Gephebase Gene	60	GephelD
Na/K-ATPase alpha-subunit (https://www.gephebase.org/search-criteria?/and+Gene Gephebase=^Na/K-ATPase alpha-subunit^#gephebase-summary-title)	GP00002361	Main curator
Entry Status Draft	Courtier	
PHENOTYPIC CHANGE		
Trait Category		
Physiology (https://www.gephebase.org/search-criteria?/and+Trait Category=^Physiology^#gephebase-summary-title)		
Trait		
Xenobiotic resistance (cardiac glycosides) (https://www.gephebase.org/search-		
criteria?/and+Trait=^Xenobiotic resistance (cardiac glycosides)^#gephebase-summary-title) Trait State in Taxon A		
- Trait State in Taxon B		
-		
Ancestral State Taxon A		
Taxonomic Status		
Interspecific (https://www.gephebase.org/search-criteria?/and+Taxonomic Status=^Interspecific^#gephebase-summary-title)		
Taxon A	Taxon B	
Latin Name	_	Latin Name
Common Name		Common Name
- Synonyms	-	Synonyms
- Rank	-	Rank
-	-	
Lineage -		Lineage
Parent -	<u>-</u>	Parent
NCBI Taxonomy ID		NCBI Taxonomy ID
- is Taxon A an Infraspecies?	-	is Taxon B an Infraspecies?
No	No	
GENOTYPIC CHANGE		
Generic Gene Name		UniProtKB Danaus plexippus
K+ ATPase alpha subunit	R4ZHW8 (http://www.uniprot.org/uniprot/R4ZHW8)	
Synonyms Na+	0	GenebankID or UniProtKB
String	·	
- Sequence Similarities		
Belongs to the cation transport ATPase (P-type) (TC 3.A.3) family. Type IIC subfamily. GO - Molecular Function		
GO:0005524 : ATP binding (https://www.ebi.ac.uk/QuickGO/term/GO:0005524)		
GO:0046872 : metal ion binding (https://www.ebi.ac.uk/QuickGO/term/GO:0046872)		
GO:0005391 : sodium:potassium-exchanging ATPase activity (https://www.ebi.ac.uk/QuickGO/term/GO:0005391)		
GO - Biological Process		
- GO - Cellular Component		
GO:0016021 : integral component of membrane		
(https://www.ebi.ac.uk/QuickGO/term/GO:0016021)		Presumptive Null
$No\ (https://www.gephebase.org/search-criteria?/and+Presumptive\ Null=^No^\#gephebase-sungle-criteria.)$	nmary-title)	·
Coding (https://www.gephebase.org/search-criteria?/and+Molecular Type=^Coding^#gepheb	vase-summary-title)	Molecular Type
_ , , , , , , , , , , , , , , , , , , ,	• •	Aberration Type

SNP Coding Change

 $SNP \ (https://www.gephebase.org/search-criteria?/and+Aberration \ Type=^SNP^\#gephebase-summary-title)$

Experimental Evidence

 $Candidate\ Gene\ (https://www.gephebase.org/search-criteria?/and+Experimental\ Evidence=^Candidate\ Gene^*\#gephebase-summary-title)$

	Taxon A	Taxon B	Position
Codon	-	-	-
Amino-acid	-	-	-

Main Reference

 $Concerted \ evolution \ reveals \ co-adapted \ amino \ acid \ substitutions \ in \ NaK-ATP as \ of \ frogs \ that \ prey \ on \ toxic \ toads. \ (2021) \ (https://pubmed.ncbi.nlm.nih.gov/33887183)$

Authors

Mohammadi S; Yang L; Harpak A; Herrera-Ālvarez S; Del Pilar RodrĀguez-Ordo±ez M; Peng J; Zhang K; Storz JF; Dobler S; Crawford AJ; Andolfatto P

Abstract

Although gene duplication is an important source of evolutionary innovation, the functional divergence of duplicates can be opposed by ongoing gene conversion between them. Here, we report on the evolution of a tandem duplication of Na, K-ATPase subunit $\hat{l}\pm 1$ (ATP1A1) shared by frogs in the genus Leptodactylus, a group of species that feeds on toxic toads. One ATP1A1 paralog evolved resistance to toad toxins although the other retained ancestral susceptibility. Within species, frequent non-allelic gene conversion homogenized most of the sequence between the two copies but was counteracted by strong selection on 12 amino acid substitutions that distinguish the two paralogs. Protein-engineering experiments show that two of these substitutions substantially increase toxin resistance, whereas the additional 10 mitigate their deleterious effects on ATPase activity. Our results reveal how examination of neo-functionalized gene duplicate evolution can help pinpoint key functional substitutions and interactions with the genetic backgrounds on which they arise.

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