

“Letter to the Editor”
From IgZ to IgT: A call for a common nomenclature for immunoglobulin heavy chain genes of ray-finned fish

Alex Dornburg¹, Tatsuya Ota², Michael F. Criscitiello³, Irene Salinas⁴, J. Oriol Sunyer⁵,
Susana Magadán⁶, Pierre Boudinot⁷, Zhen Xu⁸, Martin F. Flajnik⁹, Amy Singer¹⁰,
Francisco Gambón-Deza¹¹, John D. Hansen¹², and Jeffrey A. Yoder^{13*}

1. Department of Bioinformatics and Genomics, University of North Carolina at Charlotte, Charlotte, NC USA
2. Department of Evolutionary Studies of Biosystems, SOKENDAI (The Graduate University for Advanced Studies), Hayama, Japan
3. Comparative Immunogenetics Laboratory, Department of Veterinary Pathobiology, College of Veterinary Medicine and Biomedical Sciences, Texas A&M University, College Station, TX, USA
4. Center for Evolutionary and Theoretical Immunology (CETI), Department of Biology, University of New Mexico, Albuquerque, NM USA.
5. Department of Pathobiology, School of Veterinary Medicine, University of Pennsylvania, Philadelphia, PA, USA
6. Centro de Investigaciones Biomédicas, Universidade de Vigo, Campus Universitario Lagoas Marcosende, 36310, Vigo, Spain
7. Université Paris-Saclay, INRAE, UVSQ, Virologie et Immunologie Moléculaires, Jouy-en-Josas, France
8. Institute of Hydrobiology, Chinese Academy of Sciences, Wuhan 430072, China
9. Department of Microbiology and Immunology, University of Maryland Baltimore School of Medicine, Baltimore, MD, USA
10. Zebrafish Nomenclature Coordinator, Zebrafish Model Organism Database (ZFIN), University of Oregon, Eugene, OR, USA
11. Unidad de Inmunología Hospital do Meixoeiro, Vigo, Spain
12. U.S. Geological Survey, Western Fisheries Research Center, Seattle, WA, USA
13. Department of Molecular Biomedical Sciences, North Carolina State University, Raleigh, NC, USA

ORCID IDs:

P. Boudinot:	0000-0002-7490-9677
M.F. Criscitiello:	0000-0003-4262-7832
A. Dornburg:	0000-0003-0863-2283
M.F. Flajnik:	0000-0002-2792-5084
F. Gambón-Deza:	0000-0001-9263-7663
J.D. Hansen:	0000-0002-3006-2734
S. Magadán:	0000-0003-2968-0102
T. Ota:	0000-0002-1115-5169
I. Salinas:	0000-0002-4802-6571
A. Singer:	0000-0002-9663-3237
J.O. Sunyer:	0000-0001-5093-2429
Zhen Xu:	0000-0001-6598-2058
J.A. Yoder:	0000-0002-6083-1311

*** Corresponding author at:**

Jeffrey A. Yoder, Department of Molecular Biomedical Sciences, North Carolina State University, 1060 William Moore Drive, Raleigh, North Carolina, USA. E-mail address: jeff_yoder@ncsu.edu.
Phone: +1 919-515-7406

Ray-finned fishes comprise over half the approximately 60,000 known vertebrate species¹, and are pivotal to the functionality of aquatic ecosystems and success of global multi-billion dollar industries. Understanding ray-finned fish immune systems is essential to predicting how species will respond to known or emergent pathogens as well as to the development of effective vaccines for aquaculture. However, the diversity of species, including in aquaculture, necessitates that immunology and translational medicine research groups investigating the immune system in one or a number of species employ a common language for describing homologous immune components. Unfortunately for Immunoglobulin (Ig) genes that encode antibodies, this has not been the case.

Ig genes are restricted to jawed vertebrates (Gnathostomes) with all lineages encoding common heavy chains IgM and IgD (aka IgW in cartilaginous fish, lungfish, and coelacanths).² Prior to 2005, it was believed that bony fish encoded only IgM and IgD. In 2005, Hansen and colleagues described a new Ig heavy chain encoded within the rainbow trout heavy chain locus and named it IgT for “teleost”.³ However, during the same year, Steiner and colleagues described a new heavy chain within the heavy chain locus of zebrafish and named it IgZ, presumably for zebrafish.⁴ As these projects were being published, it became clear that IgT and IgZ encode not only very similar sequences (see note in ³) but are likely “evolutionary forms of the same antibody” isotype (Figure 1).⁵ This heavy chain sequence has since been identified in a large number of ray-finned fish species, and shown to play important roles in mucosal immunity,⁶ with many species adopting the IgT nomenclature and others (especially within cyprinids) using IgZ. Consequently, it has become routine for many authors to refer to this sequence in publications as IgT/Z.

To increase consistency in vertebrate immunogenetics, we propose a single nomenclature system is warranted for this heavy chain. IgZ continues to be used in zebrafish, a powerful model for human disease and the first fish with a reference genome. However, this convention is at odds with research that spans the remaining diversity of over 30,000 additional species of ray-finned fishes. A simple PubMed search (<https://pubmed.ncbi.nlm.nih.gov/>) using the terms “IgT antibodies” and “IgZ antibodies” identified 268 publications using IgT and only 37 using IgZ (search ran on 10/1/2021),

suggesting that IgT is either more prevalent across species, or more reports are published from species with a history of using IgT. This trend will surely accelerate given the rapid growth of genomic resources for non-model species, rendering IgZ a source of potential future confusion in comparative studies. We recognize that ideally, either IgT or IgZ would reflect an inclusive name. However, recent identification of IgT/Z from holostei (the sibling lineage of teleosts) demonstrates that this class of antibody extends outside of teleosts.^{7,8} As a consequence, neither IgT or IgZ are completely inclusive if we rely on the T as referring to “teleost-specific” and Z referring to “zebrafish-specific”. Regardless of this discrepancy in nomenclature, we feel that IgT remains the most appropriate choice as IgZ reflects a history of more taxonomically restricted usage and IgT has already been adopted in non-teleost species. Therefore, discussions with the Zebrafish Nomenclature Committee have led to the changing of the official zebrafish gene symbol for the IgZ heavy chain (ZDB-GENE-040513-8) from immunoglobulin heavy constant zeta (*ighz*) to immunoglobulin heavy constant tau (*ight*). We now encourage a shift from IgZ to IgT in all ray-finned fish species.

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Figure Legend

Figure 1. IgT and IgZ are evolutionary forms of the same antibody isotype. A maximum likelihood estimate of the phylogenetic relationships of representative IgT (orange) and IgZ (blue) sequences. The C-terminal constant domain of each Ig was aligned using MAFFT. A maximum likelihood based on phylogeny was estimated in IQ-TREE 2,⁹ and conditioned on the best-fit model of amino acid substitution selected by Bayesian information criterion. Node support was assessed via 1000 bootstrap replicates and bootstrap support (BSS) is indicated by shaded circles at nodes. 100% BSS; solid black; $90\% \leq \text{BSS} < 100\%$: dark gray; $70\% \leq \text{BSS} < 90\%$: light gray; $\text{BSS} < 70\%$: no circle. IgT and IgZ sequences were described previously⁸ or listed here: bowfin (*Amia calva*, scaff18:9770670-9770347), spotted gar (*Lepisosteus oculatus*, JH591552.1:10457-10113), European eel (*Anguilla anguilla*, NC_049202.1:63242796-63243128), zebrafish (*Danio rerio*, AAT67446.1), rainbow trout (*Oncorhynchus mykiss*, AAW66978.1), Japanese pufferfish (*Takifugu rubripes*, BAD69712.1), and olive flounder (*Paralichthys olivaceus*, ANS12795.1). IgM sequences (olive green) included: spotted gar (LG5:577726-578115), bowfin (scaff18:10347166-10347555), European eel (ABY73532.1) and nurse shark (*Ginglymostoma cirratum*, AAA50817.1). IgD sequences (tan) included: Japanese pufferfish (BAD34541.1), olive flounder (BAB41204.1), rainbow trout (AAY41237.1), zebrafish, (Chr3:33950441-33950157), European eel (NC_049202.1:63885951-63886238), spotted gar (LG5:605556-605846) and bowfin (scaff18:10369108-10368818). Nurse shark IgW (AAB08972.1) and IgNar (AAB42621.2) were employed as outgroups (black).⁷

