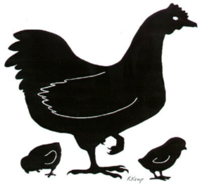
Signatures of positive adaptive selection at candidate genes for genetic resistance to avian viral diseases

Sheila Ommeh (*KU, ILRI*), Daniel Masiga (*KU, ICIPE*), David Lynn (*TCD*), Han Jianlin (*ILRI*) & Olivier Hanotte (*ILRI*)



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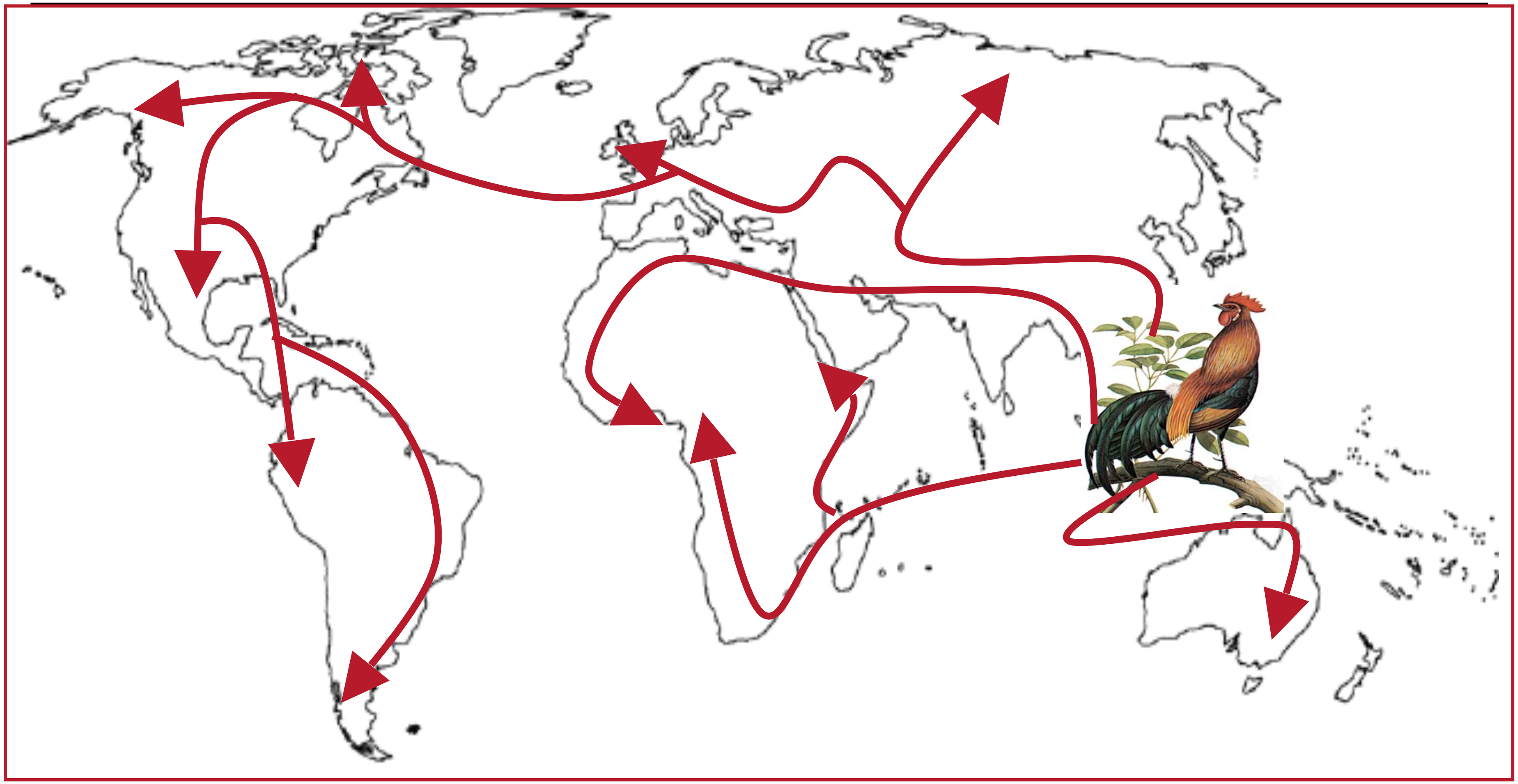
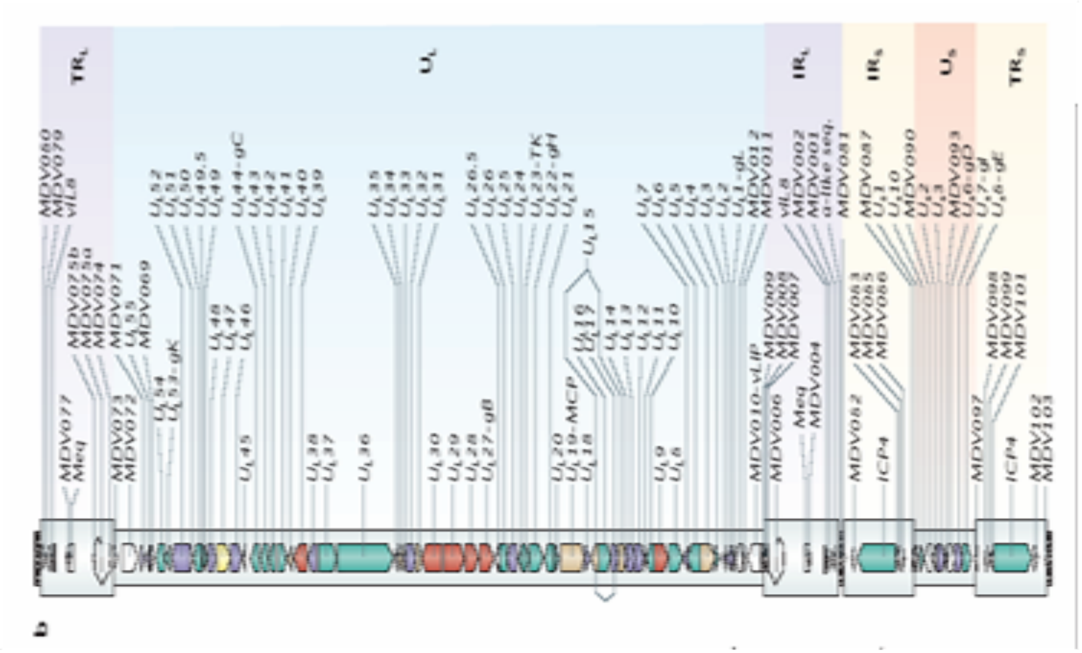
Chicken origin and domestication



Breeding of chicken

Avian tumors



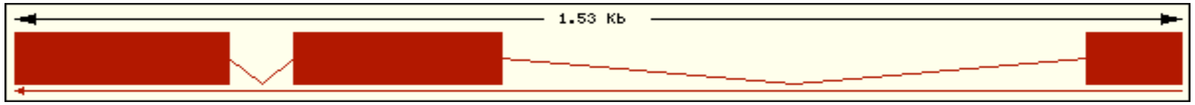
MDV: *ds*DNA virus

Family: herpesviridae

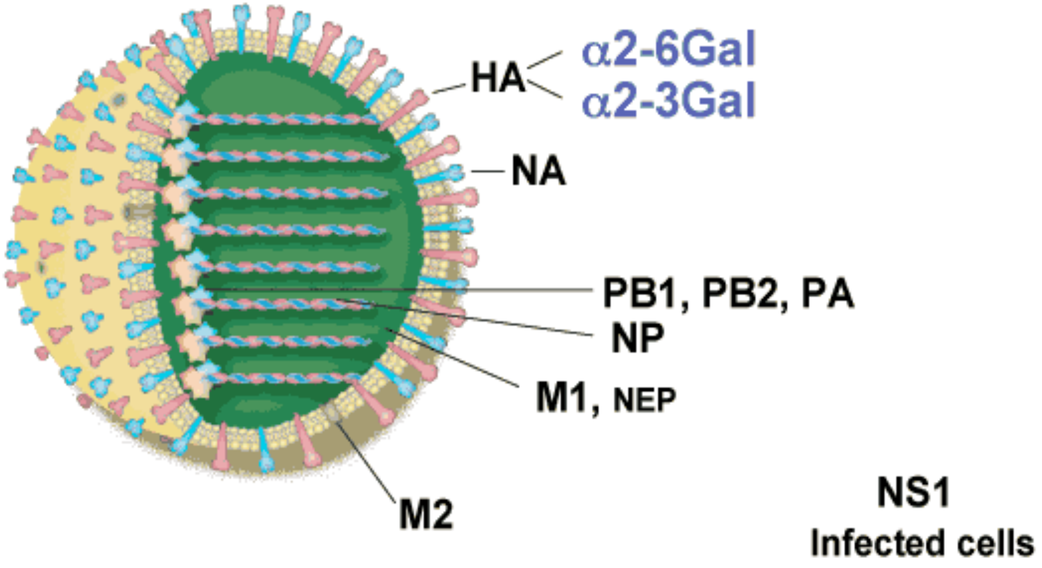
Genus: mardivirus

causes Marek’s disease

Candidate genes including BLB genes in MHC region confer resistance to MD (Juul-Madsen *et al.*, 2000)



Avian influenza



AIV: -ve *ss*RNA
Family: Orthomyxoviridae
Genus: Influenza A
Causes AI

Mx gene is a putative candidate gene to resistance to avian influenza (Ko *et al.*, 2002, 2004)

Study Objective

Search for signatures of selection present at candidate genes implicated in disease resistance to avian tumors, and avian influenza

in silico analysis

1. Species homologs of Mx (41) and BLB (35)

   NCBI Genbank & protein databases

2. Reciprocal BLAST

3. MSA & phylogeny

   T-coffee, Genedoc, MEGA, MrBayes

4. Phylogenetic Analysis by Maximum Likelihood

   http://abacus.gene.ucl.ac.uk/software/paml.html

5. RASMOL

   3D view of amino acid sites under selection

PAML codon Models

$dN/dS = \omega$ (Yang, 1998)

CODEML

Lineage models

M0: one ratio model

M1: free ratio model

(Yang, 1998)

Amino acid site models

M7: β

M8: β and ω

(Nielsen and Yang, 1998)

Likelihood ratio test (LRT):

Lineage models:
LRT =
2 (*lnl*M0 - *lnl*M1)
χ_2 (*N-1 d.f.*)

Site Models
LRT =
2 (*lnl*M7 - *lnl*M8)
χ_2 (*N-1 d.f.*)

$\omega = 1$	Neutral selection
$\omega > 1$	Positive selection
$\omega < 1$	Purifying selection

Site Model: Bayes Empirical Bayes (BEB) > 95%

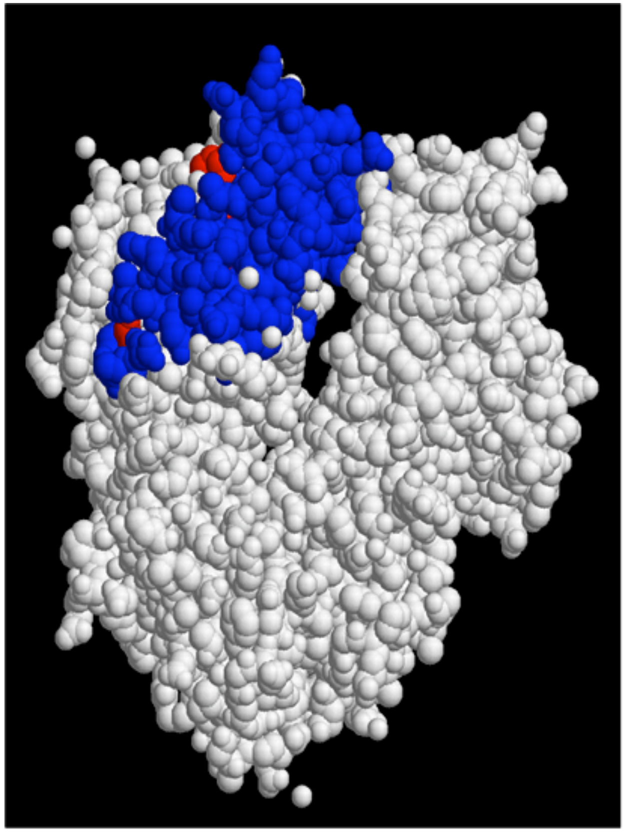
BLB gene

Likelihood ratio test (LRT) to detect adaptive evolution in BLB genes

Models	2Δl	X² Value	d.f.	p-value
Lineage analysis (M0 vs M1)	2(-8602.66-8522.23)	160.86	66	<0.0010
Site analysis (M7 vs M8)	2(-8253.47-8182.46)	142.018	2	<0.0010

BLB gene Lineage analysis; ώ values shown on lineages

BLB Amino acid site analysis



Bayes Empirical Bayes (BEB) analysis

Positively selected sites (*: P > 95%; **: P > 99%)

Position	Amino acid	Pr (w > 1)	post mean ± SE for w
2	Tyrosine	0.989*	3.823 ± 0.607
3	Serine	1.000**	3.868 ± 0.558
5	Glycine	1.000**	3.868 ± 0.558
49	Valine	1.000**	3.868 ± 0.558
59	Isoleucine	0.993**	3.839 ± 0.589
62	Aspartate	0.974*	3.775 ± 0.700
78	Valine	1.000**	3.868 ± 0.558

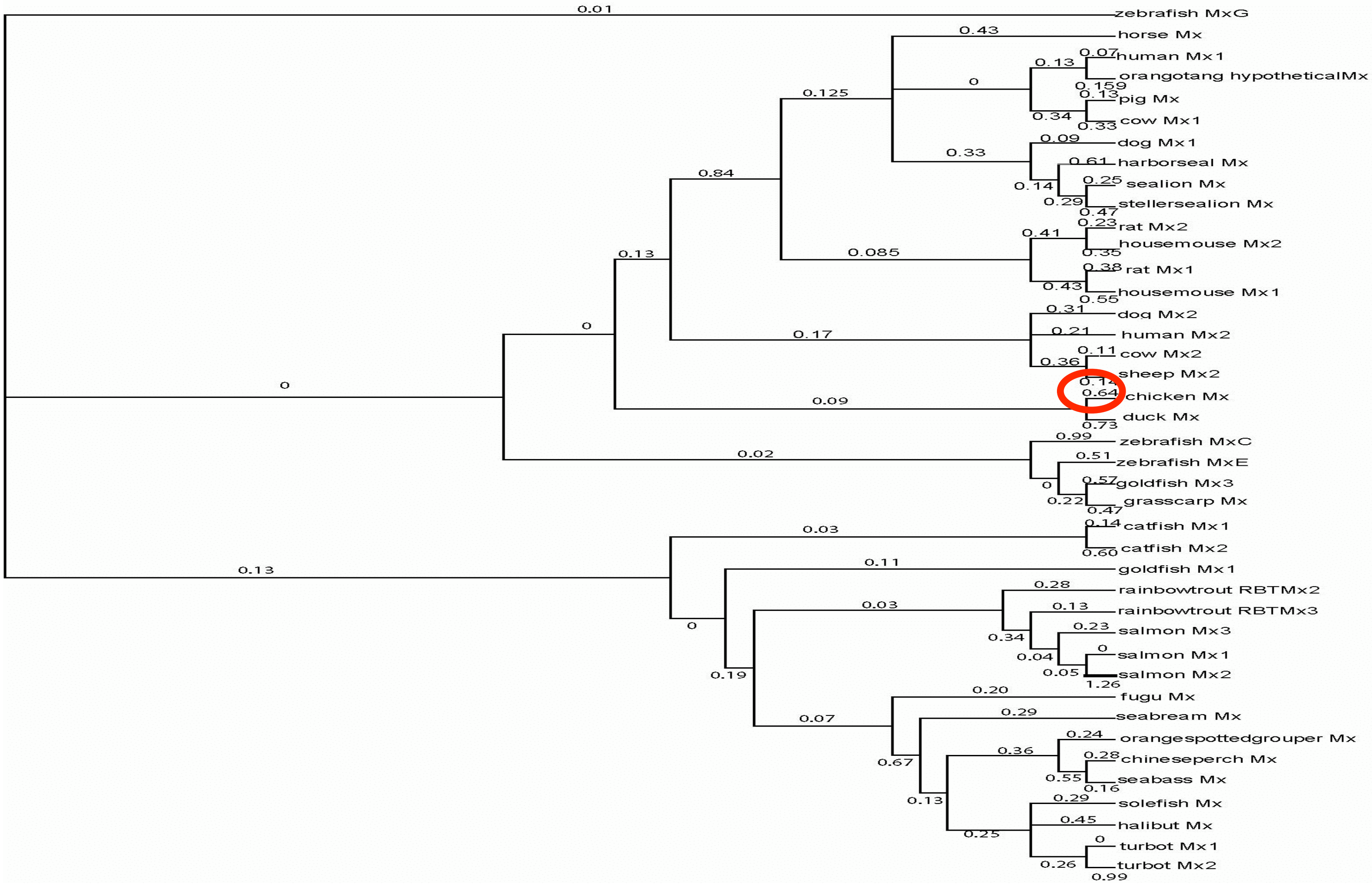
Three dimensional structure of MHC class ii protein (PDB id: ILDH)

Mx gene

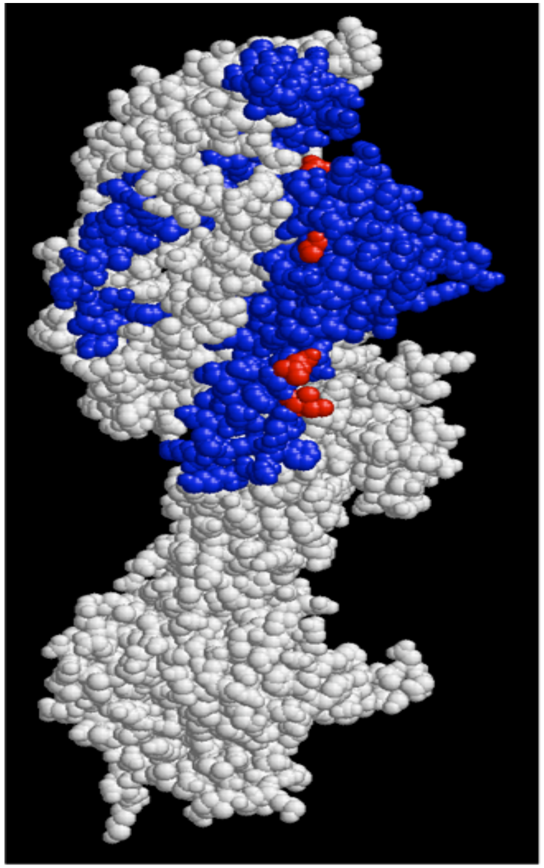
Likelihood ratio test (LRT) to detect adaptive evolution in Mx gene

Models	**$2\Delta l$**	**χ^2 Value**	**d.f.**	**p-value**
Lineage analysis (M0 vs M1)	2(-34017.99-33715.58)	604.8	75	<0.0010
Site analysis (M7 vs M8)	2(-32529.69-32507.88)	43.63	2	<0.0010

Mx gene lineage analysis;
ώ values shown on lineages



Mx Amino acid site analysis



Bayes Empirical Bayes (BEB) analysis

Positively selected sites (*: P > 95%; **: P > 99%)

Position	amino acid	Pr (w > 1)	post mean ± SE for w
321	Serine	0.956*	1.475 ± 0.127
368	Alanine	0.957*	1.476 ± 0.125
372	Methionine	1.000**	1.501 ± 0.035
386	Asparagine	0.985*	1.492 ± 0.079
444	leucine	0.990*	1.495 ± 0.0067

Three dimensional structure of the GTPase protein (PDB id: IJX2)

Key Conclusions

BLB gene:

- High *dN* at chicken lineage
- Signature of adaptive evolution at PBR

Mx gene:

- Most lineages conserved
- CID under adaptive evolution

Future studies

- SW-CODEML & branch-site models
- Assess SNPs within PBR and CID domains
- Population genetic studies at PBR and CID
- Simulation: immune response genes

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