GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 12 (369) Декабрь 2025

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

GEORGIAN MEDICAL NEWS
NO 12 (369) 2025

Содержание:

GEORGIAN MEDICAL NEWS
No 12 (369) 2025

DANIO RERIO (ZEBRAFISH) - A UNIQUE AND INTEGRATIVE PLATFORM FOR 21ST CENTURY BIOMEDICAL RESEARCH

Virina Natalia V, Kuchieva Lana M, Baturina Yulia S, Fizikova Aliya B, Gereeva Madina M, Bitiev Batraz F, Apakhaeva Karina K, Manukhova Natalia M, Rasulova Fatima Z, Kornev Egor M, Rodionova Ekaterina A.

Saint-Petersburg State Pediatric Medical University Saint-Petersburg, Russia.

NWSMU named after I.I. Mechnikova, Saint-Petersburg, Russia. Military Medical Academy named after S. M. Kirov, Saint-Petersburg, Russia.

Abstract.

Zebrafish (Danio rerio) have become an important vertebrate model in modern biomedical research due to their genetic similarity to humans, rapid embryonic development, and suitability for in vivo experimentation. Their optical transparency, high fecundity, and ease of genetic manipulation allow detailed investigation of developmental processes, disease mechanisms, and pharmacological effects. This review summarizes current applications of zebrafish in preclinical research, including toxicology, neurobiology, oncology, regenerative medicine, infectious diseases, and drug discovery. Zebrafish models enable efficient screening of therapeutic compounds, real-time observation of pathological processes, and analysis of molecular pathways involved in tissue regeneration and disease progression. Although certain physiological differences limit direct clinical translation, zebrafish provide a cost-effective and ethically advantageous platform that complements mammalian models. Their continued use significantly contributes to accelerating biomedical research and improving the early stages of translational medicine.

Key words. Zebrafish, toxicology, neurobiology, oncology, regenerative medicine, infectious diseases, drug discovery.

Introduction.

In the modern world, the production of pharmaceutical products is rapidly evolving, encompassing new fields and significantly increasing manufacturing volumes. A fundamental requirement for any medicinal product is the confirmation of its efficacy and safety, which is achieved through strictly regulated stages of preclinical and clinical research [1,2].

Preclinical studies represent a comprehensive set of experiments conducted on laboratory models, primarily involving animals, and are performed in strict compliance with international ethical standards. These studies may be carried out in vivo, meaning in living organisms, in vitro, meaning under laboratory conditions outside the organism, as well as in silico, meaning through the use of computer-based modeling [3-5].

One of the most debated aspects of contemporary preclinical science is the necessity and ethical justification of using laboratory animals, as well as the selection of the most appropriate model organisms. Traditionally, mice, rats, nonhuman primates, pigs, dogs, cats, and ferrets are utilized, along with representatives of less conventional groups, such as worms and zebrafish (Danio rerio) [4,6,7].

Zebrafish (Danio rerio) were introduced into scientific research in the 1970s–1980s, when American molecular biologist George Streisinger and his colleagues at Oregon State University proposed their use as a model organism for studying vertebrate developmental processes. Owing to a number of advantages, including low maintenance cost, ease of breeding, and high reproductive capacity, this species rapidly became an important component of biological and medical research. Zebrafish gained particular prominence in 2003 following successful genetic modifications that led to the creation of fluorescent variants known as GloFish, which further emphasized their potential in genetic and molecular experimentation [8-10].

At present, zebrafish (Danio rerio) are considered one of the unique model organisms utilized in numerous universities and research institutions worldwide. They are actively employed in studies related to developmental biology, toxicology, genetics, medicine, environmental sciences, and even space research, demonstrating their broad applicability and high significance for the global scientific community [7,11].

Objective.

The objective of the present descriptive review is to analyze current literature data concerning the wide range of applications of zebrafish (Danio rerio) as model organisms in preclinical research. The synthesis of these findings is expected to enhance the understanding of their role, advantages, limitations, and future prospects for use in contemporary biomedical and biological investigations.

Materials and Methods.

To achieve the stated objective, a descriptive review of the scientific literature was conducted. Source retrieval was performed in the PubMed electronic database for the period from 2000 to 2025. The search strategy included the following key terms: “Danio rerio,” “zebrafish model,” “preclinical research,” “toxicology,” “neurobehavior,” “embryo development,” as well as field-specific terms such as “spaceflight” and “drug screening.”

The inclusion criteria for publications comprised the following factors:

– scientific relevance, with priority given to studies published during the last five years, and direct relation to the use of zebrafish in preclinical research;

– publication type, including original research articles, narrative reviews, and meta-analyses.

The selection and analysis of the literature were carried out selectively, with emphasis placed on the most representative and methodologically significant studies that clearly demonstrate specific areas of application and methodological approaches. It should be noted that this review is not systematic and does not follow strict PRISMA guidelines. The primary aim of the present work is to provide an overall understanding of the diversity and potential applications of zebrafish (Danio rerio) in preclinical biomedical and biological research.

Main Section.

Analysis of the PubMed database demonstrates a steady increase in the number of publications devoted to zebrafish (Danio rerio) during the period from 2000 to 2025. The distribution of studies across different research fields over this time period reveals two principal trends. First, genetics and embryology remain the dominant areas in terms of publication volume. Second, there has been a significant increase in research activity in several other fields, including neurobiology, toxicology, regenerative medicine, gastroenterology, space biology, and studies related to antibacterial therapy (Figures 1 and 2) [12].

The expansion of the scope of zebrafish applications in research reflects the growing interest of the scientific community, which is driven by the unique advantages of Danio rerio (zebrafish). These advantages include embryonic transparency, a high degree of genetic homology with humans, pronounced regenerative capacity, and a rapid reproductive cycle, which collectively make zebrafish an exceptionally convenient and informative model for a wide range of biomedical investigations [7].

Zebrafish (Danio rerio) in Embryology.

Zebrafish (Danio rerio) represent a fundamental model in embryological research due to several unique advantages. These include external fertilization and development, complete transparency of embryos and larvae during the early days of life, which allows real-time observation of organogenesis, as well as a short life cycle and high fertility, which facilitate the rapid acquisition of statistically significant data.

In 2023, Zizioli D., Ferretti S., Mignani L., and colleagues conducted a study evaluating the embryonic safety of nirmatrelvir, an antiviral component of a therapeutic agent used for the treatment of coronavirus disease 2019. The investigators performed a comprehensive embryotoxicological screening

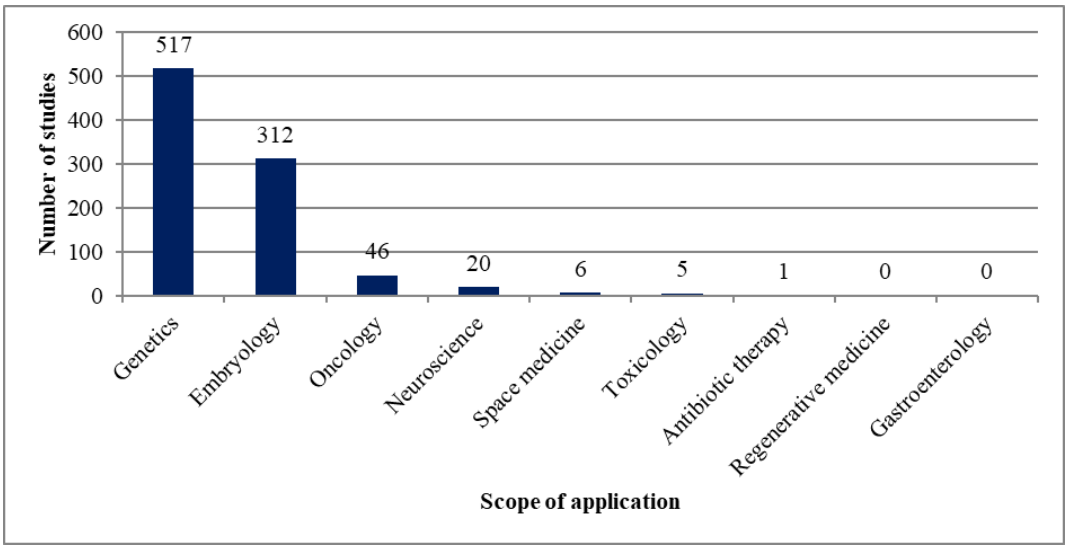

Figure 1. *Use of zebrafish (Danio rerio) in research across various scientific fields in the year 2000 (compiled by the author based on analysis of the PubMed database).*

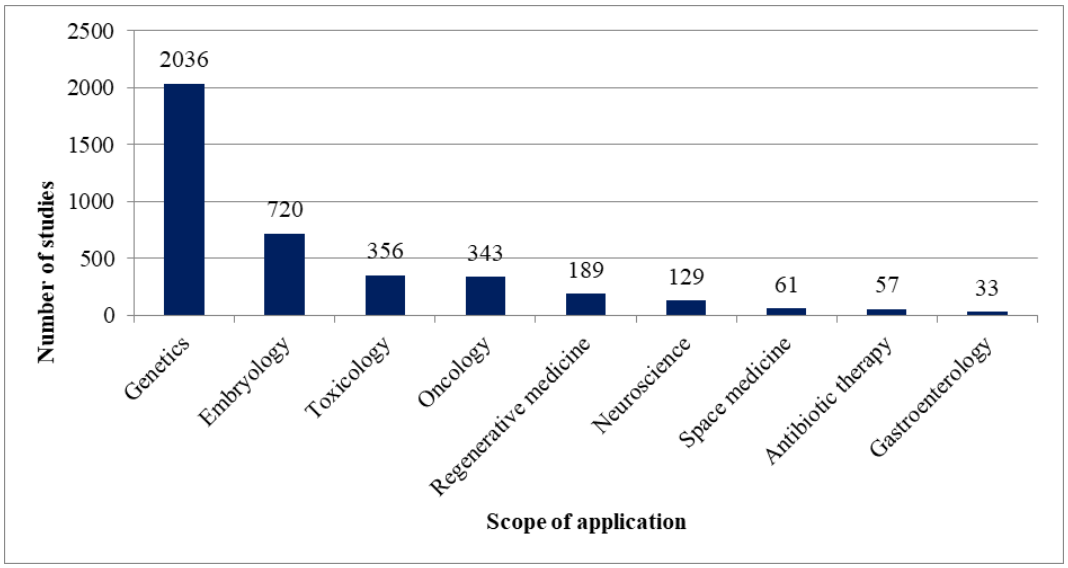

Figure 2. *Use of zebrafish (Danio rerio) in research across various scientific fields in the year 2025 (compiled by the author based on analysis of the PubMed database).*

following standardized protocols. Embryos were exposed to a wide range of substance concentrations beginning at the critical gastrulation stage, six hours post-fertilization. The findings demonstrated no statistically significant embryotoxicity, no teratogenic effects, and no impairment of neurological functions, even at concentrations substantially exceeding therapeutic levels [13].

Therefore, this study not only confirmed the favorable in vivo embryonic safety profile of nirmatrelvir, but also clearly demonstrated the value of zebrafish (Danio rerio) as a rapid, cost-effective, and highly informative model for preclinical screening of novel pharmacological compounds, enabling the acquisition of comprehensive developmental safety data prior to testing in mammalian models.

Zebrafish (Danio rerio) in Neurobiology.

In a 2024 review study conducted by O. Doszyn, T. Dulski, and J. Zmorzynska, it was demonstrated that the brain of zebrafish (Danio rerio) is relatively simple, which makes this species a convenient model for detailed investigation of neural networks. The transparency of larvae provides a unique opportunity for direct visualization of neuronal activity and developmental processes in a living organism. Of particular importance is the pronounced regenerative capacity of zebrafish, which enables effective investigation of tissue repair mechanisms, a factor that is critically important for the development of therapies for neurodegenerative disorders [14]. For example, a 2020 study examined the role of the LRRK2 gene, one of the most common genetic causes of hereditary Parkinson's disease, in zebrafish embryonic development.

The authors identified a novel association between LRRK2 and the key Wnt signaling pathway, demonstrated the consequences of mutation in vivo, and supported the hypothesis that activation of the Wnt pathway may represent a promising therapeutic strategy [15,16]. Thus, zebrafish (Danio rerio) serve as an integrative platform that accelerates the translation of fundamental neurobiological knowledge into practical therapeutic strategies for disorders such as Parkinson's disease.

Zebrafish (Danio rerio) in Modeling Neurotoxicity.

In recent years, advances in information technologies have contributed to the development of behavioral testing methods that provide objective assessment of laboratory animal behavior. Zebrafish (Danio rerio) represent a valuable model for the study of neurotoxicity due to their high sensitivity and the possibility of quantitatively evaluating behavioral alterations. For instance, in a 2025 study by Abellán-Álvaro and colleagues, automated behavioral tests were employed to assess the long-term consequences of neurotoxic exposure. The investigators examined the effects of acute exposure during the first five days post-fertilization and chronic exposure for twenty-eight days to a low, environmentally relevant concentration of a pesticide mixture. Neurobehavioral outcomes were evaluated using the DanioVision video-tracking system and EthoVision software (Noldus).

At the larval stage (five days post-fertilization), a combined light–dark transition and acoustic startle response test was used to assess stress reactivity and learning, while in juvenile fish (twenty-eight days), the classical Novel Tank Test was employed to evaluate anxiety-like behavior [17]. This study clearly demonstrates how the combination of the zebrafish model with automated behavioral analysis tools enables the detection of subtle yet long-lasting neurotoxic effects of chemical mixtures.

Zebrafish (Danio rerio) in Oncology.

Zebrafish (Danio rerio) represent a highly promising model for oncological research due to their unique characteristics, which enable real-time visualization of tumor formation and metastasis. In addition, zebrafish possess broad potential for genetic manipulation, which facilitates in-depth investigation of the molecular mechanisms of cancer and supports efficient testing of novel antineoplastic agents.

A 2024 publication systematized contemporary data on the application of xenotransplantation models involving the transplantation of human colorectal cancer cells into zebrafish embryos. Immunodeficient zebrafish embryos were used as recipients, into which both established colorectal cancer cell lines and primary patient-derived tumor cells were transplanted. This xenotransplantation model is characterized by high reproducibility and provides a unique opportunity for direct dynamic observation of tumor progression, making it a highly promising platform for preclinical investigations [18,19].

Furthermore, a 2023 study compared two key model systems—mice and zebrafish—in the context of breast cancer research. The authors emphasized that each model possesses distinct advantages: murine models provide superior physiological relevance, whereas zebrafish models enable rapid experimentation and direct visualization of tumor processes. Combined application of both models allows for a more comprehensive understanding of disease pathogenesis and accelerates the development of diagnostic and therapeutic strategies for breast cancer [20]. Therefore, zebrafish (Danio rerio) represent an effective and versatile model organism for studying malignant diseases and developing novel oncological treatment approaches.

Zebrafish (Danio rerio) in Regenerative Medicine.

Zebrafish (Danio rerio) are a valuable model for investigating regenerative processes due to their high capacity for tissue repair. In this species, regeneration typically occurs within twenty-one days, making zebrafish a convenient and practical experimental model in laboratory settings.

In 2025, a group of researchers conducted a study focused on regeneration of the zebrafish caudal fin, with particular emphasis on the non-classical interaction between the STAT3 signaling protein and the vitamin D-dependent pathway. The study demonstrated that STAT3, known for its role in cellular proliferation and inflammatory processes, interacts with components of this pathway not through traditional mechanisms but via alternative molecular crosstalks. This interaction influences the regulation of genes responsible for tissue repair, accelerates regenerative processes, and ensures control of the cell cycle in regenerating tissues [21].

Beyond fin regeneration, zebrafish demonstrate regenerative capabilities in several vital organ systems, including the cardiovascular system, nervous system, and retina. For example, in 2023, researchers identified a mechanism that promotes maturation of cardiomyocytes during cardiac tissue regeneration

in zebrafish. It was revealed that the LRRC10 protein plays a key role in signaling cells when to cease proliferation and transition to maturation, thereby contributing to effective heart regeneration [22].

Zebrafish (Danio rerio) in Gastroenterology and Genetics.

In the search for effective therapeutic strategies for conditions such as nonalcoholic fatty liver disease, researchers increasingly turn to model organisms. For instance, a 2023 study conducted by Endrina Mujica and Marcel den Hoed, dedicated to the role of lipid-associated genes in the development of nonalcoholic fatty liver disease, clearly demonstrates the uniqueness of zebrafish. Their value lies not only in their anatomical simplicity but also in their remarkable degree of genetic similarity to humans.

In this study, zebrafish were used as a model for nonalcoholic fatty liver disease by inducing a metabolic state comparable to human hepatic steatosis, for example through specialized diet-induced obesity, combined with targeted genetic modifications using CRISPR/Cas9 technology. This approach enables identification of causative genes whose dysfunction triggers steatosis, allows tracing of the entire pathogenic cascade from steatohepatitis to fibrosis, and provides an opportunity to evaluate the effectiveness of therapeutic agents by administering potential drugs to zebrafish and monitoring symptom reduction [23].

Such an integrated approach transforms the zebrafish from a simple observational organism into a highly advanced biological system for preclinical testing.

Zebrafish (Danio rerio) in Assessing the Effects of Antibacterial Agents on the Organism.

In recent years, the problem of increasing antibiotic resistance has become particularly urgent, especially considering that the development of new antibacterial drugs requires a substantial amount of time [24]. Moreover, previously established antibacterial agents are not always suitable for the treatment of multidrug-resistant infections, not only due to the development of resistance but also because of the potential risk of toxic effects on the organism. Therefore, studies evaluating the impact of such agents on model organisms are of critical importance.

For example, in a 2025 study conducted by Ling-Chun Lin, Yu-Chuan Tsai, and Nien-Tsung Lin, the synergistic interaction between bacteriophages and antibiotics in combating Pseudomonas aeruginosa biofilms was demonstrated. Zebrafish (Danio rerio) were utilized as an experimental model, and the transparency of zebrafish larvae allowed real-time visualization of biofilm destruction and assessment of the effectiveness of combined therapy directly in a living organism [25]. The use of zebrafish in this study significantly reduced the time from experimental concept to obtaining meaningful therapeutic results, owing to the possibility of direct visual monitoring and the rapid implementation of experiments in vivo.

Zebrafish (Danio rerio) in Space Research.

The prospects of long-term human presence in space have increased the relevance of research into the effects of space-related factors on living organisms. In this context, zebrafish (Danio rerio) play an important model role, determined not only by their ease of maintenance but also by several unique advantages, particularly when compared with traditional preclinical research models. These advantages include simplified maintenance requirements, as aquatic systems demand fewer resources than life-support systems for rodents, the ability to house a large number of individuals in compact conditions to achieve statistical reliability, and, critically, the ability to serve as a transparent living system for investigating fundamental cellular and molecular responses in vivo.

For instance, in 2023, a group of researchers conducted a study investigating the effects of simulated microgravity on embryonic development. The investigators reported a significant reduction in the number of cells expressing Runx2a, a key transcription factor involved in osteogenesis, along with alterations in the activity of other genes responsible for bone formation and calcium metabolism [26]. These findings directly confirm the potential of zebrafish (Danio rerio) for preclinical evaluation of risks associated with space flight, such as osteoporosis, and for the development of potential strategies for their prevention and correction.

Based on these data, zebrafish (Danio rerio) represent a powerful complementary platform in space biology. Ongoing research in this direction forms an essential foundation for future breakthrough discoveries in space biology and medicine.

Discussion of the Limitations of Using Zebrafish (Danio rerio) in Research and Comparison with Rodent Models.

Despite their well-recognized advantages, such as embryonic transparency, high fertility, and pronounced regenerative capacity, zebrafish (Danio rerio) as an experimental model also possess several important limitations that must be taken into account when designing studies and interpreting outcomes [27].

Limitations of Using Zebrafish (Danio rerio) in Research.

1. Physiological characteristics: Zebrafish lack several organ homologs, including lungs, mammary glands, the prostate gland, and a multilobular liver. They also exhibit species-specific metabolic features, including differences in pharmacokinetics, absorption, distribution, metabolism, and excretion of substances, as well as specific temperature requirements, with optimal development occurring at approximately twenty-eight to thirty degrees Celsius. The absence of homologous organs makes zebrafish unsuitable for direct modeling of certain human diseases. Metabolic peculiarities may introduce bias into drug screening outcomes and therefore require subsequent validation in mammalian systems. Temperature dependence is also highly relevant, particularly in the context of preclinical studies, as it does not correspond to mammalian physiological conditions and may influence biochemical reaction rates and the activity of tested compounds [27].

2. Genetic and molecular characteristics: Zebrafish have undergone an additional round of genome duplication, resulting in many genes existing in paralogous pairs. Certain orthologs of key human genes are absent, including selected genes associated with trophoblast differentiation. Moreover, significant differences exist in alternative splicing mechanisms and gene regulation, with gene expression patterns, particularly at the post-transcriptional level, often differing considerably

Table 1. *Comparison of Zebrafish (Danio rerio) and Rodent Models (compiled by the author based on analysis of scientific literature).*

Comparison Criterion	Zebrafish (Danio rerio)	Rodents (Mice) Practical	Significance
Cost of maintenance	Low	High	Zebrafish (Danio rerio) can be used for large-scale screening
Evolutionary proximity	Distant from humans (bony fish)	Close to humans (mammals)	Mice have higher translational potential
Immune system	Innate immunity is well developed; adaptive immunity is simple	Fully functional adaptive immune system, analogous to that of humans	The zebrafish model is limited for studying complex immune responses, whereas mice are ideal for this
Rate of development	Short (3–4 months)	Long (2.5–3 months to sexual maturity + 21 days of pregnancy)	Zebrafish allow rapid generation of genetic lines
Embryonic development	External development, transparency, technical simplicity, microinjections are easy	Intrauterine development, non-transparent, difficult access	Zebrafish are an irreplaceable model for in vivo visualization of ontogenesis
Features of pharmacological testing	Substances are added to water; systemic exposure is more difficult to control	Precise routes of administration (oral, injection)	Risks in drug administration make mice the standard for translational pharmacological research

from humans. Although approximately seventy percent of the zebrafish genome is homologous to the human genome, these intrinsic genetic features must be carefully considered, as they may substantially influence research outcomes. Genome duplication may result in functional redundancy, whereby knockout of one gene may be compensated by its paralog, masking phenotypic effects, and complicating genetic analysis, as simultaneous knockout of both paralogs may be required. These characteristics may hinder direct modeling of certain monogenic human disorders.

It is also important to note specific structural and functional features of the zebrafish nervous system, which may serve not only as advantages but also as limitations in particular research contexts.

It is also necessary to consider specific structural characteristics of the zebrafish nervous system, which may serve not only as advantages but also as limitations of this experimental model.

Neurobiological characteristics of zebrafish as limitations for research:

1. Relative structural simplicity of the brain. Although the zebrafish brain contains the principal anatomical regions, it lacks a six-layered cerebral cortex, which creates difficulties for investigating higher cognitive functions.

2. Certain neurochemical differences. Differences exist between zebrafish and humans in both the composition and distribution of neurotransmitters.

3. Restrictions in behavioral testing. The range of validated behavioral paradigms for assessing complex emotional states such as depression and anxiety is limited compared with rodents and often requires careful interpretation. Nevertheless, several reliable behavioral tests are currently available for zebrafish, including the open field test, which allows for meaningful behavioral assessment.

4. High regenerative capacity of the central nervous system. From a research perspective, this characteristic represents both an advantage and a limitation, particularly in studies focused on neurodegenerative disorders such as Alzheimer's disease and Parkinson's disease, where progressive neuronal loss plays a key pathogenic role.

The relative simplicity of the zebrafish brain therefore defines the scope of its applicability. On one hand, the absence of a complex cerebral cortex limits opportunities for accurate modeling of higher cognitive processes and severe psychiatric disorders. On the other hand, this structural simplicity, combined with the transparency of zebrafish larvae, represents a major advantage for visualization of neuronal networks and investigation of fundamental neurobiological mechanisms.

When zebrafish (Danio rerio) are compared with other laboratory animals, particularly rodents such as mice and rats, which remain the gold standard experimental models, both advantages and disadvantages of zebrafish become evident (Table 1) [27].

Thus, the selection of zebrafish (Danio rerio) as an experimental model must be strictly justified by the specific scientific objective. Zebrafish represent a powerful complementary model to existing experimental systems. Their primary strengths include suitability for large-scale genetic and pharmacological screening, investigation of embryogenesis and regenerative processes, and real-time in vivo visualization. However, in studies involving complex physiological systems, multigenic diseases with strong environmental influences, and research intended for direct clinical translation, caution is required, along with subsequent validation in mammalian models.

Conclusion.

Based on the analysis of current data regarding the wide range of applications of zebrafish (Danio rerio), it has been confirmed that this species has established a strong position as one of the most versatile and promising model organisms in modern biomedicine. However, the use of this model requires careful consideration of both its strengths and its objective limitations, depending on the specific research context. Zebrafish (Danio rerio) represent not merely a model organism but an integrative platform that unites multiple scientific disciplines. Owing to advances in genetic technologies and state-of-the-art visualization methods, this model continues to open new opportunities for an in-depth understanding of numerous biological processes that remain insufficiently explored.

REFERENCES

1. Merkulov V.A, Yagudina R.I, Serpik V.G. Global Spectrum of Development of Innovative Medicines: A Descriptive Review. Proceedings of the Scientific Center for Expertise of Medicinal Products. Regulatory Research and Expertise of Medicines. 2024;14:14-28.
2. Tulina M.A, Pyatigorskaya N.V. Special aspects of the biomedical cell products' development, non-clinical and clinical trials. RMJ. 2017;11:830-835.
3. Volskaya E. Optimization of preclinical studies: towards a humane experience. Remedium. 2016;1-2:6-12.
4. Tubau-Juni N, Hontecillas R, Ehrich M, et al. Preclinical Studies: Efficacy and Safety. In: Bassaganya-Riera J (ed.). Accelerated Path to Cures. Springer, Cham; 2018.
5. Differences between in vitro, in vivo, and in silico assays in preclinical research. 2025. https://www.zeclinics.com/blog/differences-between-in-vitro-in-vivo-and-in-silico-assays-in-preclinical-research/
6. Tyurenkov I.N, Lomkina E.M, Kurkin D.V, et al. Ethical implications of preclinical studies. Scientific Centre for Expert Evaluation of Medicinal Products Bulletin. 2015;3:36-41.
7. Kachanov D.A, Lakeenkov N.M, Levikin K.E, et al. Danio rerio (zebrafish) – an universal model object in preclinical studies. FORCIPE. 2018;1:49-53.
8. Li H.H, Huang P, Dong W, et al. A brief history of zebrafish research--toward biomedicine. 2013;35:410-420.
9. Westerfield M. The zebrafish book. A guide for the laboratory use of zebrafish (Danio rerio). 4th ed. University of Oregon Press; 2000.
10. Howe K, Clark M.D, Torroja C.F, et al. The zebrafish reference genome sequence and its relationship to the human genome. Nature. 2013;496:498-503.
11. Shen C, Zuo Z. Zebrafish (Danio rerio) as an excellent vertebrate model for developmental, reproductive, cardiovascular, neural and ocular toxicity studies. Environ Sci Pollut Res. 2020;27:43599-43614.
12. Danio rerio. https://pubmed.ncbi.nlm.nih.gov/?term=danio+rerio&filter=years.1995-2025&timeline=expanded.
13. Virina N, Kesova E, Gadzhieva D, et al. Effect of some immunomodulatory drugs on embryonic development of Danio rerio. Georgian Med News. 2024;346:98-101.
14. Doszyn O, Dulski T, Zmorzynska J. Diving into the zebrafish brain: exploring neuroscience frontiers with genetic tools, imaging techniques, and behavioral insights. Front Mol Neurosci. 2024;17:1358844.
15. Seegobin S.P, Heaton G.R, Liang D, et al. Progress in LRRK2-associated Parkinson's disease animal models. Front Neurosci. 2020;14:674.
16. Wint J.M, Sirotkin H.I. Lrrk2 modulation of Wnt signaling during zebrafish development. J Neurosci Res. 2020;98:1831-1842.
17. Zairkhanova Kh.A, Virina N.V, Nogaeva S.G, et al. Assessment of the neurotoxicity of antitumor drugs in Danio rerio fish in an experiment. Bulletin of the North-Western State Medical University named after I.I. Mechnikov. 2024;16:94-103.
18. Fontana C.M, Van Doan H. Zebrafish xenograft as a tool for the study of colorectal cancer: a review. Cell Death Dis. 2024;15:23.
19. Xiao J, Glasgow E, Agarwal S. Zebrafish xenografts for drug discovery and personalized medicine. Trends Cancer. 2020;6:569-579.
20. Singhal S.S, Garg R, Mohanty A, et al. Recent advancement in breast cancer research: insights from model organisms—mouse models to zebrafish. Cancers (Basel). 2023;15:2961.
21. Virina N.V, Kosolapova E.A, Kachanov D.A. The effect of some antitumor drugs on caudal fin regeneration in Danio rerio. In: St. Petersburg Scientific Readings – 2024, Abstracts of the X International Youth Medical Congress; 2024.
22. Nguyen P.D, Gooijers I, Campostrini G, et al. Interplay between calcium and sarcomeres directs cardiomyocyte maturation during regeneration. Science. 2023;380:758-764.
23. Mujica E, Hoed M. Investigating the role of lipid genes in liver disease using models of steatotic liver disease in zebrafish (Danio rerio). Liver Int. 2023;43:2348-2350.
24. Mariyko V.A, Mariyko V.V. The current state of the antibiotic resistance problem. Bulletin of New Medical Technologies. 2025;19:147-159.
25. Lin L.C, Tsai Y.C, Lin N.T. Phage-antibiotic synergy enhances biofilm eradication and survival in a zebrafish model of Pseudomonas aeruginosa infection. Int J Mol Sci. 2025;26:5337.
26. Carvajal-Agudelo J.D, McNeil A, Franz-Odendaal T.A. Effects of simulated microgravity and vibration on osteoblast and osteoclast activity in cultured zebrafish scales. Life Sci Space Res. 2023;38:39-45.
27. China is sending zebrafish to the Tiangong space station. https://www.space.com/china-tiangong-space-station-zebrafish