

## GEPHE SUMMARY

**Gephebase Gene**  
pepsinogen A1

**Entry Status**  
Published

**GepheID**  
GP00001917

**Main curator**  
Courtier

## PHENOTYPIC CHANGE

**Trait Category**  
Physiology

**Trait**  
Digestion (absence of stomach)

**Trait State in Taxon A**  
presence of stomach and gastric acid production

**Trait State in Taxon B**  
loss of stomach and no gastric acid production

**Ancestral State**  
Taxon A

**Taxonomic Status**  
Intergeneric or Higher

### Taxon A #1

**Latin Name**  
*Gadus morhua*

**Common Name**  
Atlantic cod

**Synonyms**  
Atlantic cod; Gadus morhua Linnaeus, 1758

**Rank**  
species

**Lineage**  
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii; Teleostei; Osteoglossocephalai; Clupeccephala; Euteleostomorpha; Neoteleostei; Eurypterygia; Ctenosquamata; Acanthomorphata; Paracanthomorphacea; Zeiogadaria; Gadariae; Gadiformes; Gadoidei; Gadidae; Gadus

**Parent**  
Gadus () - (Rank: genus)

**NCBI Taxonomy ID**  
8049

**is Taxon A an Intraspecies?**  
No

### Taxon B

**Latin Name**  
*Danio rerio*

**Common Name**  
zebrafish

**Synonyms**  
Brachydanio rerio; Brachydanio rerio frankei; Cyprinus rerio; Danio frankei; Danio rerio frankei; zebrafish; leopard danio; zebra danio; zebra fish; Cyprinus rerio Hamilton, 1822; Danio rerio (Hamilton, 1822); Brachidanio rerio

**Rank**  
species

**Lineage**  
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii; Teleostei; Osteoglossocephalai; Clupeccephala; Otomorpha; Ostariophysii; Otophysi; Cypriniphysae; Cypriniformes; Cyprinoidei; Cyprinidae; Danio

**Parent**  
Danio () - (Rank: genus)

**NCBI Taxonomy ID**  
7955

**is Taxon B an Intraspecies?**  
No

### Taxon A #2

**Latin Name**  
*Gasterosteus aculeatus*

**Common Name**  
three-spined stickleback

**Synonyms**  
three-spined stickleback; three spined stickleback; Gasterosteus aculeatus Linnaeus, 1758

**Rank**  
species

**Lineage**  
cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii; Teleostei; Osteoglossocephalai; Clupeccephala; Euteleostomorpha; Neoteleostei; Eurypterygia; Ctenosquamata; Acanthomorphata; Euacanthomorphacea; Percormorphaceae; Eupercaria; Perciformes; Cottioidei; Gasterosteales; Gasterosteidae; Gasterosteus

**Parent**  
Gasterosteus () - (Rank: genus)

**NCBI Taxonomy ID**  
69293

is Taxon A an Intraspecies?

No

### Taxon A #3

Latin Name

*Oreochromis niloticus*

Common Name

Nile tilapia

Synonyms

*Oreochromis nilotica*; *Tilapia nilotica*; Nile tilapia; *Oreochromis niloticus* (Linnaeus, 1758)

Rank

species

Lineage

cellular organisms; Eukaryota; Opisthokonta; Metazoa; Eumetazoa; Bilateria; Deuterostomia; Chordata; Craniata; Vertebrata; Gnathostomata; Teleostomi; Euteleostomi; Actinopterygii; Actinopteri; Neopterygii; Teleostei; Osteoglossocephalai; Clupeocephala; Euteleostei; Neoteleostei; Eurypterygia; Ctenosquamata; Acanthomorpha; Euacanthomorpha; Percormorpha; Ovalentaria; Cichlomorpha; Cichliformes; Cichlidae; African cichlids; Pseudocrenilabrinae; Oreochromini; Oreochromis

Parent

*Oreochromis* () - (Rank: genus)

NCBI Taxonomy ID

8128

is Taxon A an Intraspecies?

No

## GENOTYPIC CHANGE

Generic Gene Name

PGA4

UniProtKB Homo sapiens

P0DJD7

Synonyms

-

GenebankID or UniProtKB

String

9606.ENSP00000367391

Sequence Similarities

Belongs to the peptidase A1 family.

GO - Molecular Function

GO:0004190 : aspartic-type endopeptidase activity

GO - Biological Process

GO:0006508 : proteolysis

GO:0044267 : cellular protein metabolic process

GO:0007586 : digestion

GO:0030163 : protein catabolic process

GO - Cellular Component

GO:0070062 : extracellular exosome

GO:0097486 : multivesicular body lumen

Presumptive Null

Yes

Molecular Type

Gene Loss

Aberration Type

Deletion

Deletion Size

-

Molecular Details of the Mutation

Absence of the gene in the genome sequence - high synteny

Experimental Evidence

Candidate Gene

Main Reference

Recurrent gene loss correlates with the evolution of stomach phenotypes in gnathostome history. (2014)

Authors

Castro LF; GonÁsalves O; Mazan S; Tay BH; Venkatesh B; Wilson JM

### Abstract

The stomach, a hallmark of gnathostome evolution, represents a unique anatomical innovation characterized by the presence of acid- and pepsin-secreting glands. However, the occurrence of these glands in gnathostome species is not universal; in the nineteenth century the French zoologist Cuvier first noted that some teleosts lacked a stomach. Strikingly, Holocephali (chimaeras), dipnoids (lungfish) and monotremes (egg-laying mammals) also lack acid secretion and a gastric cellular phenotype. Here, we test the hypothesis that loss of the gastric phenotype is correlated with the loss of key gastric genes. We investigated species from all the main gnathostome lineages and show the specific contribution of gene loss to the widespread distribution of the agastric condition. We establish that the stomach loss correlates with the persistent and complete absence of the gastric function gene *kit-H(+)/K(+)-ATPase* (*Atp4A* and *Atp4B*) and pepsinogens (*Pga*, *Pgc*, *Cym*)--in the analysed species. We also find that in gastric species the pepsinogen gene complement varies significantly (e.g. two to four in teleosts and tens in some mammals) with multiple events of pseudogenization identified in various lineages. We propose that relaxation of purifying selection in pepsinogen genes and possibly proton pump genes in response to dietary changes led to the numerous independent events of stomach loss in gnathostome history. Significantly, the absence of the gastric genes predicts that reinvention of the stomach in agastric lineages would be highly improbable, in line with Dollo's principle.

### Additional References

## RELATED GEPHE

### Related Genes

4 (*ATP4A*, *ATP4B*, pepsinogen A2, pepsinogen A3)

### Related Haplotypes

No matches found.

## COMMENTS

There are three pepsinogen A genes in teleost fishes - their nomenclature and phylogenetic relationships are different from Mammals pepsinogen genes