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Recent Trends in Applied Zoology

Dr.D.S.Rathod

Editor

Associate Editors

Dr. K.S.Raut

Mr.Datta Nalle

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Editor
Dr.D.S.Rathod
Head
Department of Zoology and Fishery Science,
Rajarshi Shahu Mahavidyalaya (Autonomous),

Latur- 413531, Maharashtra

Associate Editors
Dr. K.S.Raut
Mr.Datta Nalle
Department of Zoology and Fishery Science, Rajarshi Shahu Mahavidyalaya (Autonomous),
Latur- 413531, Maharashtra

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Chapter 2

Review on Important role of *Danio rerio* in Animal and human vaccination research

Datta Ashok Nalle and Dnyaneshwar S. Rathod

Department of Zoology and Fishery Science, Rajarshi Shahu Mahavidyalaya, (Autonomous) Latur-413512 (MS)

Abstract

Animal models are used extensively in medical research to better understand the origins of both human and animal diseases as well as to facilitate the creation of novel treatments. Though rodents are still the most popular study model used globally, zebrafish (Danio rerio) models have rapidly gaine:d popularity among scientists in recent years. This is due to the fact that a little tropical freshwater teleost fish shares significant physiological, anatomical, and genetic similarities with mammals. Zebrafish are a great experimental model for behavioural, genetic, and toxicological research that helps to understand the causes of numerous human disorders. Testing novel therapeutics, including the security of novel vaccinations, is also beneficial. This review's objective was to offer a systematic literature analysis of the most recent studies conducted on the subject. It highlights increases in time and cost savings of research and analyses by outlining a number of benefits of using this kind of animal model in studies of the safety and efficacy of both animal and human vaccines.

Keywords: health; Immunity; Vaccine safety, Danio rerio

Introduction

The function of the immune system is to defend the body from invasions by bacteria, viruses, or other foreign antigens. Vaccination is used to increase immunity against diseases brought on by microorganisms in order to improve protection. It often contains a less dangerous substance that causes a reaction and prompts the immune system to identify it as foreign. Every time an invasion is recognised, a body's defence mechanism gains the ability to identify and eliminate a bacterium, its poisons, or its surface proteins [1].

The use of vaccinations is crucial because it encourages the body's defence mechanisms to be stimulated and the growth of both individual and group immunity. In contrast to immunostimulants, which solely affect innate immunity, vaccinations can affect both nonspecific (innate) and specific (adaptive) immune responses. It is important to remember the function vaccines play in disease control both as prophylactic and non-therapeutic strategies. As a result, the body can create antibodies that recognise, alert, and neutralise infections or specialised cellular responses that recognise the antigens in concern. with high efficiency and affinity.

Despite the fact that research on fish immunology is more recent than that on humans and other animals, the concepts and methods employed are comparable [3]. The research of vaccine usage in fish is a rapidly expanding field. Commercial vaccination of various fish types is already a reality in many nations as aquaculture develops and the need to control infections becomes more urgent. It assists in preventing illnesses that could endanger the shoal's health as well as in preventing financial losses brought on by infection-related mortality. It lessens the quality of finished fish products and the overuse of antibiotics that might contaminate water sources [4, 5, 6, 7, 8,9, 10].

The Zebrafish model has been extensively employed in studies on the health of both humans and animals as well as, more recently, in aquaculture. Despite rodents being the most popular study model in the world, zebrafish (Danio rerio) models have become increasingly popular among scientists in recent years. It adheres to the 3Rs (replacement, reduction, and refinement) philosophy as demanded by numerous national and international regulatory agencies. In addition, compared to the models made from those more well-known animals, using the zebrafish model saves time and resources. When compared to in vitro outcomes, it also offers a larger capacity for information and prediction [11].

Challenge trials for vaccine development measure the vaccine's effectiveness and safety against various infections when designing immunisation tests. These are typically evaluated using animal models, primarily mammalian ones, which are typically inaccurate in simulating human diseases [12], not to mention time-consuming and requiring a lot of animals. Additionally, laboratory testing, clinical symptoms, and mortality are typically examined to determine if an immune system response was innate (non-specific) or adaptive (specific). T and B lymphocytes, which emerge from the thymus and kidneys, respectively, are the components of Zebrafish's adaptive immune system, which is similarly well-maintained to that of mammals. Fish appear to contain memory cells of the type B and T, albeit, when it comes to the maturation of memory lymphocytes [13,14,15,16,17].

There isn't enough evidence to support that in zebrafish. The enzyme system involved in the genetic rearrangement process that gives rise to the B (BCR) and T (TCR) lymphocyte receptors is also seen in zebrafish. The rearrangement of gene segments V, D, and J in Zebrafish, like in humans, is governed by recombination activator genes, which create the variety of antibodies and lymphocyte receptors. Additionally, the immune system of the zebrafish is five orders of magnitude less complex than that of humans and three orders of magnitude less than that of mice since it only has about 300,000 antibody-producing B cells [18,19 20.21,22].

Due to the antibodies' greater affinity, the humoral reaction is more effective. In comparison to mammals, affinity maturation of antibody responses is less effective in cold-blooded animals. Despite this, zebrafish data showed that directed mutations were occurring in areas of the BCR receptor that targeted particular nucleotides. Therefore, it was hypothesised that affinity maturation and activation-induced deaminase both contributed to the diversification of antibodies in fish [23,24,25,26,27]. When teleost fish were immunised with the TNP-KLH antigen (linked to trinitrophenyl to keyhole limpet hemocyanin), for instance, the production of specific, low affinity antibodies was stimulated. These antibodies were replaced in 5 weeks by intermediate affinity antibodies, and in 15 weeks by antibodies with higher affinity for the antigen [28,29]

The most common immunological tests include erythrocyte count, thrombocyte and leukocyte counts, differential white cell counts, hematocrit measurements, glucose readings, organ histology, and immunological essays like serology, specific antibody titration, and agglutination [30,31,32]toxicity tests can also be carried out on zebrafish, including those for embryotoxicity, hepatotoxicity, neurotoxicity, endocrine toxicity, and genotoxicity. Until recently, these tests were carried out on rats, but in recent years, the Zebrafish model has emerged as a crucial resource for the investigation of infections and immune reactions. This approach has the benefit of OECD-specific rules for acute toxicity testing of chemical compounds, which is completed in 96 hours [33,34]. Real-time observations can also be obtained on the effects of vaccines on the cardiovascular, hepatic, neurological, and endocrine systems as well as the monitoring of embryogenesis

To prevent harm, including death, to animals, especially to immunosuppressed organisms, young children, and the elderly, vaccinations should be evaluated using animal models before being used on humans, cattle, or pets [35]. Zebrafish have additional biological benefits over other vertebrates, such as high fecundity, external fertilisation, optical transparency, and quick development. A highly developed immune system that is strikingly similar to the human immune system is also present in zebrafish. It follows that it would be reasonable to assume that the majority of the signalling pathways and molecules involved in the immune response in humans exist in fish and operate similarly [36].

Fish include components of innate and adaptive immunity, which makes them susceptible to infections from gram-positive and gram-negative bacteria, protozoa, viruses, fungi, and mycobacteria. As a result, this makes it possible to study infectious processes.A sizable number of mutants were identified thanks to the development of specialised cloning, mutagenesis, and transgenesis procedures. The ability to produce knockout zebrafish for whole organism gene studies is made possible by commercial mutant zebrafish lines and the recently created CRISPR/Cas9 genome modification system [37]. Additionally, Casper zebrafish and other non-pigmenting mutants have enhanced the visibility of interior organs [38,39]

Fish Mucosal tissues were examined for a Th17-like immune response following the injection of live, attenuated V. anguillarum via several vaccination methods. Immersion vaccination induced robust Th17-like immune responses in the gastrointestinal tissue of zebrafish when compared to injection vaccination. During a study on zebrafish responses to vaccine, Vibrio vulnificus, an aquatic bacterium that can cause primary sepsis and soft tissue infection, was also examined. A sort of crucial immunomodulator known as CpG oligodeoxynucleotides was found to protect zebrafish.[4041,42]

Up to 165 million cases of shigellosis occur each year due to Shigella, which is a leading cause of dysentery globally [43]. Although a vaccine is not currently available, observational studies in Shigella-endemic areas as well as human and animal challenge-rechallenge experiments with virulent Shigella are encouraging. Following Shigella infection, the disease's incidence dropped, indicating the biological viability of a vaccination [44]. Using adult zebrafish to explore the immune response to Shigella was suggested by [45] and Mani et al. [46]. Understanding the interplay between Shigella and T-lymphocytes [47] is essential for the development of vaccination methods.

References

1. Bailone RL, Aguiar LK, Roça RO, Borra RC, Corrêa T, Janke H, et al. Zebrafish as an animal model for food safety research: trends in the animal research. *Food Biotechnol.* 2019;33(4):283–302.
2. Bailone RL, Fukushima H, Roça R, Corrêa T, Janke H, Setti P, et al. Potenciais usos do Modelo animal zebrafish *Danio rerio* em pesquisas na medicina veterinária. Rev Educ Cont Med Vet e Zoo CRMV-SP. 2019b; Just Accepted.
3. Benard EL, Van der Sar AM, Ellett F, Lieschke GJ, Spaink HP, Meijer AH. Infection of zebrafish embryos with intracellular bacterial pathogens. *JoVE (J Vis Exp)* 2012;61:e3781.
4. Burnham LA, Jaishankar D, Thompson JM, Jones KS, Shukla D, Tiwari V. Liposome-mediated herpes simplex virus uptake is glycoprotein-D receptor-independent but requires heparan sulfate. *Front Microbiol.* 2016;7:973.
5. Chen H, Zhang L, Li S, Ling K, Chen X, Lin C. CpG-ODN 2007 protects zebrafish against *Vibrio vulnificus*-induced infection. bioRxiv. 2019:780742. 10.1101/780742
6. Ding C, Liu Q, Li J, Ma J, Wang S, Dong Q, et al. Attenuated *Listeria monocytogenes* protecting zebrafish (*Danio rerio*) against vibrio species challenge. *Microb Pathog*. 2019;132:38–44.
7. Ding CB, Zhang JP, Zhao Y, Peng ZG, Song DQ, Jiang JD. Zebrafish as a potential model organism for drug test against hepatitis C virus. *PLoS One.* 2011;6(8):e22921.
8. Ding CB, Zhao Y, Zhang JP, Peng ZG, Song DQ, Jiang JD. A zebrafish model for subgenomic hepatitis C virus replication. *Int J Mol Med.* 2015;35(3):791–797.
9. . Fehr A, Eshwar AK, Neuhauss SC, Ruetten M, Lehner A, Vaughan L. Evaluation of zebrafish as a model to study the pathogenesis of the opportunistic pathogen *Cronobacter turicensis*. *Emerg Microbes Infect*. 2015;4(1):1–9.
10. . Ferrairo F. Os riscos reais da vacina. Revista Superinteressante. 2015; https://super.abril.com.br/saude/os-riscos-reais-da-vacina/ Accessed 27 Feb 2020.
11. . Fukushima HCS, Leal CAG, Cavalcante RB, Figueiredo HCP, Arijo S, Moriñigo MA, et al. *Lactococcus garvieae* outbreaks in Brazilian farms Lactococcosis in *Pseudoplatystoma* sp.– development of an autogenous vaccine as a control strategy. *J Fish Dis.* 2017;40(2):263–272.
12. Gabor KA, Goody MF, Mowel WK, Breitbach ME, Gratacap RL, Witten PE, et al. Influenza a virus infection in zebrafish recapitulates mammalian infection and sensitivity to anti-influenza drug treatment. *Dis Model Mech*. 2014;7(11):1227–1237.
13. . Guo Z, Lin Y, Wang X, Fu Y, Lin W, Lin X. The protective efficacy of four iron-related recombinant proteins and their single-walled carbon nanotube encapsulated counterparts against *Aeromonas hydrophila* infection in zebrafish. *Fish Shellfish Immunol. 2*018;82:50–59.
14. Harjula SKE, Saralahti AK, Ojanen MJ, Rantapero T, Uusi-Mäkelä MI, Nykter M, et al. Characterization of immune response against *Mycobacterium marinum* infection in the main hematopoietic organ of adult zebrafish (*Danio rerio*) *Dev Comp Immunol.* 2020;103:103523.
15. Hodgkinson JW, Belosevic M, Elks PM, Barreda DR. Teleost contributions to the understanding of mycobacterial diseases. Dev Comp Immunol. 2019.

16. Howe K, Clark MD, Torroja CF, Torrance J, Berthelot C, Muffato M, et al. The zebrafish reference genome sequence and its relationship to the human genome. *Nature.* 2013;496(7446):498.
17. Ji J, Torrealba D, Thwaite R, Gomez AC, Parra D, Roher N. Nanostructured TNFα protein targets the zebrafish (*Danio rerio*) immune system through mucosal surfaces and improves the survival after *Mycobacterium marinum* lethal infection. *Aquaculture.* 2019;510:138–149.
18. Kavaliauskis A, Arnemo M, Speth M, Lagos L, Rishovd AL, Estepa A, et al. Protective effect of a recombinant VHSV-G vaccine using poly (I: C) loaded nanoparticles as an adjuvant in zebrafish (*Danio rerio*) infection model. *Dev Comp Immunol.* 2016;61:248–257
19. Kim YS, Yoon NK, Karisa N, Seo SH, Lee JS, Yoo SS, et al. Identification of novel immunogenic proteins against *Streptococcus parauberis* in a zebrafish model by reverse vaccinology. *Microb Pathog*. 2019;127:56–59.
20. . Lagos L, Tandberg JI, Becker MI, Winther-Larsen HC. Immunomodulatory properties of *Concholepas concholepas* hemocyanin against francisellosis in a zebrafish model. *Fish Shellfish Immunol.* 2017;67:571–574.
21. Lieschke GJ, Currie PD. Animal models of human disease: zebrafish swim into view. *Nat Rev Genet.* 2007;8(5):353.
22. Lohi O, Parikka M, Rämet M. The zebrafish as a model for paediatric diseases. *Acta Paediatr.* 2013;102(2):104–110.
23. López V, Risalde MA, Contreras M, Mateos-Hernández L, Vicente J, Gortázar C, et al. Heat-inactivated *Mycobacterium bovis* protects zebrafish against mycobacteriosis. *J Fish Dis.* 2018;41(10):1515–1528.
24. MacRae CA, Peterson RT. Zebrafish as tools for drug discovery. *Nat Rev Drug Discov.* 2015;14(10):721.
25. Mani S, Wierzba T, Walker RI. Status of vaccine research and development for Shigella. *Vaccine.* 2016;34:2887–2894.
26. Mantilla Galindo A, Ocampo M, Patarroyo MA. Experimental models used in evaluating anti-tuberculosis vaccines: the latest advances in the field. *Expert Rev Vaccines.* 2019;18(4):365–377.
27. Marianes AE, Zimmerman AM. Targets of somatic hypermutation within immunoglobulin light chain genes in zebrafish. *Immunology*. 2011;132(2):240–255.
28. McFetridge R, Sobanjo-ter Meulen A, Folkerth SD, Hoekstra JA, Dallas M, Hoover PA, et al. Safety, tolerability, and immunogenicity of 15-valent pneumococcal conjugate vaccine in healthy adults. *Vaccine*. 2015;33(24):2793–2799.
29. Membrebe JD, Yoon NK, Hong M, Lee J, Lee H, Park K, et al. Protective efficacy of *Streptococcus iniae* derived enolase against streptococcal infection in a zebrafish model. *Vet Immunol Immunopathol.* 2016;170:25–29.
30. Nguyen-Chi M, Phan QT, Gonzalez C, Dubremetz JF, Levraud JP, Lutfalla G. Transient infection of the zebrafish notochord with *E. coli* induces chronic inflammation. *Dis Model Mech*. 2014;7(7):871–882.

31. Ojanen M. *Reverse genetics to study immunity against mycobacteria in zebrafish (Danio rerio)* 2019. [Google Scholar]
32. Oksanen KE, Halfpenny NJ, Sherwood E, Harjula SKE, Hammarén MM, Ahava MJ, et al. An adult zebrafish model for preclinical tuberculosis vaccine development. *Vaccine.* 2013;31(45):5202–5209.
33. Palha N, Guivel-Benhassine F, Briolat V, Lutfalla G, Sourisseau M, Ellett F, et al. Real-time whole-body visualization of chikungunya virus infection and host interferon response in zebrafish. *PLoS Pathog*. 2013;9(9):e1003619.
34. Patterson H, Saralahti A, Parikka M, Dramsi S, Trieu-Cuot P, Poyart C, et al. Adult zebrafish model of bacterial meningitis in *Streptococcus agalactiae* infection. *Dev Comp Immunol.* 2012;38(3):447–455.
35. Phalipon A, Mulard LA, Sansonetti PJ. Vaccination against shigellosis: is it the path that is difficult or is it the difficult that is the path? *Microbes Infect.* 2008;10(9):1057–1062.
36. Ravindran C, Varatharajan GR, Raju R, Vasudevan L, Anantha SR. Infection and pathogenecity of *Myroides odoratimimus* (NIOCR-12) isolated from the gut of grey mullet (*Mugil cephalus* (Linnaeus, 1758)) *Microb Pathog.* 2015;88:22–28.
37. Risalde MA, López V, Contreras M, Mateos-Hernández L, Gortázar C, de la Fuente J. Control of mycobacteriosis in zebrafish (*Danio rerio*) mucosally vaccinated with heat-inactivated *Mycobacterium bovis. Vaccine.* 2018;36(30):4447–4453.
38. Rocker AJ, Weiss AR, Lam JS, Van Raay TJ, Khursigara CM. Visualizing and quantifying *Pseudomonas aeruginosa* infection in the hindbrain ventricle of zebrafish using confocal laser scanning microscopy. *J Microbiol Methods.* 2015;117:85–94.
39. Salgado-Pabón W, Konradt C, Sansonetti PJ, Phalipon A. New insights into the crosstalk between Shigella and T lymphocytes. *Trends Microbiol.* 2014;22(4):192–198.
40. Saralahti A. *A zebrafish model for host-pathogen interactions in streptococcal infections.* 2019
41. Saralahti A, Rämet M. Zebrafish and streptococcal infections. *Scand J Immunol.* 2015;82(3):174–183.
42. Scapigliati G, Fausto AM, Picchietti S. Fish lymphocytes: an evolutionary equivalent of mammalian innate-like lymphocytes? *Front Immunol.* 2018;9:971.
43. Shahin K, Shinn AP, Metselaar M, Ramirez-Paredes JG, Monaghan SJ, Thompson KD, et al. Efficacy of an inactivated whole-cell injection vaccine for nile tilapia, *Oreochromis niloticus* (L), against multiple isolates of *Francisella noatunensis* subsp. orientalis from diverse geographical regions. *Fish Shellfish Immunol.* 2019;89:217–227.
44. Shan Y, Fang C, Cheng C, Wang Y, Peng J, Fang W. Immersion infection of germ-free zebrafish with *Listeria monocytogenes* induces transient expression of innate immune response genes. *Front Microbiol.* 2015;6:373.

45. Shan Y, Zhang Y, Zhuo X, Li X, Peng J, Fang W. Matrix metalloproteinase-9 plays a role in protecting zebrafish from lethal infection with *Listeria monocytogenes* by enhancing macrophage migration. *Fish Shellfish Immunol.* 2016;54:179–187.
46. Sullivan C, Matty MA, Jurczyszak D, Gabor KA, Millard PJ, Tobin DM, Kim CH. Infectious disease models in zebrafish. In: Methods in cell biology, vol. 138: Academic; 2017. p. 101–36. 10.1016/bs.mcb.2016.10.005.
47. Tandberg J, Oliver C, Lagos L, Gaarder M, Yáñez AJ, Ropstad E, Winther-Larsen HC. Membrane vesicles from Piscirickettsia salmonis induce protective immunity and reduce development of salmonid rickettsial septicemia in an adult zebrafish model. *Fish Shellfish Immu.* 2017;2017(67):189–198.