Viral hemorrhagic septicemia (VHS):
recent advance in molecular characterization

Argelia Cuenca, Niels Jørgen Olesen

Viral Haemorrhagic Septicaemia virus (VHSV)

- Isolated from first time from fresh water cultured rainbow trout,
- To date it has been found in more than 80 marine and fresh water species
- Assumed to be endemic among many marine and anadromous fish species in the north hemisphere

- Family: Rhabdovirus, Genus: Novirhabdoviridae

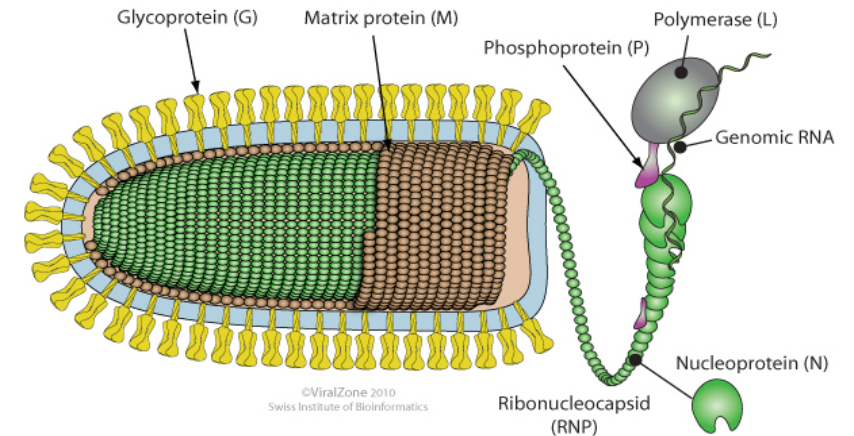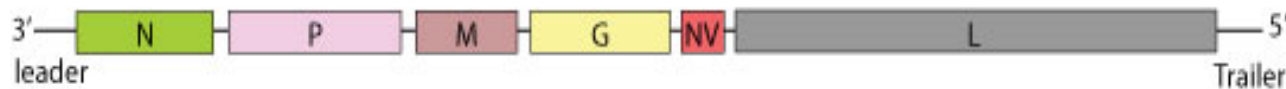- Negative ssRNA virus with a linear genome of about 11 kb
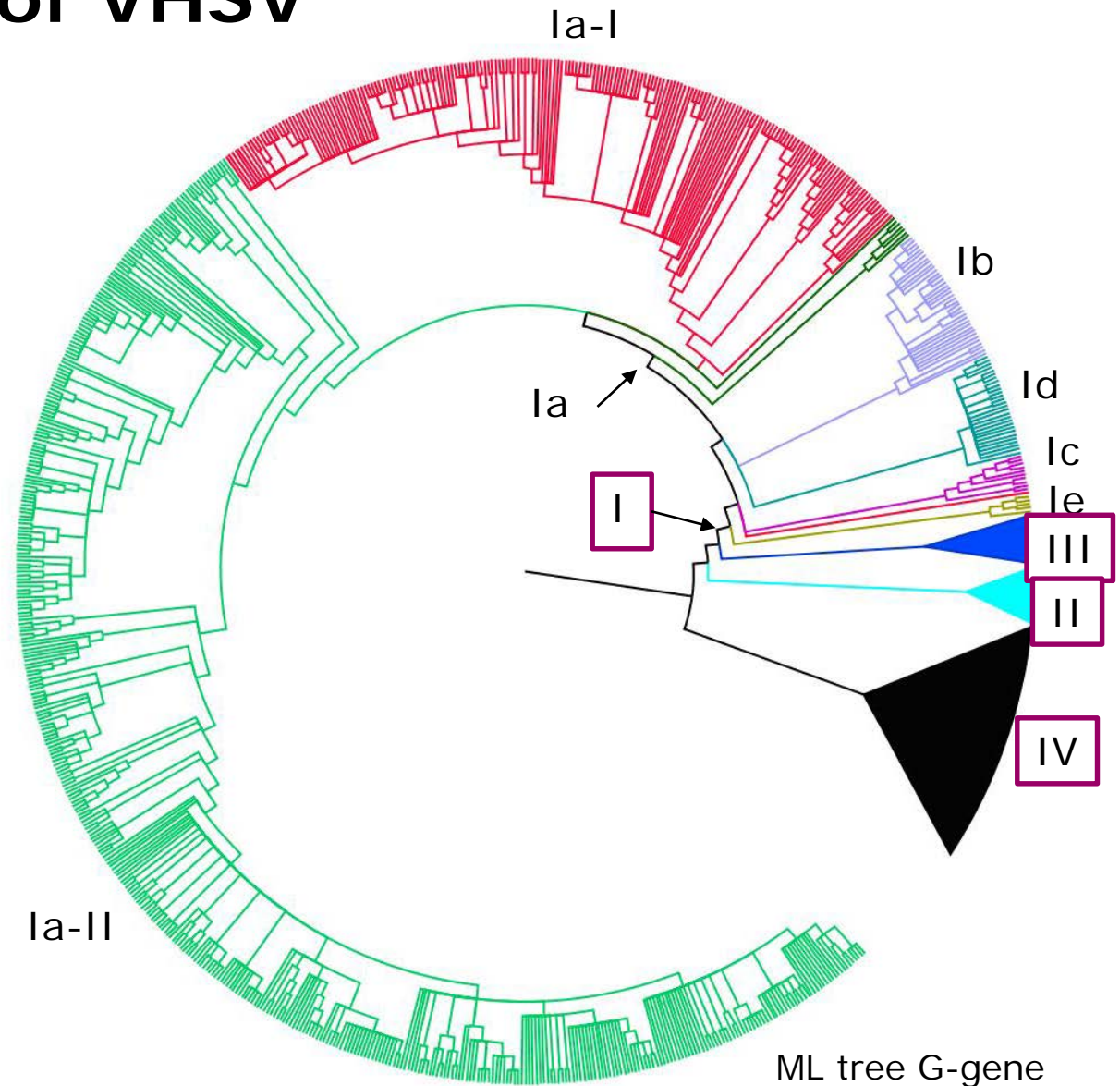
Illustration from Viral Zone

Molecular characterization of VHSV

- Genotype classification based on the glycoprotein

    – Four genotypes:
        - I, II, III, IV

    – Eight subgenotypes:
        - Ia, Ib, Ic, Id, Ie, IVa, IVb, Ivc

    – Two groups:
        - Ia-1, Ia-2,
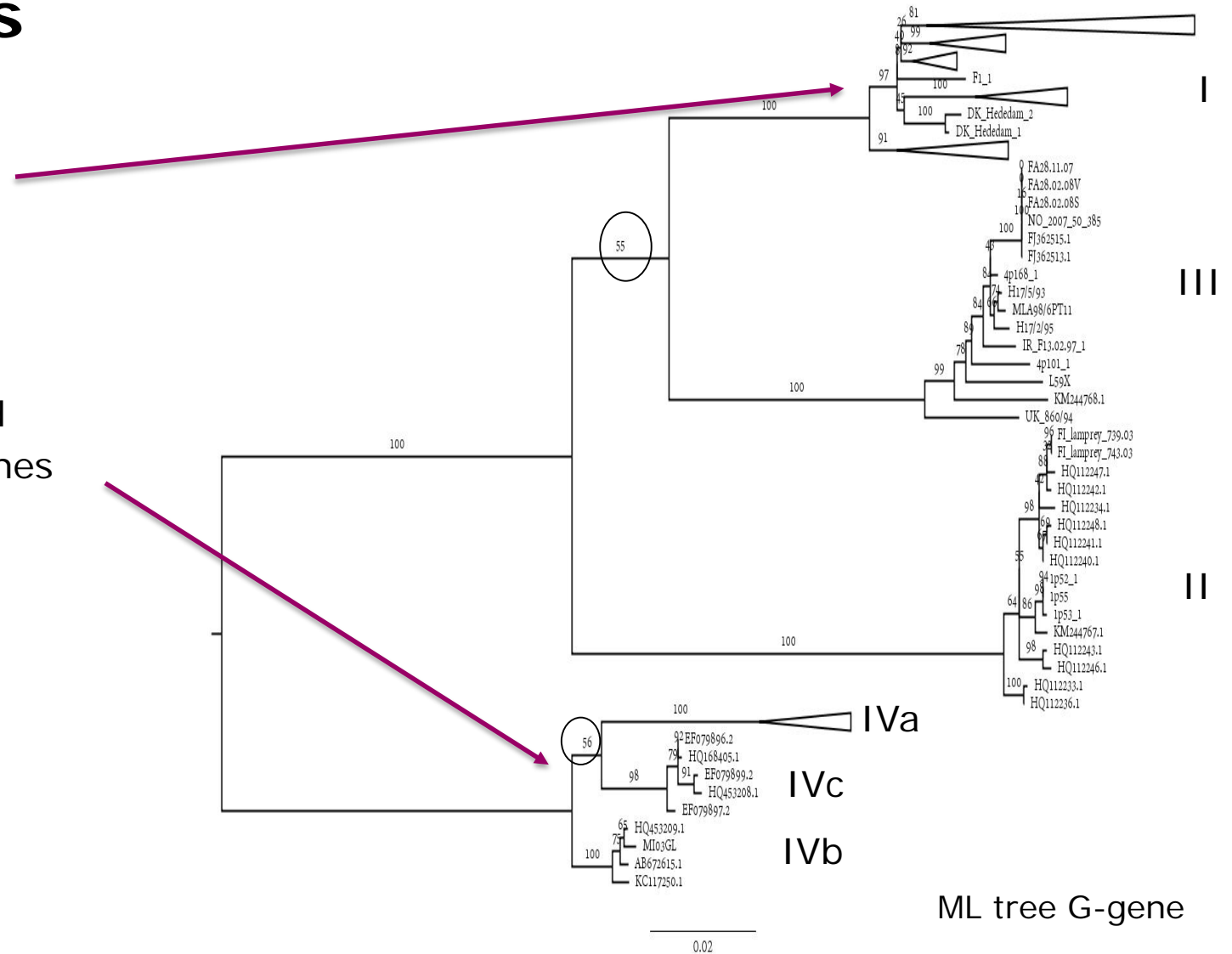
Subgenotype IVd (lumpfish 2015)

Subgenotype If and clades Ia-3 and Ia-4

(Schönherz et al. 2018)

ML tree G-gene

Unresolved questions

- Phylogenetic relationship among I subgenogroups
  - Very rapid radiation

- Placement of subgenotypes IVc and IVd
  - Conflicting signal using different genes
    - Taxon sampling?

ML tree G-gene

Datasets

- In the frame of NOVIMARK project:
  - 112 full genome sequences
  - representatives of all genotypes, except Id

- Consensus sequences:
  - annotated (in house database and scripts)
  - aligned MATTF (v7.388)

- Dataset characteristics
  - Size and coverage variation in their leader and trailer parts of the genome (as a result of assembling strategy)
  - Size variation in intergenic regions

- Dataset was pruned to include protein coding regions only
  - 118 taxa
  - 10323 nt

- Coding regions were analysed individually and with the six regions concatenated.

Phylogenetic analysis based in the whole genome

Whole genome analysis:

Largely consistent with phylogeny using G-gene,
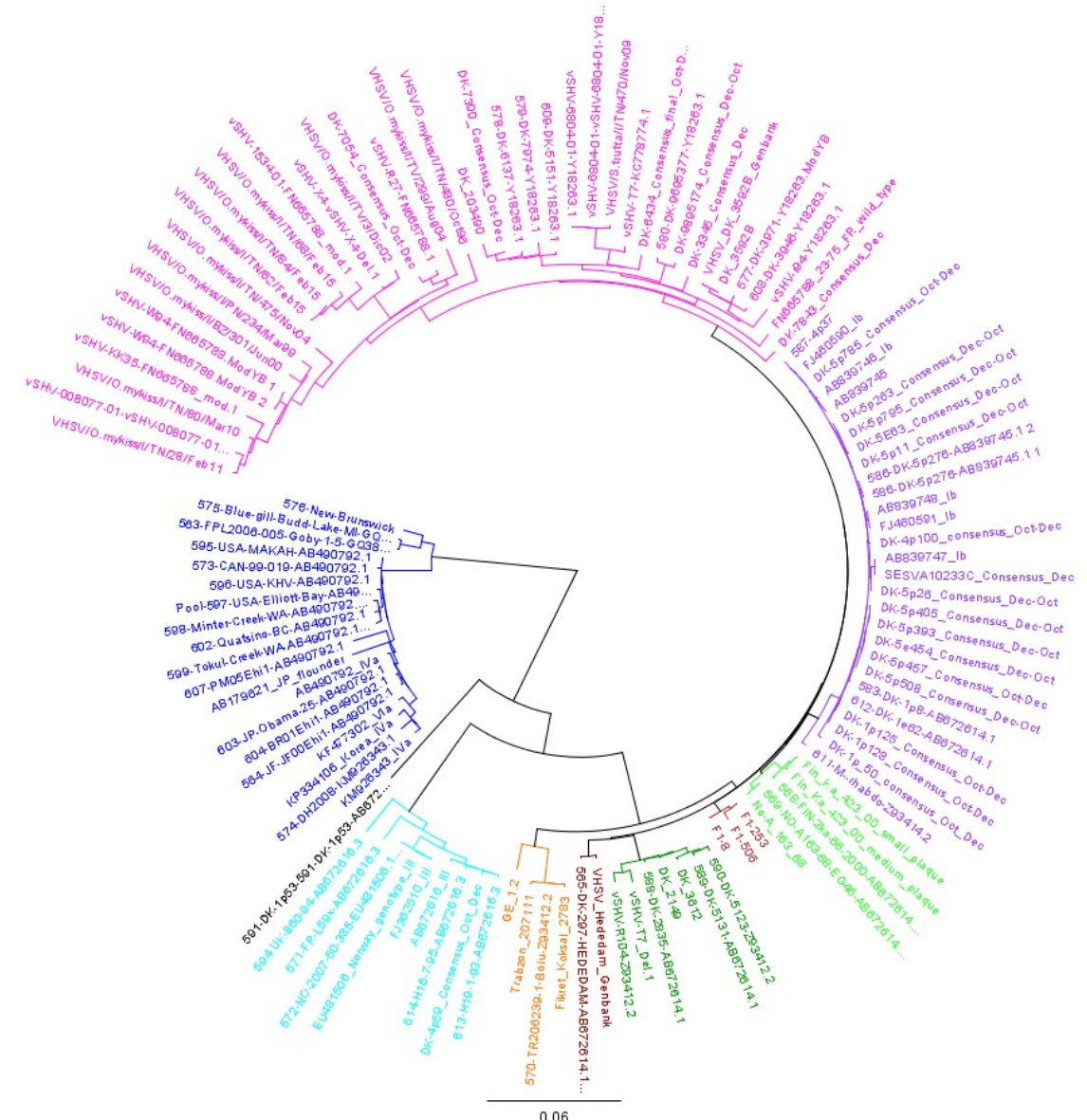
Except small changes genotype IV

Individual gene analyses:

- Somehow (strong) phylogenetic incongruences depending of which coding region was using for the analysis

- But most of the incongruence was caused by some few isolates

ML tree -RAxML (v. 8.2.11)

100 bootstrap replicates

Tree rooted with genotype IV

Whole genome dataset:
Analysis of topological incongruence – GARD

BPs	AIC$_c$	Δ AIC$_c$	Segments
0	110684.92		1 - 10323
1	110627.93	56.99	1 - 3620 / 3621 - 10323

Topological incongruence report ℹ

Breakpoints	LHS p-value	RHS p-value	Significance
3621	0.0002	0.9182	

Comparing the AIC$_c$ score of the best fitting GARD model, that allows for different topologies between segments (110627.9), and that of the model that assumes the same tree for all the partitions inferred by GARD the same tree, but allows different branch lengths between partitions (110814.4) suggests that because the multiple tree model can be preferred over the single tree model by an evidence ratio of 100 or greater, *at least of one of the breakpoints reflects a true topological incongruence.*
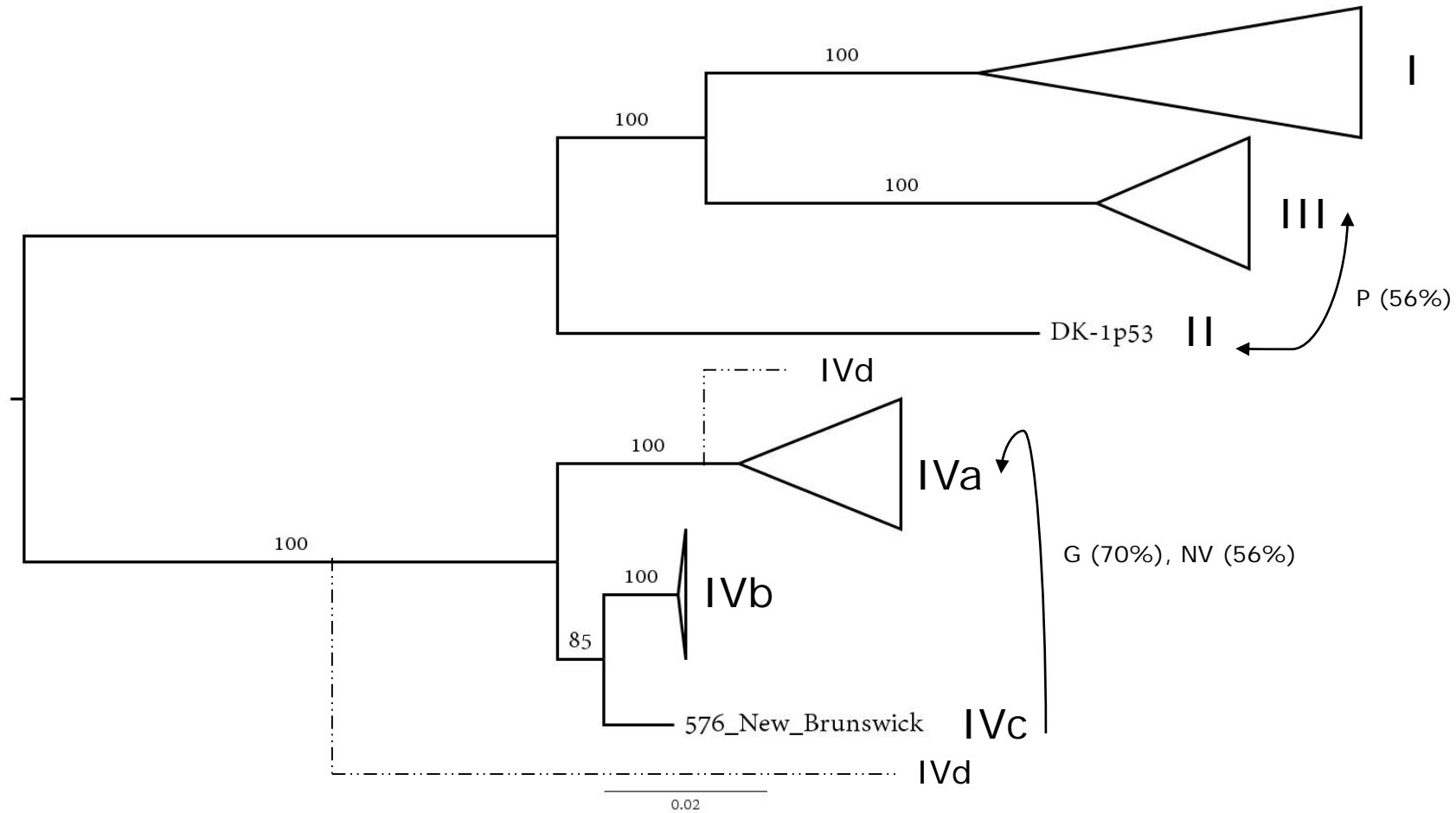
Removed all "recombinant" sequences – further exploration
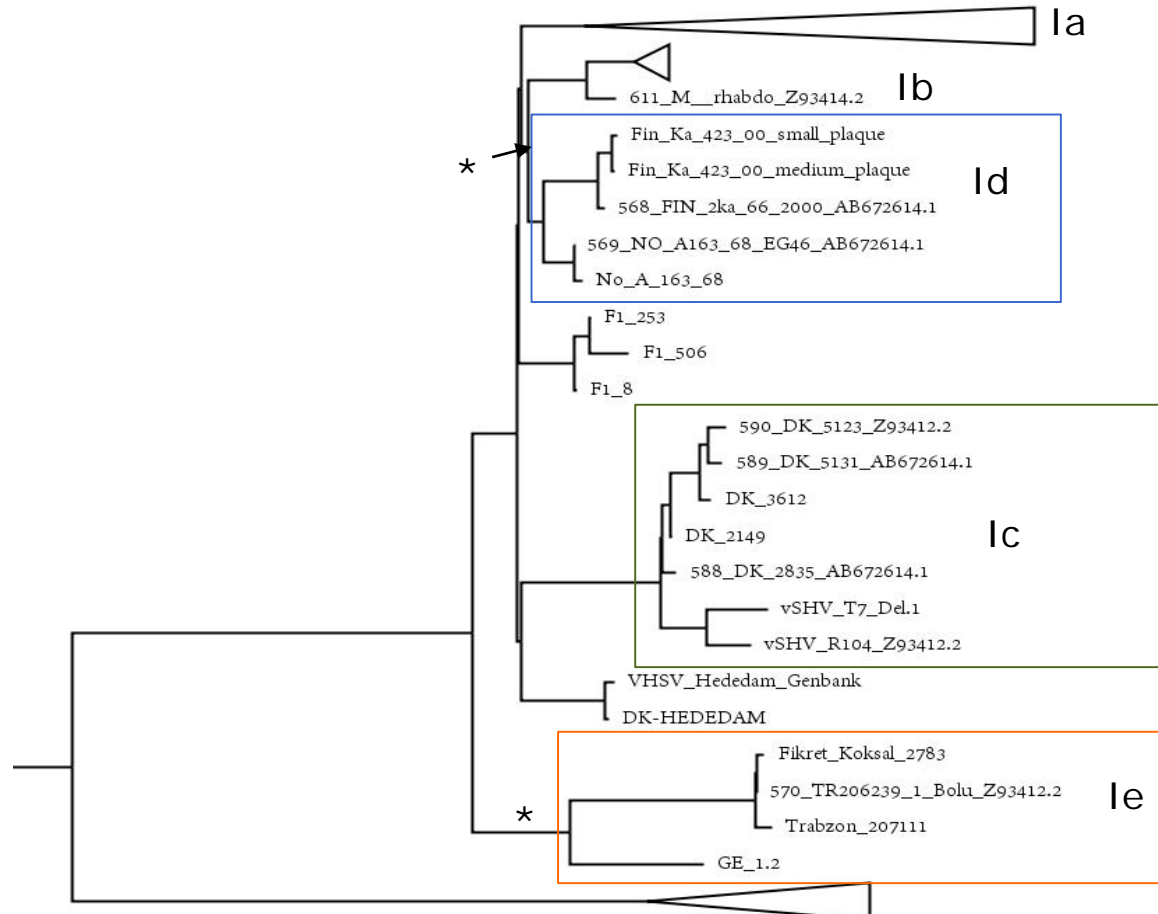
Phylogenetic consistency among genes

- Using a panel of <u>16 isolates</u>, the same overall phylogenetic typing was found with the N, G and Nv gene (Einer-Jensen et al. 2005)
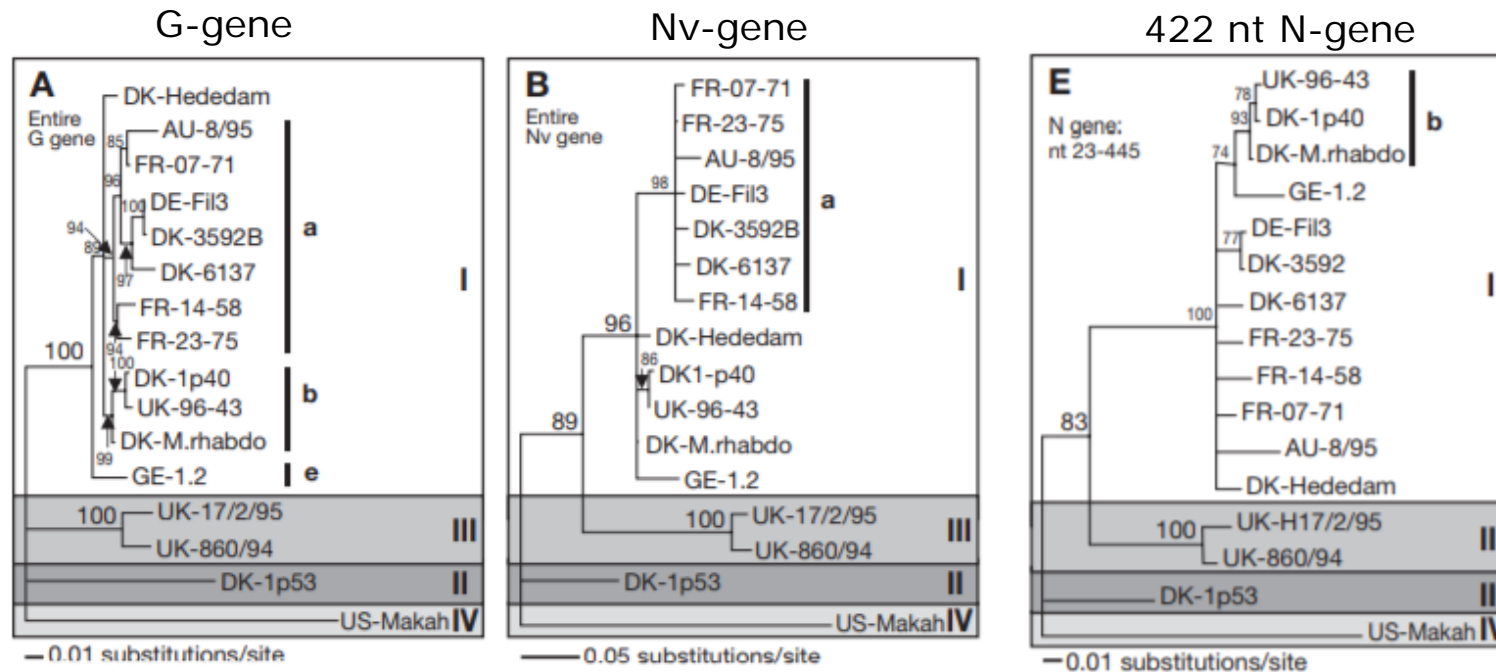
Whole genome analysis:
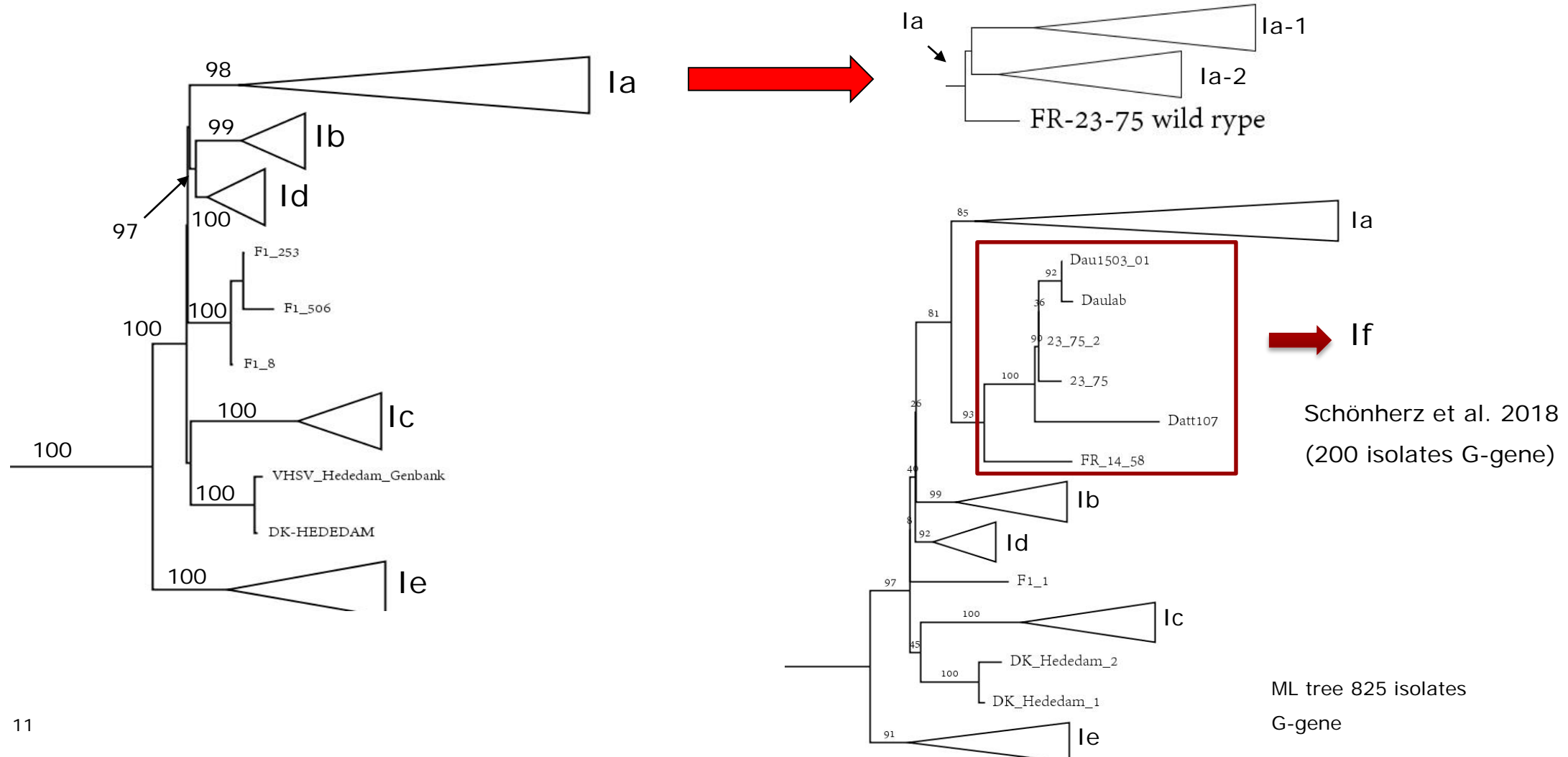# Relationship among genotypes

Whole genome analysis: Relationships among genotype I subgroups
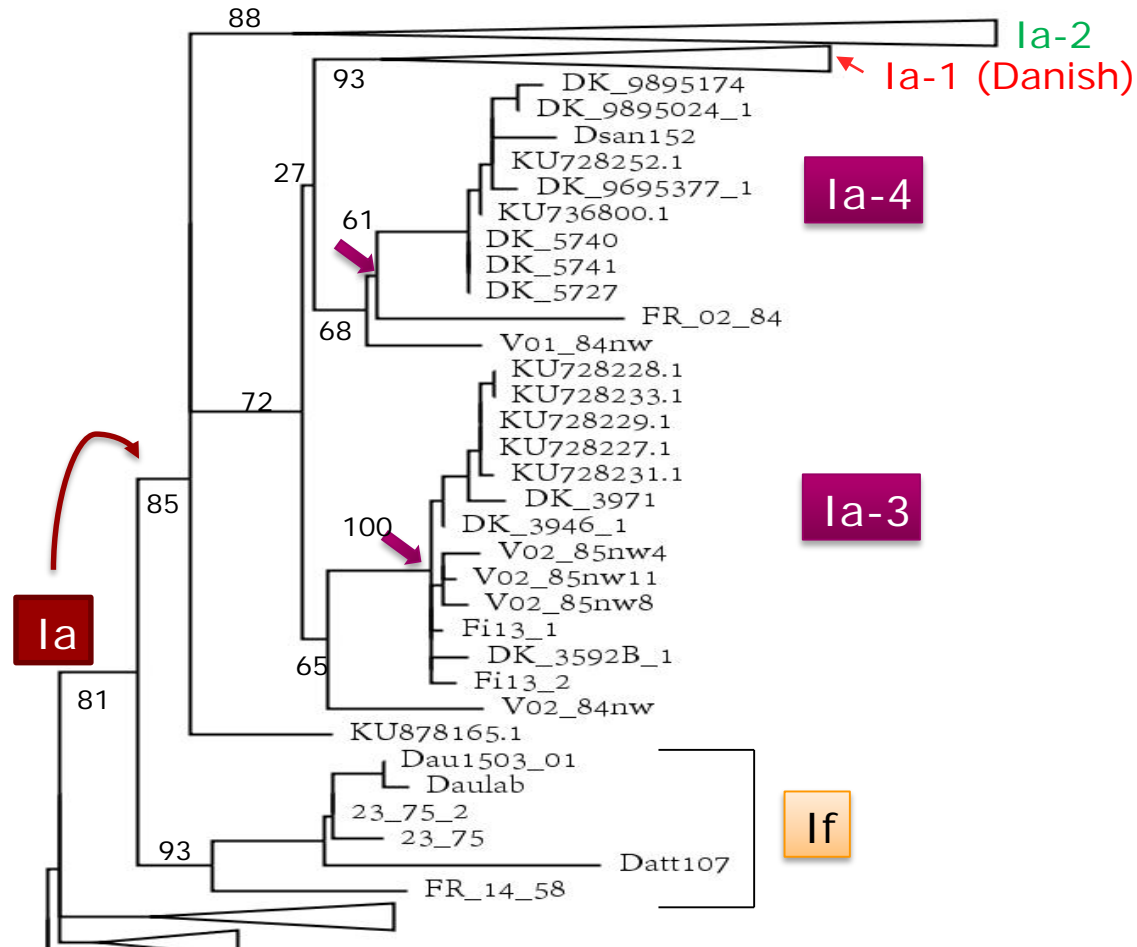

- Supported relationships:

- All subgroups monophyletic

- Genotype Ie first branching group

- Genotypes Ib and Id are sister groups

Whole genome analysis:
Relationships among genotype I subgroups

Schönherz et al. 2018
(200 isolates G-gene)

ML tree 825 isolates
G-gene

New classification within Ia – is this necessary?

New clades proposed by:

Schönherza A, Forsberg K, Guldbrandtsen B, Buitenhuisa AJ, K. Einer-Jensen.

Journal of Virology, In press

ML tree, G-gene

Thank you

Origin of VHSV

- Phylogenetic analyses indicate a marine origin for VHSV

- VHSV emergence from the marine environment into cultured rainbow trout might occur occasionally

- Marine isolates are usually low virulent to rainbow trout

- A trend to increment virulence is observed in isolates from genotype Ia, which is adapted to cultured rainbow trout