for signal transduction (Verstak, *et al.*, 2009). Three hundred and fifteen non-synonymous mutation sites and 202 synonymous mutation sites were observed in the avian *TLR3*, including 60 sites for *Numida meleagris* and 44 sites for the *Phasianus colchicus*. Sixty-two variable sites were located in the extracellular domain, including 34 sites in LRR regions. Eighteen variable sites were also located in the cytoplasmic domain, including 9 sites in the TIR region. Two hundred and



twenty-seven non-synonymous mutation sites and 174 synonymous mutation sites were observed in the avian TLR7, including 58 sites for Numida meleagris and 64 sites for the Phasianus colchicus. Eight-two variable sites were located in the extracellular domain, including 34 sites in the LRR domain, and 8 variable sites were located in the cytoplasmic domain, including 2 sites in the TIR domain. Two sites were located in the transmembrane domain. Among these sites, 44 amino acid sites were observed in LRR and TIR region of TLR3 and used common variation of amino acids in most avian species (Table 3), including G64R, L163F, and H627Y in α -helix structure, V123M, V224R, N381S, and E383Q in β -sheet structure (Figure 1). Forty-five mutation sites were also observed in LRR and TIR region of TLR7 and used common variation of amino acids in most avian species (Table 4), including T175N, F176L, and E341Q sites in α -helix structure, F51S, R56T, V216I, Q664E, 1689V, and 1739M in β -sheet structure (Figure 1). These sites located in α -helix or β -sheet may affect structure of TLR and recognition function.

Three-dimensional structures of avian TLR3 and TLR7 were helpful for further speculating on the role of these variable sites (Choe et al., 2005). The sites that are located at the external and LRR domains may be more important than others (Botos, et al., 2011). Moreover, it reported that two N-terminal half-sites in both dimer subunits of TLR3 are the viral dsRNA binding sites (Alexopoulou et al., 2001; Leonard et al., 2008; Liu et al., 2008; Zhang et al., 2017). In this study, H59Y, E60K, G64R, E93K, L112S, K117E, N118K, R120H, V123M, L163F, R443Q, R459K, E460D, C485H, and F511L for avian TLR3 were considered in all 51 avian species (Figure 1). The sites located at long loop of TLR7, termed 'Z-loop', may also be the viral ssRNA binding sites (Zhang et al., 2016; Zhang et al., 2017; Diebold et al., 2004). In this study, I432V, M437V, and T732S for avian TLR7 were considered in all 49 avian species (Figure 1). These sites may bind to ligands and play crucial roles in viral recognition. Fully characterizing the functions of these sites would require a large number of experiments.



Figure 1 – Visualization of amino acids corresponding to nonsynonymous single nucleotide variations in the extracellular domain of avian *TLR3* (left) and *TLR7* (right) based on the protein structure predicted by CPHmodels 3.0. The predicted liqand binding sites were marked with dotted box.



There is mounting evidence suggesting that there are species-specific components to TLR (Werling *et al.*, 2009). Differences in avian TLR3 and TLR7 reflect the differences in geography and microbial environments (Liu *et al.*, 2006; Alcaide & Edwards, 2011). These variable TLRs recognize the same or similar pathogens and perform the same functions. Different avian TLR3 and TLR7 sequences could also affect the host's resistance to viruses. These variable sites in the extracellular LRR domain, especially the viral binding sites that have been reported, play a dramatic role in recognizing viruses. Further functional research regarding these differences may clarify the impacts of these variable sites in avian *TLR3 and 7*.

The dS/dN represents the proportion between the Ka (Synonymous mutation) and the Ks (nonsynonymous mutation). This ratio determines whether there was any selective pressure on the *TLR3* and *7* genes. This finding indicates positive selection occurred in avian *TLR3* and *7* genes because the frequency of synonymous (dS)/frequency of non-synonymous (dN) (dS/dN of *TLR3* is 0.64; dS/dN of *TLR7* is 0.77). Mutations will be retained in avian *TLR3* and *7*. This property was highly conserved through gene evolution and the more important function of recognizing viruses (Liu *et al.*, 2006; Bergman *et al.*, 2010; Alcaide & Edwards, 2011).

Based on the TLR3 and 7 polymorphisms and their correlations with human and mouse susceptibility to viral infections, we propose that avian TLR3 and 7 differences may be associated with either resistance or susceptibility to avian infectious diseases (Schott *et al.*, 2007; Lee *et al.*, 2013; Piaserico *et al.*, 2015; He *et al.*, 2017). This study may be helpful to further understand the varied resistance to viral diseases that exist between different avian species.

AUTHOR CONTRIBUTIONS

Conceived and designed the experiments: WR. Performed the experiments: YL QL. Analyzed the data: YL WR. Contributed reagents/materials/analysis tools: WR. Wrote the paper: WR.¹

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¹ Tables 1 to 4 are presented in the pages that follow the references.



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Tables 1 to 4:

Table 1 – PCR primers used in this study.

	Primers (5'-3')
avTLR3p1	ATGCTGGAGGAGGTGAAGA
avTLR3p2	TGCAGTCCCTGGAGAGTTAA
avTLR3p3	ACACAGGATGTTTACATGCGATTGG
avTLR3p4	CCCTTGAAAACATGAACTGGAATCTC
avTLR3p5	AAGCAGGAATATCTGAGTTTGAAGC
avTLR3p6	GCATAGTATCTAAACGTTTGTGACCC
avTLR7p1	ATGACAAATCTTTCAGAGGTGGCT
avTLR7p2	GGGGATATGGTTAATAGTCAGGGTC
avTLR7p3	GAAACGCTACTAACCTGACCCTGAC
avTLR7p4	CAGCGTCACCGATCTCCTTTATG
avTLR7p5	CCAAGCAGCTGGTTTAAGAACATCA
avTLR7p6	TCGGGGAACGGTAGTCAGAAGGT
avTLR7p7	GAGCATTCAGCTGAGCAAAAAG
avTLR7p8	CAGTTTCCTGGAGAAGTTTGTTGTA

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Table ;	2 – Avian names	and GenBank acc	cession numbers.						
No.	0	1	2	m	4	5	9	7	∞
Name	Gallus gallus	Acanthisitta chloris	Anser anser	Apteryx austrailis mantelli	Apteryx rowi	Athene cunicularia	Buceros rhinoceros	Calypte anna	Cariama cristata
TLR3	NM001011691	XM009072290	KC292270	XM013942085	XM026054760	XM026847033	XM010135016	XM008491852	XM009700362
TLR7	NM001011688			XM013950523		XM026856297		XM008494759	XM009696068
No.	6	10	11	12	13	14	15	16	17
Name	Chartura pelagica	Charadrius vociferus	Chlamydotis macqueenii	Colius striatus	Columba livia	Phasianus colchicus	Corapipo altera	Cuculus canorus	Cyanistes caeruleus
TLR3	XM010002467	XM009883901	XM010122732	XM010203505	AB618533	MG604331/2	XM027636061	XM009565656	XM023925083
TLR7			XM010119851	XM010209014	XM005512700	MG604329		XM009555971	
No.	18	19	20	21	22	23	24	25	26
Name	Egretta gazetta	Eurypyga helias	Ficedula albicollis	Fulmarus glacialis	Gavia stellata	Numida meleagris	Haliaeetus albicilla	Haliaeetus leucocephalus	Leptosomus discolor
TLR3	XM009642418	XM010156014	XM005045153	XM009585392	XM009811989	MG604330	XM009915940	XM010570028	XM009953213
TLR7	XM009646337	XM010146638	XM005037400	XM009572361	XM009813692	MG604328	XM009913820	XM010581565	XM009960331
No.	27	28	29	30	31	32	33	34	35
Name	Lonchura striata domestica	Manacus vitellinus	Merops nubicus	Mesitomis unicolor	Neopelma chrysocephalim	Nestor notabilis	Nipponia nippon	Nothoprocta perdicara	Opisthocomus hoazin
TLR3	XM021556089	XM018069963	XM008943939	XM010181262	XM027676546	XM010013832	XM009474837	XM026033588	XM009940192
TLR7	XM021528936	XM008932256	XM008935272			XM010019975	XM009476283	XM026047305	
No.	36	37	38	39	40	41	42	43	44
Name	Passer domesticus	Pelecanus crispus	Phaethon lepturus	Phalacrocorax carbo	Picoides pubescens	Pseudopodoces humilis	Pterocles gutturalis	Struthio camelus	Sturnus vulgaris
TLR3	GU229788	XM009486220	XM010281742	XM009505917	XM009902217	XM014263168	XM010074246	XM009676700	XM014889663
TLR7	KF212180	XM009489888	XM010290259	XM009501983		XM014252874	XM010076693	XM009683661	XM014894280
No.	45	46	47	48	49	50	51	52	53
Name	Taeniopygia guttata	Tauraco erythrolophus	Tinamus guttatus	Tyto alba	Caprimulgus carolinensis	Zonotrichia albicollis	Anas platyrhynchos	Anser cygnoides	Balearica regulorum gibbericeps
TLR3	XM002190852	XM009986371	XM010219604	XM009970053	XM_010170240	XM005483864			
TLR7		XM009991025		XM009975060	XM_010175260		XM005029176	KJ022638	XM010309901
No.	54	55	56	57	58	59	60	61	62
Name	Parus major	Corvus cornix cornix	Coturnix japonica	Dromaius novaehollandiae	Empidonax traillii	Falco cherrug	Falco peregrinus	Serinus canaria	Pavo cristatus
TLR3									
TLR7	XM015629850	XM019283098	AB553582	XM026116653	XM027905403	XM027798644	XM027785411	XM018913537	KX712249
No.	63								
Name	Pygoscelis adeliae								
TLR3									
TLR7	XM009318873								



Identification of Avian Toll-Like Receptor 3 and 7 and Analysis of Gene Variation Sites



Table 3 – Avian TLR3 diffe	erences sites at functional region.
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Instrument Instrument Instrument 178 187 OCCAAD 02-4727Ad/3540442 File		Stru	Aa	Avian number	Aa	Avian number
Site L <thl< th=""> L <thl< th=""> <thl< th=""></thl<></thl<></thl<>			(codon)		(codon)	
57 188 0.CAA 0.2-42724939414407 105A 115-12152224-3228390323335739414424-46950 68 188 5(CAA) 0.2-4734938-114697 YTAB 15-1215-12224-32293032333574 68 188 5(CAA) 0.2-4734938-1244524 NAAC 15-1215-12224-32339-1244526 711 188 L(CAC) 0.2-47174578-1175-1791-12224-3233-124244548-125 S(CAC) 3-44727333444445560 712 188 L(CAC) 0.2-4717567 (01.87192-1722-42028)33537- KAAC 0.7-1717567 1771727273444444550 713 188 NAAC 0.7-1717567 (01.87192-1722-42028)33537- KAAC 0.772027741424444550 713 188 VICTG 0.2-474473539474-9 MATO 15-17172027414244445450 713 188 VICTG 0.2-474473539474-9 MATO 15-171720273141244445450 713 188 VICTG 0.2-44473539474-9 MATO 15-171720273141244445450 713 188 VICTG 0.2-44473539474-9 MATO 15-1717202731412444454550 713 188 VICTG 0.2-444	Site					
59 88 IICAQ 00-44172438-114647 VITA 15-80701216182224-32024-30333582772424490 64 88 CIGAQ 0024172443574244490 RIAQQ 11-75-111512472435737347844449454700 64 88 CIGAQ 002417244357474244490 RIAQQ 11-75-1115112472435784 RIAQQ 71 88 CITGS 00151715115121224245058-31433037 RIAQQ 37027736814444540 717 88 RIGT 0015711151101212224245028-3335577 RIAQQ 370775814444550 718 88 RIGT 00257-11110101212224-3628-3335577 RIAQ 1071727278814444550 718 88 RIGT 00257-11110101212224-3628-335577 RIAQ 1157172027481444550 718 RIA 00257-11110101212224-3628-335577 RIAQ 11571720274814444550 718 RIA 00257-11110101212224-362935367-7 RIAQ 11571720274814444550 718 RIA 00257-11110101212224-362935367-7 RIAQ 11571720227483738144444550 718 RIA 00257-1111010121224-36293353577 RIAQ 115717202272833738414424445	57	LRR	Q(CAA)	0/2-4/27/34/39/40/47	E(GAA)	1/5-12/15-22/24-26/28-31/33/35/37/38/41/42/44-46/48-50
60 IR8 EGAA 02-4342847 KAAB 16-12/15-22/4-3355/7-2404/1-46 91 IR8 EGAA D-36-12/15-12/45/26-23 RAGA 17-29/1-1175-12073/344444543/80 112 IR8 KTTG 01/3-11/15-19/1-22/2-3337-42444493/81-50 STGC 3-4170/6 117 IR8 KAAD 01/3-11/15/16/18/312/22/4-32/8-3337-52 KAAA 6/17/20/27/31/4444550 118 IR8 NAAC 01/3-11/15/16/18/312/22/4-26/28/35/37-1 RIGA 17/20/27/31/44/44550 113 IR8 NGTG 01/3-11/15/16/18/312/22/4-26/28/35/37-2 RIGA 1/20/27/11/4/44/550 113 IR8 NGTG 02/4/44/8 MATG 1/51/17/20/27/8/31/41/44/550 113 IR8 NGTG 02/4/44/8 MATG 1/51/17/20/27/8/31/41/44/550 113 IR8 NGTG 02/4/44/8 MATG 1/51/17/20/31/41/44/550 114 IR8 NGTG 02/4/44/8 MATG 1/51/17/20/27/83/14/14/44/550 114 IR8 NGGG 02/4/14/9/47/47/14/3 NATG 1/51/17/20/27/28/31/14/44/550<	59	LRR	H(CAC)	0/2-4/17/34/38-41/46/47	Y(TAT)	1/5-8/10/12/16/18-22/24-26/29/30/32/33/35/37/42/44/48-50
64 Rev CircGA D2/R122/435774-2/44-90 RevGA 1/17-76/11/15-18020-22 7 PER CircGA D2/R122/435762-3133742/44-90 STGC 3-4/2027322/34/44/67/050 117 Rev KAAAQ D2/R22/43578-11/21/15/1671-22/24-2628-313/3627- KAAA 3-4/2027328/14/44/560 118 Rev NAAC D2/R7-12/15/16/11/21/22/24-2628-3335637- KCAA 3/47/201-17/201/24/14/44/560 118 Rev NAAC D2/R7-12/15/16/11/21/22/24-2628-3335637- KCAA 3/47/201-17/2022/41/42/44/550 113 Rev NTTO D2/R7-11/16/11/21/22/24-2628-35937- RTTC 7/917/202741/12/44/45/48/50 113 Rev NCTO D2-A/44/35/98/27-4 MACA 1/15/17/2022/41/24/44/57/98/14/24/44/56 113 Rev NCTO D2-A/44/35/98/27-4 MACA 1/15/17/2022/41/24/44/56 113 Rev NCTO D2-A/44/35/98/27-2 MCAD 1/15/17/2022/41/24/44/56 113 Rev NCTO D2-1/14/16/18/92/22/24/26/23/35/37-4 NCAD 1/15/17/2022/24/25/23/35/37/24/44/45/50 114 RA	60	LRR	E(GAA)	0/2-4/34/39/47	K(AAG)	1/5-12/15-22/24-33/35/37/38/40/41/44-46/48-50
93 IRR EIGAG 0.2/25-12/15-10/21-22/22-62/08-31/3/32/93/93-7 KIAAG 3-4/17/46 112 IRR (TTG) 0/15-111/51019-12/22/4-2028-313/7-21/4/4/54/8-50 STGCG 3-4/17/46 112 IRR NAAG 0/15-211/51019/12/22/4-2028-23/93-74/14/44/9550 IZ/20/27/95/44/44/9550 112 IRR NAAG 0/15-211/51019/12/22/4-2028-33/95/97- HICA1 1/3/1/2115-17/20/22/26-29/31/34/11/65/07-50 1120 IRR NGTO 0-2/9/11/81/91/12/22/4-2028-33/95/97- HICA1 1/3/1/2115-17/20/22/26-29/31/34/11/65/07-50 113 IRR VIGTO 0-2/4/34/93/94/14/91/12/22/4-20/23/93/92-35/97- HICA1 1/3/1/21/15-17/20/23/38/31/14/24/44/95/06 1143 IRR VIGTO 0-2/9/14/94 VIGTO 1/15/17/15/20/22/26-29/31/33/14/14/24/45/06 1143 IRR NAGC 0-2/9/14/94 VIGTO 1/15/17/15/20/22/24/9/37/20/37/83/14/14/24/46/9/3 224 IRR KGAG 0-2/14/23/24/9/17 VIGTO 1/15/17/15/20/22/24/9/37/33/31/14/44/46/9/3 224 IRR KGAG 0-2/14/14/23/24/9/17 VIGTO 1/15/17/11/17/17/17/17/17/17/17/1	64	LRR	G(GGA)	0/2/8/12/24/35/37-42/44-50	R(AGA)	1/3-7/9-11/15-18/20-22
112 LRR LUTG: 0./15./11/S10719/21/23.337.34/44/3495.00 STCC0 3-41/746 117 LRR KAAG 0./15./11/S10719/21/22.4262829/03-3437. EGAG 17200/27/54/14/44/550 118 LRR NAAC 026/71.31/S16718/19/21/22.425/29/03022/33/S37.37 KAAA 617/007/41/44445/50 120 LRR VGT0 0.24/445/349 MACA 1521/5.327.33/344/14/547.50 133 LRR VGT0 0.24/445/349 MACA 1512/1.527.323.37/384/14/24/44/550 134 LRR VGT0 0.24/447.359/347.49 MACA 1512/1.527.02.23/37/384/14/24/44/550 135 LRR NACC 0.25-12/1.43/16/18/19/21.22/24.2628.35/37.7 TACA 15.517.52.02.24/22/27.228/33/33/33.3359.37/364/14/24/44/550 224 LRR KAAA 0.24/14/23/43/49/47 QCAA 15.517.52.02.24/22/27.228/33/33/33.3359.37/364/14/24/44/550 225 LRR KAAAA 0.24/14/23/43/49/47 QCAA 15.577.677.073/15/16/11/39/27.24/24/32/33/39/47 226 LRR KAAAA 0.24/14/23/43/49/47 QCAA 15.277.677.073/15/16/17/39/27/24/24/24/24/24/24/24/24/24/2	93	LRR	E(GAG)	0-2/5-12/15-19/21-22/24-26/28-31/33/35/37- 42/46/48/49	K(AAG)	3-4/20/27/32/34/44/45/47/50
117 IPR KAA60 01/12-12/15/01/01/92/22/24/26/28/29/01-3/437- EGA60 17/20/27/35/41/44/45/90 118 IVR NAAC) 0-25/71-12/15/16/18/19/21/22/24-26/28/33/5/37- KIAAA) 6/17/20/27/45/41/44/44/590 120 IER RCG1 02/57-11/8/19/21/22/24-26/28/33/5/37- HCA1 1/4/4/21/5-17/20/22/26-28/31/34/41/45/47-50 123 IER VCG10 02-4/34/25/99/30/32/35/37- HCA1 1/4/4/24/44/44/950 123 IER VCG10 02-4/34/25/99/30/32/35/37- HCA1 1/5/12/20/27/34/34/24/44/950 124 IER VCG10 02-1/31/51/81/21/22/2-25/9/32/35/37- IVCA 1/51/27/20/37/38/34/1/24/44/550 124 IER VCG10 02-1/47/23/34/39/47 VCCA0 1/51/27/20/27/28/31/1/14/44/550 225 IER ECA60 0-8/11-1/21/4-16/18/19/21-26/28/39/27-40/22/49 NAAT 1/151/20/27/28/31/1/14/44/550 226 IER HCA70 0-8/11-2/31/4-16/18/19/21-26/28/39/27-40/22/49 NAAT 1/151/27/20/27/28/31/1/14/44/550 227 IER ICCA60 0-9/11-2/31/4-16/18/19/21-26/28/39/27-40/22/49 NAAT 1/	112	LRR	L(TTG)	0/1/5-11/15/16/19-22/24-33/37-42/44/45/48-50	S(TCG)	3-4/17/46
118 IAR NUACC 0-25/57-12/15/16/18/102/12/26-26/28-33/35/37- 20/26/24/4464 KAAA F1720027/14/14/44/35/0 120 IAR RICGT 0/05/57-11/18/102/12/25/29/30/23/33/53/7- 20/26/24/446 HCAT 13/41/21/5-1720022/25-28/31/34/41/45/47-50 123 IAR VGTD 0-24/34/35/39/47-49 MATO 15-12/15-12/10/22/26-28/31/34/44/45/40-50 124 IAR L(TTA) 0-24/34/35/39/47-49 MATO 15-12/15-12/16/18/19/12/12-26/29/30/32-35/37- TICO 125 IAR ACCG 0/01/11/16/18/19/12-26/28/30/32-35/37- TICO 19/17/02/27/8/314/14/44/55/0 124 URR KIAAA 0/24/49/49 VIAA 105/17/20/27/8/314/14/44/55/0 1247 IRR ECGAC 0/24/14/23/44/39/47 QCAA 15-12/15-02/22/12/23/13/34/14/24/4-46/48-50 1247 IRR ECGAC 0/24/14/23/44/39/47 QCAA 15-12/15-16/12/22/12/23/33/35/37/38/40-42/46/44-56 1247 IRR ECGAC 0/24/14/23/44/39/47 QCAA 15-12/15-16/27/22/23/23/35/37/38/40-42/46/44-56 1247 IRR ECGAC 0/24/14/23/44/39/47 QCAA	117	LRR	K(AAG)	0/1/3-12/15/16/18/19/21/22/24-26/28/29/31-34/37- 40/42/46-49	E(GAG)	17/20/27/35/41/44/45/50
120 IRR RCGT1 00257-11181/02174252/93032333537- 02484426 HCAT1 13441215-17202226-2831344144548750 123 IRR VIGT30 0-2-4843539847-49 MATD1 15-1215-1210-5337584142444548950 124 IRR LITR1 0-2-48445539847-49 FITC1 79/17202714142444548950 125 IRR ACGC5 0-2-121618191021224-262893032-3537- VIA1 115/17272891141444454950 224 IRR VIGT10 0-2-44432349497 QCAA 15-1715-70272475777890-333553778840424544648-50 227 IRR EGA5 0-2-414232403947 QCAA 15-1715-70618-222424272-224-39/13-3355377884042454648-50 227 IRR EGA5 0-2-414232403947 QCAA 15-1715-1618 1224242923-3355377884042454 223 IRR EGA5 0-2-4142324039447 QCAA 15-1715-1618 122424291-33353778840424454 223 IRR EGA5 0-2-41423240394444 HCACD 15-275778393-3357788404424444850 224 IRR HCAD 0-2-414232403944444 HCAD 15-267571383953778840442444850 224 IRR	118	LRR	N(AAC)	0-2/5/7-12/15/16/18/19/21/22/24-26/28-33/35/37- 40/42/46/48/49	K(AAA)	6/17/20/27/41//44/45/50
123 UR VIGTO 02-493559947-49 MAIG0 VISTD15-2102-3973798414244454650 163 IRR LITAI 0-660115-12/15/16/18/19/21/22/24-2628-35/37- RTC0 77917/202714142/444546950 165 IRR AIGCG 02-12/16/18/19/21/22/24-2629/30/32-35/37- TIACA 115117/27/28/31/41/44/4548050 224 IRR KIAAA 02-4112/33/33/347 QICAAI 151-12716-2022/24/25/27/30-33/35/37/38/41/42/44-46/48-50 229 IRR KIAAA 02-4112/33/33/347 QICAAI 151-12716-2012/24/25/27-32/35/37/38/41/42/44-46/48-50 224 IRR EIGAG 00-414/23/33/34/47 QICAAI 145-12715/0102/22/24/29/3-33/35/37/8/41/42/44-46/48-50 224 IRR EIGAG 00-414/23/33/34/47 QICAAI 145-12715/0102/22/24/29/3-33/35/37/8/40/42/44/54 226 IRR MICACI 02/64/43/34/34/44 XIACI 15-6891/215-22/2-43/35/37/8/40/42/44/550 235 IRR PICACI 0-6891/215-22/2-33/35/37/8/40/42/44/550 125/1791012/15/17/12/22/24/37/33/7/8/40/42/44/550 242 IRR MICACI 0/26/14/39/47 YICAI 1-66991/215-22/24/37/33	120	LRR	R(CGT)	0/2/5/7-11/18/19/21/24/25/29/30/32/33/35/37- 40/42/44/46	H(CAT)	1/3/4/12/15-17/20/22/26-28/31/34/41/45/47-50
163 LRR LITA) 0.660710.211251678319212224-262293032-3537- 400467749 FITC0 7/9172027411424445450 165 LRR AIGCG 0.7-19161819212224-26293032-3537- 404042664749 TIACA 1/15/172022741142444550 224 LRR VIGT1 0.25-121140101819121-26293032-3537- 404042664749 IIAT1 1/15/1720227414424454550 223 LRR KIAAA 0.24-14233343947 QICAA 1/5-1215-2022724252772830-3335/37784/4142/44-4648-50 234 LRR DIGAT0 0.8711-12714-161881921-26293032-35937-4040474-649 NIAAT0 1/15/1618-222442527-3235377884/041424644849 235 LRR EIGAG0 0.6714/23003946-50 KIAAG1 1/5-12716612122742527-3335377884/04144-4648490 232 LRR HICAT0 0.42443236947 YITAC1 1-68971712-527781/012-11171-333783784/0414444648490 233 LRR NIAAT0 0.02614394/1 YITAC1 1-68971712-2827-3333377840/41444648490 234 LRR NIAAT0 0.02614394/1 YITAC1 1-68971712-2827-28333377840/41444648490 234 LRR NIAAT0 0.02614394/7 YITAC1 1-	123	LRR	V(GTG)	0/2-4/34/35/39/47-49	M(ATG)	1/5-12/15-21/26-33/37/38/41/42/44/45/46/50
404644749 156 LR A(GCG) 002-17.167/B179212222-826290032-35/37- 4042/46-49 TACA 1/157172/272831141144/45/60 224 LR V(GT) 002-17.167/B179212222-826290032-35/37- 4042/46/7709 I/AT 1/157172/272831141144/45/60 229 LR K(AAA) 02-41142334/39/47 Q(CAA) 1/51172/224252728/33/35/373840/42/45/46/48-50 229 LR E(GA6) 0-6111-12/14-16181/921-26/28-33/35/37.4042/46-49 N(AAT) 107702072714144/45 227 LR E(GA6) 0-6111-12/14-16181/921-26/28-33/35/37.84004/24-64/84-50 N(AAT) 175-172151021/222/28/37.33/35/37/384004/24/64/84/90 228 LR E(GA6) 0-6141/33/03/94/65 K(AAC) 155-77810012/152/27-23/33/35/37/384004/24/64/84/90 229 LR H(CAC) 0.26614/39/47 Y(TAC) 1-689/17/15-25/27-33/35/37/384/0-42/46/48/90 238 LR P(CAC) 0.2641/23/03/94/64 S(AAT) 2/5-121/1618/67/14/44/950 244 LR N(AAT) 0.7571/11/22/72/38/31/44/44/950 Q(CAA) 1-9/11-12/15/18/21/22/24/28/37/38/40-42/44/48/80 248 LR R(CAGG) 0.77	163	LRR	L(TTA)	0-6/8/10-12/15/16/18/19/21/22/24-26/28-35/37-	F(TTC)	7/9/17/20/27/41/42/44/45/48/50
168 188 0.6CG) 0.2021/01/01/01/02/224-26/29/30/32-35/37- 04/24/64/37 TACA) 115/172072/8314114445/50 224 188 0.6Th 0.205-12/14/16/18/19/21-26/29/30/32-35/37- 04/24/64/37 0.ATh 115/172007728/3141144445/89/50 223 188 0.74-114/23/34/39/47 0.CAM 15-12/15-20/22/42/52/73/23/53/73/84/14/24/54/64/8-50 223 188 E(GAG 0.74-114/33/43/94/T 0.CAM 17-12/15-20/27/42/52/73/23/53/73/84/04/24/54/64/8-50 224 188 E(GAG 0.641/42/33/39/47 KIAB 17-25/73/10/12/15/22/4-29/31/33/53/73/84/04/24/54/64/8-50 225 188 0.CAM 0.24-114/23/64/39/01/47 KICAT 15-25/73/73/23/53/73/84/04/24/54/64/8-50 226 188 HCAG 0.75/14/11/61/81/97/12/26/29/03/2-55/37 QICA 17-5/78/10/11/51/73/20/73/83/44/64/8-50 227 188 NAAT 0.71/14/16/18/97/12/26/29/03/2-35/37 QICA 175/78/10/11/41/23/26/83/37/38/40/41/44/550 228 188 RICGA 0.22-10/14/16/18/97/12/26/29/30/32-35/37 QICA 175/78/10/11/41/23/26/83/33/38/40/41/44/45/50 228 188 RICAG 0.22-10/14/15/17			_(,	40/46/47/49	. (/	
224 LR VIGTD 0/2/5-12/14/16/18/19/21-26/29/30/32-35/37- IATD 11/5/17/20/27/28/31/41/44/45/49/50 229 LR KIAAA 0/2-41/42/34/39/47 QICAA 1/5-12/15-20/22/42/52/72/83/0-33/55/37/38/41/42/44-66/48-50 227 LR D(GAT) 0-8111-12/14-16/18/19/21-26/28-33/25/37-40/42/46-44 NIAAT) 1017/20/27/14/44-45 228 LR E(GAG) 0-2/41/42/34/39/39/47 H(CAT) 1/5-12/15/20/22/4/52/73-32/57/37/84/24/64/84/9 253 LR HCAD 0-3-4/8/23/39 RCGT) 1/5/7-8/10/12/16/27/8-2/8/3/35/37/84/04/24/54/64/84/9 254 LR HCAD 0-2-4/14/23/48/49/44/9 RCGT) 1/5/7-8/10/12/15/27/2-2/9/3/3/5/37/84/04/24/54/64/84/9 252 LR HCAD 0-2/6/13/9/47 H(CAT) 1/6-8/9/12/15-26/23/37/38/24/64/84/9 254 LR NCAD 0-2/6/14/9/15/12/12/26/29/30/22-35/37 QICAD 1/5/17/10/10/21/8/17/38/24/64/44/84/50 254 LR NCAD 0-2/6/14/15/11/9/12/22/35/39/4 QICAD 1/5/17/81/12/16/8/1-26/28-35/37/38/4/44/44/84/50 254 LR NCAD 0-2/6/14/15/11/11/19/12/22/24-26/29/30/32/33/37-3	165	LRR	A(GCG)	0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- 40/42/46-49	T(ACA)	1/15/17/27/28/31/41/44/45/50
128 KRA 0.02-41/42/314/39/47 QICAN 115/12/15/2022/42/52/28/30-33/35/37/38/41/42/44.648-50 127 LRR DIGATI 0.06/11 0.06/11 0.07/112/12/26/28/33/39/47 QICAA 115/12/15/07/12/12/22/28/30/33/25/73/84/04/24/54/648-50 125 LRR EIGAG 0.07/41/42/33/03/94/50 KIAAG 1-2/5/78/01/21/52/28/33/35/37/84/04/24/54/64/8-50 126 LRR HICAT 0.3-4/8/33/9 RICGT 1-2/5/78/01/21/52/28/33/35/37/84/04/24/45/64/8-50 126 LRR HICAT 0.3-4/8/33/9 RICGT 1-2/5/78/01/21/52/29/33/33/38/40/24/44/54/8-50 128 LRR NICAT 0.07/51/41/72/35/59/46 YICA 1-6/8/91/21/52/29/33/33/38/40/24/44/54/8-50 128 LRR RIGGS 0.01/14/15/17/19/20/27/39/41/44/49/50 QICAG 1/15/17/20/27/28/31/40/41/44/45/8-50 443 LRR RIGGS 0.01/14/15/17/19/20/27/39/31/33/35/37-41/44/45/84-50 QICAG 1/15/17/20/27/28/31/40/41/44/45/80-50 128 LRR RIGGS 0.01/24/35/71/19/22/23/33/37-39/41/42/45-50 QICAT 1/27/28/31/41/44/45/50 111 LRR RIGAA 0.02-5/	224	LRR	V(GTT)	0/2/5-12/14/16/18/19/21-26/29/30/32-35/37- 40/42/46/47/49	I(ATT)	1/15/17/20/27/28/31/41/44/45/48/50
123 IRR D(GAT) 0-8/11-12/14-16/18/19/21-26/28-33/35/37-40/42/46-49 N(AAT) 10/17/20/27/14/44/5 247 ILR E(GAG) 0/2-4/14/23/03/39/46-50 KIAAG) 1/6-11/15/16/18-22/24/29/3-33/55/37/38/40/42/45/46/49/9 252 ILR P(GAT) 0/2-4/14/23/06/34/39/40/47 H(CAT) 1/5-12/15/16/21/22/24/25/2-33/55/37/38/40/42/45/46/48/9 252 ILR H(CAT) 0/2-4/14/23/06/34/39/40/47 H(CAT) 1/5-12/15/16/18-21/24-29/31-33/57/38/40/42/45/46/48/9 252 ILR H(CAT) 0/2-4/14/23/16/24/39/40 Y(TAC) 1-6/9/9/121-55/27-33/55/37/38/40/42/45/46/48/9 252 ILR H(CAT) 0/2-4/6-12/11/41/17/3/35/39/46 S(AGT) 2/5-17/15/16/18-21/24-29/31-33/77/38/40/42/45/46/48/50 254 ILR N(AAT) 0/15/14/17/17/19/28/30/32-35/37- Q(CAG) 1/15-6/7/10/11/16-32/26-28/30/32/34/35/37-41/44/45/48-50 254 ILR R(CAG) 0/11/15/17/19/28/26-38/33/35/37-41/44/45/48-50 H(CAT) 1-5/7/8/11/12/15-18/2-22/27-28/31/33/36/40/24/4-46/48 254 ILR R(CAG) 0/2-12/16/18/21/22/24-26/29/30/23/37-39/41/42/45-50 H(CAT) 1-5/7/8/11/12/15-18/2-22/24-28/3-33/38/40/42/44-46/50 <td>229</td> <td>LRR</td> <td>K(AAA)</td> <td>0/2-4/14/23/34/39/47</td> <td>Q(CAA)</td> <td>1/5-12/15-20/22/24/25/27/28/30-33/35/37/38/41/42/44-46/48-50</td>	229	LRR	K(AAA)	0/2-4/14/23/34/39/47	Q(CAA)	1/5-12/15-20/22/24/25/27/28/30-33/35/37/38/41/42/44-46/48-50
247 IRR E(GAG) 0.02-41/4233439347 Q(CAA) 1/6-11/16/(1-2)/22/42/93/35/37/38/4042/45/46/48-50 252 IRR E(GAG) 0.6/14/23/0393/46-50 KAAQ) 1-2/57/-8/101/215-22/24/93/1-33/35/37/38/4042/45/46/49-50 252 IRR H(CAT) 0.9-4/14/23/26/33/31/04/7 H(CAT) 1/5-12/15/16/21/22/42/52/8-33/35/37/38/40-42/45/46/49-50 252 IRR H(CAT) 0.9-4/14/23/26/33/31/36/2 S(CAT) 1/5-6/99/12/15-25/27/33/35/37/38/40-42/45/46/49-50 253 IRR NIAAT) 0.1/5/14/17/23/37/39/46 S(ACT) 2/6-12/15/16/18-21/24-29/31-33/35/37/38/40-42/44/54/8-50 264 IRR R(CAG) 0.2/4/15/17/19/20/27/29/31/44/49/50 Q(CAA) 1/3-10/17/10/20/27/28/31/40/14/44/45/50 443 IRR R(CAG) 0.7/91/22/42/29/39 X(AAA) 1/3-68/10/11/14-23/02-83/37/38/40/42/44-46/48/50 4443 IRR R(CAG) 0.7/91/22/42/29/39 X(AAA) 1/3-68/10/11/14-23/20-28/37/38/40/42/44-46/48/50 4443 IRR R(CAG) 0.7/91/22/42/52/33/37/37/41/44/45/48-50 D(GAA) 3-4/12/16/18/34/34/37 4459 IRR R(CAG) 0.2/	237	LRR	D(GAT)	0-8/11-12/14-16/18/19/21-26/28-33/35/37-40/42/46-49	N(AAT)	10/17/20/27/41/44/45
252 LRR EGAGS 016/14/23/30/39/46-50 KIAAG 1-2/5/7-8/10/12/15-22/24/25/43/33/40/47 253 LRR D16/A7 02-4/14/23/26/34/39/40/7 H(CAT) 105-12/7/97/10/12-15/62/12/24/25/83/35/37/38/40-42/45/46/48-50 252 LRR H(CAC) 00/3-4/8/33/39 R(CGT) 1-2/5/7/97/10/12-15/22/73/35/37/38/40-42/45/46/48-50 253 LRR H(CAC) 00/2-4/6-12/14/16/18/19/21-26/29/30/32-35/37- Q(CAG) 1/15/117/12/02/78/31/44/45/50 381 LRR R(CGG) 0/10/14/15/17/19/20/27/39/41/44/49/50 Q(CAG) 1/15/117/11/12/26/28-35/37/36/42/45-48 459 LRR R(CGG) 0/10/14/15/17/19/20/27/39/41/44/45/50 Q(CAG) 1/15/117/11/14/16/18/12/26/28-35/37/36/42/45-50 450 LRR R(CGG) 0/10/14/15/17/19/20/27/39/37/37/41/44/45/850 D(GAT) 3-4/12/16/18/21/46/27 451 LRR R(CGG) 0/10/14/15/17/19/20/27/39/37/37/37/37/39/42/45-48 H(CAT) 0/3/12/24/55/37/37/38/42/45-49 453 LRR C(CGA) 0/2/12/16/18/21/22/22/29/39/37/37/39/41/42/45-50 H(CAT) 1/5/7/11/11/17/18/22/22/29/2 5111 LRR R(CGG)	247	LRR	E(GAG)	0/2-4/14/23/34/39/47	Q(CAA)	1/6-11/15/16/18-22/24/25/27-32/35/37/38/40/42/45/46/48-50
253 LR D(GAT) 0/2-4/14/23/26/34/39/40/47 H(CAT) 1/5-12/15/16/21/22/24/25/28-33/35/37/38/42/4/46/48/90 252 LRR H(CAT) 0/2-6/14/39/47 Y(TAC) 1-6/89/21/25/25/73/31/37/38/40/41/44/46/48/90 381 LR N(AAT) 0/15/1/41/17/23/35/39/46 S(AGT) 2/6-12/15/16/18-21/24-29/31-33/37/38/40-42/44/5/48-50 383 LR E(GAG) 0/2-4/16-12/14/16/18/19/21-26/29/30/32-35/37- Q(CAG) 1/15/17/20/27/28/31/40/41/44/45/50 443 LR R (GGG) 0/10/14/15/17/19/20/27/39/41/44/45/45 Q(CAG) 1-9/11-12/16/18/32/46/47 445 LR R (AGG) 0/179/122/42/5/29/39 K(AAA) 1/3-6/10/11/14-23/26-28/30/32/37/37/38/40-42/44-49 456 LR R (GAG) 0/2-12/16-18/17/19-20/32/3/35/37-41/44/54/545 Q(CAG) 3-4/12/16/18/32/44/64/7 460 LRR R (GGA) 0/2-2/3/4/39/31/17 LCTT 1/5/79/11/12/1-22/24-28/30/32/37/37/38/40/4/24-46/49/50 511 LR R(GAG) 0/7/21/24-26/29/30/32-35/37- D(GAT) 1/5/70/22/72/8/31/41/44/45/50 604 LR Q(CAG) 0-4/12/24-26/29/30/32-35/37-	252	LRR	E(GAG)	0/6/14/23/30/39/46-50	K(AAG)	1-2/5/7-8/10/12/15-22/24-29/31-33/35/37/38/40-42/45
262 IRR H(CAT) 0/3-4/8/33/39 R(CGT) 1-2/57/9/10/12-15/17-32/37/38/40/41/44-46/48/50 292 LRR H(CAC) 0/4/4/39/47 V(TAC) 1-6/8/9/12/15-2527-33/35/57/38/40-42/44/54/8-50 381 LRR N(AAT) 0/1/5/14/17/2/35/39/46 S(AGT) 2/6-12/15/16/18-21/24-29/31-33/37/38/40-42/44/45/48-50 383 LRR E(GAG) 0/2-4/6-12/4/16/18/19/21-26/29/30/32-35/37- Q(CAG) 1/15/17/20/27/28/31/40/44/44/5/50 443 LRR R(CGG) 0/10/14/15/17/19/20/27/39/41/44/49/50 Q(CAA) 1-9/11-12/16/18/21-26/28-35/37/38/42/45-48 459 LRR R(CGG) 0/10/14/15/17/19/20/27/39/31/35/37-41/44/5/48-50 D(GAT) 1-5/7/8/11/14/44/5/0 460 LRR E(TGT) 0/31/23/43/5/37-42/44-50 H(CAT) 1/5/9/11/12/15-18/20-22/27.429 511 LRR R(TTT) 0/2-4/34/39/41/47 L(CTT) 1/5/9/11/12/15-18/20-32/36/3/38/40/42/44-46/48/50 604 LRR V(TAT) 0/2-2/6/8/11/16/18/19/21/22/4-26/29/30/32-35/37- D(GAT) 1/15/20/22/21/8/31/41/44/45/50 610 LRR Q(CAG) 0-4/12/16/18/19/21/22/24-26/29/30/32-	253	LRR	D(GAT)	0/2-4/14/23/26/34/39/40/47	H(CAT)	1/5-12/15/16/21/22/24/25/28-33/35/37/38/42/46/48/49
292 LRR H(CAC) 0/26/14/39/47 Y(TAC) 1-6/8/9/12/15-25/27-33/35/37/38/40-42/44/54/8-50 381 LRR N(AAT) 0/1/5/14/17/23/35/39/46 S(AGT) 2/6/12/15/16/18-21/24-29/31-33/37/38/40-42/44/45/48-50 383 LRR E(GAG) 0/2-4/6-12/14/16/18/19/21-26/29/30/32-35/37- Q(CAG) 1-9/11-12/16/18/21-26/28-35/37/38/40-42/44/45/48-50 443 LRR R(CGG) 0/10/14/15/17/19/22/25/9/39 K(AAA) 1-9/11-12/16/18/21-26/28-35/37/38/42/45-48 459 LRR R(AGG) 0/7/9/12/24/25/25/9/39 K(AAA) 1-9/11-12/16/18/21-26/28-35/37/38/40-42/44-49 460 LRR E(GAA) 0-2/5-10/14/15/17/19-28/30-33/35/37-41/44/45/8-50 D(GAT) 3-4/12/16/18/34/26/47 478 LRR C(TGT) 0/31/32/34/5/37-42/44-50 H(CAT) 15/7/8/11/12/15-18/20-22/27/30/32-33/38/40/42/44-46/48/50 603 LRR A(GCA) 0/2-12/16-18/21/24-26/29/30/32-35/37- D(GAT) 1/15/20/22/27/28/31/44/44/45/50 604 LRR Y(TAT) 0/2-46/24/39/49/47 R(AGG) 5/79-11/16-18/20-22/27/30/33/37/37/41/44/44/5/50 605 LRR Q(CAG) <t< td=""><td>262</td><td>LRR</td><td>H(CAT)</td><td>0/3-4/8/33/39</td><td>R(CGT)</td><td>1-2/5/7/9/10/12-15/17-32/37/38/40/41/44-46/48/50</td></t<>	262	LRR	H(CAT)	0/3-4/8/33/39	R(CGT)	1-2/5/7/9/10/12-15/17-32/37/38/40/41/44-46/48/50
381 LRR N(AAT) 0/1/5/14/17/23/35/39/46 S(AGT) 2/6-12/15/16/18-21/24-29/31-33/37/38/40-42/44/45/48-50 383 LRR E(GAG) 0/2-4/6-12/14/16/18/19/21-26/29/30/32-35/37- 39/42/46/17/49 Q(CAG) 1/15/17/20/27/28/31/40/41/44/45/50 443 LRR R(GG) 0/10/14/15/17/19/20/27/39/41/44/49/50 Q(CAA) 1-9/11-12/16/18/21-26/28-35/37/38/40-42/44-548 459 LRR R(GG) 0/79/12/24/25/29/39 K(AAA) 1-3-4/12/16/18/31/46/47 460 LRR E(GAA) 0-2/5-10/14/15/17/19-28/30/33/35/37-41/44/45/85-0 D(GAT) 3-4/21/16/18/31/46/47 461 LRR C(TGT) 0/31/32/34/35/37/42/44-50 H(CAT) 1-5/7/81/11/21/5-18/20-22/24-29 511 LRR K(TT) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- U(CAT) 17/5/02/27/28/31/44 604 LRR V(TAT) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- V(TAT) 17/5/7/28/31/41/44/45/50 603 LRR Q(CAG) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- V(TAT) 17/5/7/28/31/41/44/45/50 604 LRR V(ATAT) 0/2-2/12/16/18/19/21/22/24-26/29/30/3	292	LRR	H(CAC)	0/26/14/39/47	Y(TAC)	1-6/8/9/12/15-25/27-33/35/37/38/40-42/45/46/48-50
383 LRR E(GAG) 0/2-4/6-12/14/16/18/19/21-26/29/30/32-35/37- 39/42/46/47/49 Q(CAG) 1/15/17/20/27/28/31/40/41/44/45/50 443 LRR R(CGG) 0/10/14/15/17/19/20/27/39/41/44/49/50 Q(CAA) 1-9/11-12/16/18/21-26/28-35/37/38/42/45-48 459 LRR R(AGG) 0/79/12/24/25/29/39 K(AAA) 1/3-6/8/10/11/14/23/26-28/30/32/34/5/37/38/40-42/44-49 460 LRR E(GAA) 0-2/5-10/14/15/17/19-28/30-33/35/37-41/44/45/48-50 D(GAT) 3-4/12/16/18/34/46/47 460 LRR C(TGT) 0.31/32/34/35/37-42/44-50 H(CAT) 1-5/7/8/11/12/15-18/20-22/24-29 511 LRR R (TTT) 0/2-6/8-12/16/18/19/21/22/24-26/29/30/32-35/37- U(GA) 11/5/7/8/11/12/15-18/20-22/27/38/31/44 604 LRR Y(TAT) 0/2-6/8-12/16/18/19/21/22/24-26/29/30/32-35/37- U(GA) 11/5/7/20/27/28/31/41/44/45/50 609 LRR Q(CAG) 0-4/12,24-26/29/30/32-35/37- Y(TAT) 11/5/17/20/27/28/31/41/44/45/50 617 LRR H(CAT) 0/2-5/6/8/11/15/17/19-22/24-29/31-33/35/38-42/44- D(GAT) 3/49/10/16/18/30/34/37/47 718 R(AAG) 0/2/17/	381	LRR	N(AAT)	0/1/5/14/17/23/35/39/46	S(AGT)	2/6-12/15/16/18-21/24-29/31-33/37/38/40-42/44/45/48-50
Instructure 39/42/46/7/49 Number of the second sec	383	LRR	E(GAG)	0/2-4/6-12/14/16/18/19/21-26/29/30/32-35/37-	O(CAG)	1/15/17/20/27/28/31/40/41/44/45/50
IAB IRR R(CGG) 0/10/14/15/17/19/20/27/39/41/44/49/50 Q(CAA) 1-9/11-12/16/18/21-26/28-35/37/38/42/45-48 ISR IRA R(AGG) 0/79/12/24/25/29/39 K(AA) 1/3-6/8/10/11/4-23/6-28/30/32/34/35/37/38/40-42/44-59 IER E(GAA) 0-2/5-10/14/15/17/19-28/30-33/35/37-41/44/45/8-50 D(GAT) 3-4/12/16/18/21/26/28/30/32/34/35/37-42/44-50 III IRR C(TGT) 0/31/32/34/35/37-42/44-50 H(CAT) 1-5/7/8/11/12/15-28/20-22/24-29 511 I.RR R(TTT) 0/2-4/34/39/41/47 ICCTT) 1/5-9/11/12/15-22/24-28/30-33/38/40/42/44-46/48/50 603 I.RR R(GCA) 0/2-12/16-18/19/21/22/24-26/29/30/32-35/37- V(GA) 1/15/20/22/27/8/31/44 604 I.RR Y(TAT) 0/2-42/4/39/34/34/9/40/47 R(AGG) 5/7/9-11/16/18/20/22/27/30/33/37/38/41/42/4-46/50 607 I.RR H(CAT) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- Y(TAT) 1/15/17/20/27/28/31/41/44/5/50 617 I.RR N(AAT) 0-2-5/5/6/8/11/15/17/19-22/24-29/31/33/53/37.84/24/4- D(GAT) 3/4/9/10/16/18/30/34/37/47 716 TIR K(AAG) 0/3/4/12/16/			-(-:-)	39/42/46/47/49	2(0)	
459 LRR R(AGG) 0/7/9/12/24/25/9/9 KIAAA 1/3-6/8/10/11/14-23/26-28/30/32/34/35/37/38/40-42/44-49 460 LRR E(GAA) 0-2/5-10/14/15/17/19-28/30-33/35/37-41/44/5/48-50 D(GA) 3-4/12/16/18/34/46/47 461 LRR C(TGT) 0/3/32/34/35/37-42/44-50 H(CAT) 1-57/8/11/12/15-1820-22/24-29 511 LRR R(TT) 0/2-4/34/39/41/47 L(CT) 1/5-9/11/12/15-1820-22/24-28/30-33/38/40/42/44-46/48/50 603 LRR A(GCA) 0/2-12/16-18/21/24-26/29/30/32-35/37- V(GTA) 1/15/02/22/7/28/31/41/44/45/50 604 LRR Q(CAG) 0-4/12,24-26/29/32/34/39/40/47 R(AGG) 5/7/9-11/16-18/20-22/7/30/33/37/38/41/42/44-46/50 627 LRR H(CAT) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- Y(TA) 1/15/17/20/27/28/31/41/44/45/50 627 LRR H(CAT) 0-2/3/6/8/11/15/17/19-22/24-29/31-33/35/38/34/24/4- D(GAT) 3/49/10/16/18/30/34/37/47 617 TIR N(AAT) 0-2/3/6/8/11/15/17/19-22/24-29/31-33/35/37/38/4/4/4/44/5/85 D(GAT) 3/49/10/10/17/18/20/22/26/31/33/5/37/38/4/4/4/45/48-50 719 TIR N(AA	443	LRR	R(CGG)	0/10/14/15/17/19/20/27/39/41/44/49/50	Q(CAA)	1-9/11-12/16/18/21-26/28-35/37/38/42/45-48
460 LRR E(GAA) 0-2/5-10/14/15/17/19-28/30-33/35/37-41/44/45/48-50 D(GAT) 3-4/12/16/18/34/46/47 485 LRR C(TGT) 0/31/32/34/35/37-42/44-50 H(CAT) 1-5/7/8/11/12/15-18/20-22/24-29 5111 LRR F(TT) 0/2-4/34/39/41/47 L(CT) 1/5-7/8/11/12/15-18/20-22/24-29 603 LRR A(GCA) 0/2-12/16-18/21/24-26/29/30/32/33/37-39/41/42/45-50 V(GTA) 1/15/20/22/27/8/31/41 604 LRR Y(TAT) 0/2-6/8-12/16/18/19/21/22/24-26/29/30/32-35/37- D(GAT) 1/15/17/20/27/8/31/41/44/45/50 609 LRR Q(CAG) 0-4/12/42-49/9 RAGG) 57/9-11/16-18/20-22/27/30/3/37/38/41/42/44-46/50 627 LRR H(CAT) 0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- Y(TAT) 1/15/17/20/27/8/31/41/44/45/50 627 LRR N(AAT) 0/2-12/16/18/19/21/22/24-26/29/30/32- V(TAT) 1/15/17/20/27/8/31/41/44/45/50 710 TIR N(AAT) 0-2/5/6/8/11/15/17/19-22/24-29/31-33/35/37-8/42/44 D(GAT) 1/2/5/11/15/17-22/24-31/33/53/37/84/04/14/44/5/48-50 711 TIR Q(CAA) 0/3-6/11/16/18/19/21/22/24	459	LRR	R(AGG)	0/7/9/12/24/25/29/39	K(AAA)	1/3-6/8/10/11/14-23/26-28/30/32/34/35/37/38/40-42/44-49
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705 TIR N(AAT) 0-2/5/6/8/11/15/17/19-22/24-29/31-33/35/38-42/44- 46/48-50 D(GAT) 3/4/9/10/16/18/30/34/37/47 716 TIR E(GAA) 0/3/4/12/16/24/25/32/34/39/46/47 K(AAA) 1/2/5-11/15/17-22/26-31/33/35/37/38/40/41/44/45/48-50 719 TIR Q(CAA) 0/2-5/16/39 H(CAC) 6-9/11/15/17-22/24-31/33/35/37/38/40/41/44/45/48-50 721 TIR Q(CAA) 0/3-9/11/16/18/19/21/22/24-26/29/33/35/37- 39/46/48/49 E(GAA) 1/2/15/17/20/27/28/31/41/44/45/50 723 TIR K(AAG) 0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50 R(AGG) 2-6/8/11/15/18/19/21/22/24/25/28/29/31/33/35/37/48/49 735 TIR I(ATA) 0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49 V(GTA) 6/11/17/19/20/24/25/27/38/41/44/45/50 741 TIR I(ATA) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48-50 746 TIR R(AGG) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-19/21/22/26-28/31-33/35/37/38/41/42/44-66/48-50 747 TIR R(AGG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40	627	LRR	H(CAT)	0/2-12/16/18/19/21/22/24-26/29/30/32-35/37- 40/42/46-49	Y(TAT)	1/15/17/20/27/28/31/41/44/45/50
TIR E(GAA) 0/3/4/12/16/24/25/32/34/39/46/47 K(AAA) 1/2/5-11/15/17-22/26-31/33/35/37/38/40/41/44/45/48-50 719 TIR Q(CAA) 0/2-5/16/39 H(CAC) 6-9/11/15/17-22/26-31/33/35/37/38/40/41/44/45/48-50 721 TIR Q(CAA) 0/3-9/11/16/18/19/21/22/24-26/29/33/35/37- 39/46/48/49 E(GAA) 1/2/15/17/20/27/28/31/41/44/45/50 723 TIR K(AAG) 0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50 R(AGG) 2-6/8/11/15/18/19/21/22/24/25/28/29/31/33/35/37/48/49 735 TIR I(ATA) 0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49 V(GTA) 6/11/17/19/20/24/25/27/38/41/44/45/50 741 TIR I(ATA) 0-2/7/9/39/46/47/49 T(ACA) 1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48/50 746 TIR R(AGG) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-31/33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2/2/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/31/41/42/44/45/48-50(9/40 749 TIR N(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/22-24-31/33/35/37/34/41/42/44/45/48-50(9/40 799 <td>705</td> <td>TIR</td> <td>N(AAT)</td> <td>0-2/5/6/8/11/15/17/19-22/24-29/31-33/35/38-42/44- 46/48-50</td> <td>D(GAT)</td> <td>3/4/9/10/16/18/30/34/37/47</td>	705	TIR	N(AAT)	0-2/5/6/8/11/15/17/19-22/24-29/31-33/35/38-42/44- 46/48-50	D(GAT)	3/4/9/10/16/18/30/34/37/47
TIR Q(CAA) 0/2-5/16/39 H(CAC) 6-9/11/15/17-22/24-31/33/35/37/38/40/41/44/45/48-50 721 TIR Q(CAA) 0/3-9/11/16/18/19/21/22/24-26/29/33/35/37- 39/46/48/49 E(GAA) 1/2/15/17/20/27/28/31/41/44/45/50 723 TIR K(AAG) 0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50 R(AGG) 2-6/8/11/15/18/19/21/22/24/25/28/29/31/33/35/37/48/49 735 TIR I(ATA) 0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49 V(GTA) 6/11/17/19/20/24/25/27/38/41/44/45/50 741 TIR I(ATA) 0-2/7/9/39/46/47/49 T(ACA) 1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48/50 746 TIR R(AGA) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/14/14/2/44/45/48-50(9/40 799 TIR N(AAT) 0/2-4/34/37-39/41/42/47 Y(TAT) 1/5-9/12/15-19/21/22/24-28/31-33/35/38/40-42/45/46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) <t< td=""><td>716</td><td>TIR</td><td>E(GAA)</td><td>0/3/4/12/16/24/25/32/34/39/46/47</td><td>K(AAA)</td><td>1/2/5-11/15/17-22/26-31/33/35/37/38/40/41/44/45/48-50</td></t<>	716	TIR	E(GAA)	0/3/4/12/16/24/25/32/34/39/46/47	K(AAA)	1/2/5-11/15/17-22/26-31/33/35/37/38/40/41/44/45/48-50
T21 TIR Q(CAA) 0/3-9/11/16/18/19/21/22/24-26/29/33/35/37- 39/46/48/49 E(GAA) 1/2/15/17/20/27/28/31/41/44/45/50 723 TIR K(AAG) 0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50 R(AGG) 2-6/8/11/15/18/19/21/22/24/25/28/29/31/33/35/37/48/49 735 TIR I(ATA) 0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49 V(GTA) 6/11/17/19/20/24/25/27/38/41/44/45/50 741 TIR I(ATA) 0/2/7/9/39/46/47/49 T(ACA) 1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48/50 746 TIR R(AGG) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40 799 TIR N(AAT) 0/2-4/39/47 Y(TAT) 1/5-9/12/12-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-19/21/22/24-31/33/35/38/40-42/45/46/48-50 810	719	TIR	Q(CAA)	0/2-5/16/39	H(CAC)	6-9/11/15/17-22/24-31/33/35/37/38/40/41/44/45/48-50
723 TIR K(AAG) 0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50 R(AGG) 2-6/8/11/15/18/19/21/22/24/25/28/29/31/33/35/37/48/49 735 TIR I(ATA) 0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49 V(GTA) 6/11/17/19/20/24/25/27/38/41/44/45/50 741 TIR I(ATA) 0/2/7/9/39/46/47/49 T(ACA) 1/3-6/8/10/12/15-22/24-35/37/38/40-42/44/45/48/50 746 TIR R(AGA) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40 799 TIR N(AAT) 0/2-4/39/47 Y(TAT) 1/5-9/12/12-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-19/21/22/24-31/33/35/44-46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/69/10/18-22	721	TIR	Q(CAA)	0/3-9/11/16/18/19/21/22/24-26/29/33/35/37- 39/46/48/49	E(GAA)	1/2/15/17/20/27/28/31/41/44/45/50
735TIRI(ATA)0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49V(GTA)6/11/17/19/20/24/25/27/38/41/44/45/50741TIRI(ATA)0/2/7/9/39/46/47/49T(ACA)1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48/50746TIRR(AGA)0/2/7/30/34/39/40/47K(AAA)1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50747TIRR(AGG)0/2-4/20/29/34/39/40/44/47M(ATG)1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50767TIRK(AAG)0/10/15-22/24/28/30/31/33/39/46N(AAT)1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40)799TIRN(AAT)0/2-4/39/47Y(TAT)1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50803TIRC(TGC)0/2-4/39/47H(CAC)5-10/12/15-19/21/22/24-28/31-33/35/38/40-42/45/46/48-50810TIRR(AGA)0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50K(AAA)4/9/16/18/19/21/22/33/37/49812TIRC(TGC)0/15/24/25/28/31/39R(CGC)2/3/69/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	723	TIR	K(AAG)	0/1/7/9/10/12/17/20/26/27/34/38-41/44/45/47/50	R(AGG)	2-6/8/11/15/18/19/ 21/ 22/ 24/25/ 28/ 29/ 31/33/35/37/48/49
THR I(ATA) 0/2/7/9/39/46/47/49 T(ACA) 1/3-6/8/10/12/15-22/24-35/37/38/40-42/44/45/48/50 746 TIR R(AGA) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40) 799 TIR N(AAT) 0/2-4/39/47 Y(TAT) 1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-1921/22/24-31/33/35/38/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/69/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	735	TIR	I(ATA)	0-5/7-10/12/16/18/21/22/26/29/30/32- 35/37/39/40/42/48/49	V(GTA)	6/11/17/19/20/24/25/27/38/41/44/45/50
746 TIR R(AGA) 0/2/7/30/34/39/40/47 K(AAA) 1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50 747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/5/48-50(9/40) 799 TIR N(AAT) 0/2-4/39/47 Y(TAT) 1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-19/21/22/24-28/31-33/35/38/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/8/31/39 R(CGC) 2/3/69/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	741	TIR	I(ATA)	0/2/7/9/39/46/47/49	T(ACA)	1/3-6/8/10/12/15-22/2435/37/38/40-42/44/45/48/50
747 TIR R(AGG) 0/2-4/20/29/34/39/40/44/47 M(ATG) 1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50 767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40) 799 TIR N(AAT) 0/2-4/34/37-39/41/42/47 Y(TAT) 1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-1921/22/24-28/31-33/35/38/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	746	TIR	R(AGA)	0/2/7/30/34/39/40/47	K(AAA)	1/3-6/8-10/12/15-22/24-29/31-33/35/37/38/41/42/44-46/48-50
767 TIR K(AAG) 0/10/15-22/24/28/30/31/33/39/46 N(AAT) 1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40 799 TIR N(AAT) 0/2-4/34/37-39/41/42/47 Y(TAT) 1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-1921/22/24-31/33/53/8/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	747	TIR	R(AGG)	0/2-4/20/29/34/39/40/44/47	M(ATG)	1/6-12/15-19/21/22/26-28/31-33/35/37/38/41/46/48-50
799 TIR N(AAT) 0/2-4/34/37-39/41/42/47 Y(TAT) 1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50 803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-19/21/22/24-31/33/35/38/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	767	TIR	K(AAG)	0/10/15-22/24/28/30/31/33/39/46	N(AAT)	1/5-8/11/12/25-27/29/32/35/37/41/42/44/45/48-50(9/40
803 TIR C(TGC) 0/2-4/39/47 H(CAC) 5-10/12/15-1921/22/24-28/31-33/35/38/40-42/45/46/48-50 810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	799	TIR	N(AAT)	0/2-4/34/37-39/41/42/47	Y(TAT)	1/5-9/12/15-19/21/22/24-31/33/35/44-46/48-50
810 TIR R(AGA) 0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50 K(AAA) 4/9/16/18/19/21/22/33/37/49 812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	803	TIR	C(TGC)	0/2-4/39/47	H(CAC)	5-10/12/15-1921/22/24-28/31-33/35/38/40-42/45/46/48-50
812 TIR C(TGC) 0/15/24/25/28/31/39 R(CGC) 2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50	810	TIR	R(AGA)	0-3/5/6/8/10-12/15/17/20/24-32/34/35/38-42/44-48/50	K(AAA)	4/9/16/18/19/21/22/33/37/49
	812	TIR	C(TGC)	0/15/24/25/28/31/39	R(CGC)	2/3/6/9/10/18-22/26-27/29/30/32-35/37-38/40-42/44-50

Abbreviations: Stru (structural character), Aa (amino acid), LRR (leucine-rich repeat domain), TIR (Toll/interleukin-1 receptor domain)



Table 4 – Avian TLR7 differences sites at functional region.

	Stru	Aa (codop)	Avian number	Aa (codoo)	Avian number
Cito		(codon)		(codon)	
51	IDD	E/TTT\	0/11/22 25/22/24/26/48/56/62/62	S(TCT)	5/7/0/11 12/16/10/10/21/22/26/20/22/27 20/42/46/40/51 52/50/60
56	LRR	R(AGA)	0/14/23/36/48/51/52/56/62	$T(\Delta \subset \Delta)$	3/5/7/8/11/13/18-22/24/22/23/37-39/41-43/49/53-55/58-61/63
60	LRR	S(AGT))	0/3/14/36/43/48/56/57/62	T(ACT)	7/13/20/26/29/32/38/39/41/42/44/46/49/53-55/59-61
135	LRR	S(TCA)	0/8/36	T(ACA)	5/7/11/13/18/19/21-29/33/34/37-39/41-44/46/48/49/51-63
149	LRR	K(AAA)	0/36	E(GAA)	3/5/7/8/11-13/16/18-29/32-34/37-39/41-44/46/48/51-63
152	LRR	R(CGG)	0/3/5/12/13/22/23/26/29/32-34/36/38/48/51/52/56/57/62	Q(CAG)	7/8/14/18/19/21/24/25/37/39/42-43/49/53/63
159	LRR	R(CGT)	0/3/14/26/34/36/42/43/56/57/62	S(AGT)	5/7/11-13/16/18/19/21-25/29/32/33/37-39/46/48/49/51-53/59/60/63
175	LRR	T(ACT)	0/14/23/36/56/58/62	N(AAT)	3/7/8/13/16/18/19/21-22/24-26/29/32-34/37-39/42/43/ 46/48-49.51-53/57/63
176	LRR	F(TTT)	0/7/14/23/36/56/62	L(TTG)	3/5/11-13/16/18/19/22/24/25/28/29/32/34/37/38/42/43/46/48/53/57-60/63
213	LRR	N(AAT)	0/3/14/23/34/36/43/51/52/56-58/62	K(AAA)	5/7/8/11/13/16/18/19/21/22/24-26/28/32/33/37-39/ 42/46/48/49/53/59/60/63(12/20/27/29/41/44/54/55/61
216	LRR	V(GTA)	0/14/23/26/33/3652/56/62	I(ATA)	3/5/7/8/11-13/16/18-22/24/25/27/28/32/34/37-39/41-44/46/48/53-55/57- 60/63
244	LRR	R(AGA)	0/12/14/23/27/28/36/56/62	M(ATG)	3/5/7/8/11/13/16/19-22/24-26/29/33/37-39/41/42/46/48/49/53-55/57/59- 61/63
247	LRR	E(GAG)	0/5/14/16/20/23/27/34/36/41/44/51/52/54/56/61/62	V(GTG)	3/7/8/11-13/18/19/21/22/24-26/28/29/32/33/37-39/42/43/46/48/49/55/57- 60/63
248	LRR	V(GTT)	0/13/14/23/36/39/51/52/56/62	I(ATT)	3/5/7/8/11/12/16/18-22/24-29/32-34/37/38/41-44/46/48/49/53-55/57-61/63
298	LRR	K(AAA)	0/14/34/36/41/51/52/54/56/62	N(AAT)	5/7/8/11-13/16/18-22/24-26/28/29/32-33/37/39/42/44/46/48/49/53/55/58- 61/63
321	LRR	K(AAG)	0/5/14/20/23/27-29/36/44/48/55-58/61/62	R(AGG)	3/7/8/11-13/16/18/21/22/24-26/32/33/37-39/41-43/46/49/51-54/59/60/63
341	LRR	E(GAG)	0/14/20-29/32-34/36-39/41/42/54/59/60/62	Q(CAG)	3/5/7/8/11-13/16/18/19/43/44/46/49/51-53/55-58/61/63
418	LRR	I(ATT)	0/7/14/16/20/33/41/53/54/56/62	V(GTT)	3/5/8/11/12/18/19/21-29/32/34/36-39/42-44/46/48/49/51/52/55/57-61/63
428	LRR	R(CGA)	0/18	P(CCA)	3/5/7/812/13/16/19-22/24-29/32-34/36-38/41-44/46/48/49/53-55/57-61/63
429	LRR	S(TCC)	0	A(GCT)	3/8/11-14/16/18-22/24/25/28/29/32-34/36-39/41-44/48/49/51-55/57/59- 61/63
432	LRR	I(ATC)	0/14/23/62	L(CTC)	5/7/8/11-13/19/24/25/29/38/42/46/49/53/59/60
437	LRR	M(ATG)	0/24-26/29	V(GTG)	3/5/7/11-14/16/19-23/27/28/32-34/36-39/41-44/48/49/51-63
445	LRR	G(GGT)	0/3/5/8/14/16/18/21-26/32/33/38/ 39/42/43/48/49/53/56/57/62	S(AGT)	19/46/51/52/59/60/63
528	LRR	F(TTC)	0/8/11/12/14/21-25/33/34/36/37/43/ 46/49/51- 53/56/57/62/63	S(TCC)	5/13/16/18/20/26-29/38/41/42/44/48/54/55/59-61
530	LRR	K(AAA)	0/7/12/14/20/23/27/36/37/41/44/54-56/61/62	R(AGA)	3/5/8/11/13/16/19/21/22/24-26/29/32-34/38/42/43/46/48/49/51-53/57-60/6
573	LRR	K(AAA)	0/3/8/13/14/18-25/27-29/33/34/36-39/41-44/48/53- 56/58/61-63	E(GAA)	16/26/46/49/51/52/57/59/60
596	LRR	S(AGC)	0/14/36/49/56/62	T(ACT)	5/7/8/11/13/16/18/19/22/24-29/38/39/41-43/46/48/51/52/54/55/58/61/63
661	LRR	N(AAT)	0/23/36/39/56/62	S(AGC)	5/7/8/11-13/16/18/20-22/24-29/32-34/37/38/41-43/46/48/49/53-55/57- 60/63(3)
664	LRR	Q(CAA)	0/3/5/7/8/11-13/16/18/19/21-26/29/33/36 /37/39/42/43/46/48/49/52/53/56/59/60/62/63	E(GAA)	20/27/28/32/34/41/44/54/55/57/58/61
671	LRR	M(ATG)	0/14/23/36/56/62	S(TCA)	7/8/13/16/20/24/25/27/29/32/37/41/42/44/49/51/52/54/59/60/61
689	LRR	I(ATA)	0/3/14/34/36/43/51/52/57/62	V(GTC)	12/13/29/46/59/60
694	LRR	S(AGT)	0/3/14/23/36/56/58/62	N(AAT)	7/8/11/13/16/18-22/24-29/33/34/37/39/41-44/46/48/49/51-55/57/59/60/63
697	LRR	L(TTG)	0/12/14/23/28/36/43/51/52/56/58/61/62	M(ATG)	5/7/8/16/19/22/24-26/29/32/37-39/42/46/48/53/63
698	LKK	H(CAC)	0/36	K(AAG)	3/5///11-14/18-29/32/33/34/3/-39/41-44/46/48/49/51-63
726	LRR	r(CGA)	0/3/11/36/43/57/62 0/3/7/13/14/16/18/22-26/28/29/33/36/ 27/20/14/24/6/18/22-26/28/29/33/36/	Q(CAA)	5/8/12-14/18/20-29/33/3//38/41/42/44/46/48/49/53-56/58-61/63 5/8/12/21/27/32/38/43/59/60/63
727	IRR	K(AAG)	0/1/23/36/62	E(GAA)	3/5/7/8/11/-13/16/18-22/26/28/29/32-34/37-30/41-44/48/40/51-55/57 61/62
732		T(ACT)	0/14/23/30/02	S(TCT)	3/5/7/8/11_13/16/18/19/21/22/24/23/52-54/57-59/41-44/46/43/51-55/57-61/05
152	LINIX	1(ACT)	0/14/20/20/2///00/4//4/3//02/00/02	5(101)	61/63
739	LRR	I(ATA)	0/3/7/14/23/34/36/56/57/62	M(ATG)	5/8/11/-13/16/18-22/24-29/33/37-39/42/43/46/48/49/53/55/58-61
744	LRR	R(CGT)	0/14/20/23/29/36/57/58/62/	H(CAC)	18/32-34/37/51/59/60
748	LRR	I(ATA)	0/14/23/36/44/62	L(CTA)	3/7/8/11/-13/16/18/19/21/22/24-29/32/34/37-39/41-43/46/48/49/51-54/57- 60/63
751	LRR	Y(TAT)	0/7/13/14/20/23-27/36/44/46/51/52/55 /56/61/62	H(CAT)	3/5/8/11/12/16/18/19/21/22/28/29/32-34/37-39/41-43/48/49/53/54/57-60/63
757	LRR	I(ATT)	0/14/23/36/44/51/52/56/62/	F(TTT)	3/5/7/8/11-13/16/18-22/24-29/32-34/37-39/41-43/46/48/49/53- 55/57/58/61/63
771	LRR	I(ATA)	0/3/5/7/8/13/14/18/19/21/22/26/27/29/33/34/36/37/39/41- 44/48/49/51-57/59-63	V(GTA)	12/20/23-25/28/46

Abbreviations: Stru (structural character), Aa (amino acid), LRR (leucine-rich repeat domain).