ZEBRAFISH

A MODEL ORGANISM IN BIOMEDICAL SCIENCES

MEDSCIEN9502

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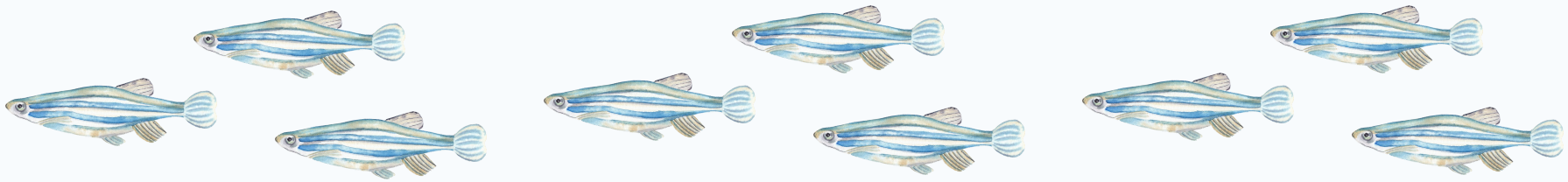
Agenda

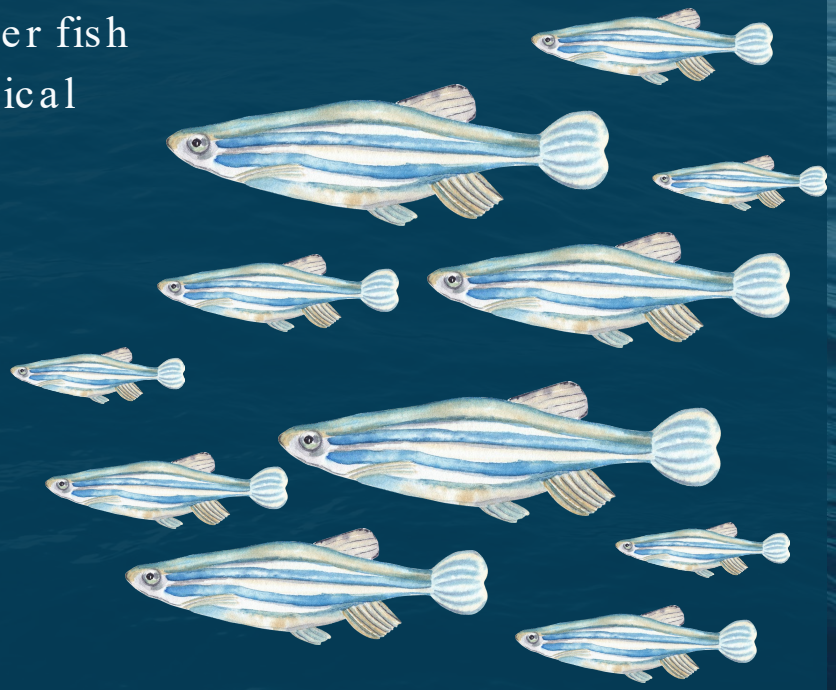
1. INTRO TO ZEBRAFISH
2. HISTORY OF STUDY
3. ADVANTAGES & LIMITATIONS
4. ZEBRAFISH CASE STUDIES



INTRODUCTION

Introduction

- Zebrafish (*Danio rerio*) are small freshwater fish
- Widely used as model organisms in biological and medical research
- Native to South Asia
- Key features:
  - Short generation time
  - High fertility
  - Rapid development
  - Eggs develop externally
  - Sexually mature by 12 weeks



Chia et al. (2022)

HISTORY AND KEY EVENTS

History

1822

First described by the British physician Francis Hamilton

Early 20th Century

Popular as aquarium fish in Europe and the U.S

1934

Charles W. Creaser published a paper describing the suitability of zebrafish for embryological research

1960s

George Streisinger transitioned to working with zebrafish as a model for vertebrate genetics

1981

First major breakthrough in zebrafish research by developing a technique to generate homozygous diploid zebrafish through artificial parthenogenesis

1983

Mutagenesis techniques were established

Ankeny et al., (2012)
Chia et al. (2022)
JP., (2002)

History

1988

The first study analyzing a neuronal necrosis mutant from mutagenesis experiments was published

1990s

Charles Kimmel, a developmental biologist, published the first fate map for zebrafish

Christiane Nüsslein-Volhard initiated preparations for large-scale mutagenesis screen

1993-1996

Large-scale mutagenesis screens were conducted

1996

Results from these screens were published in Development journal

2001

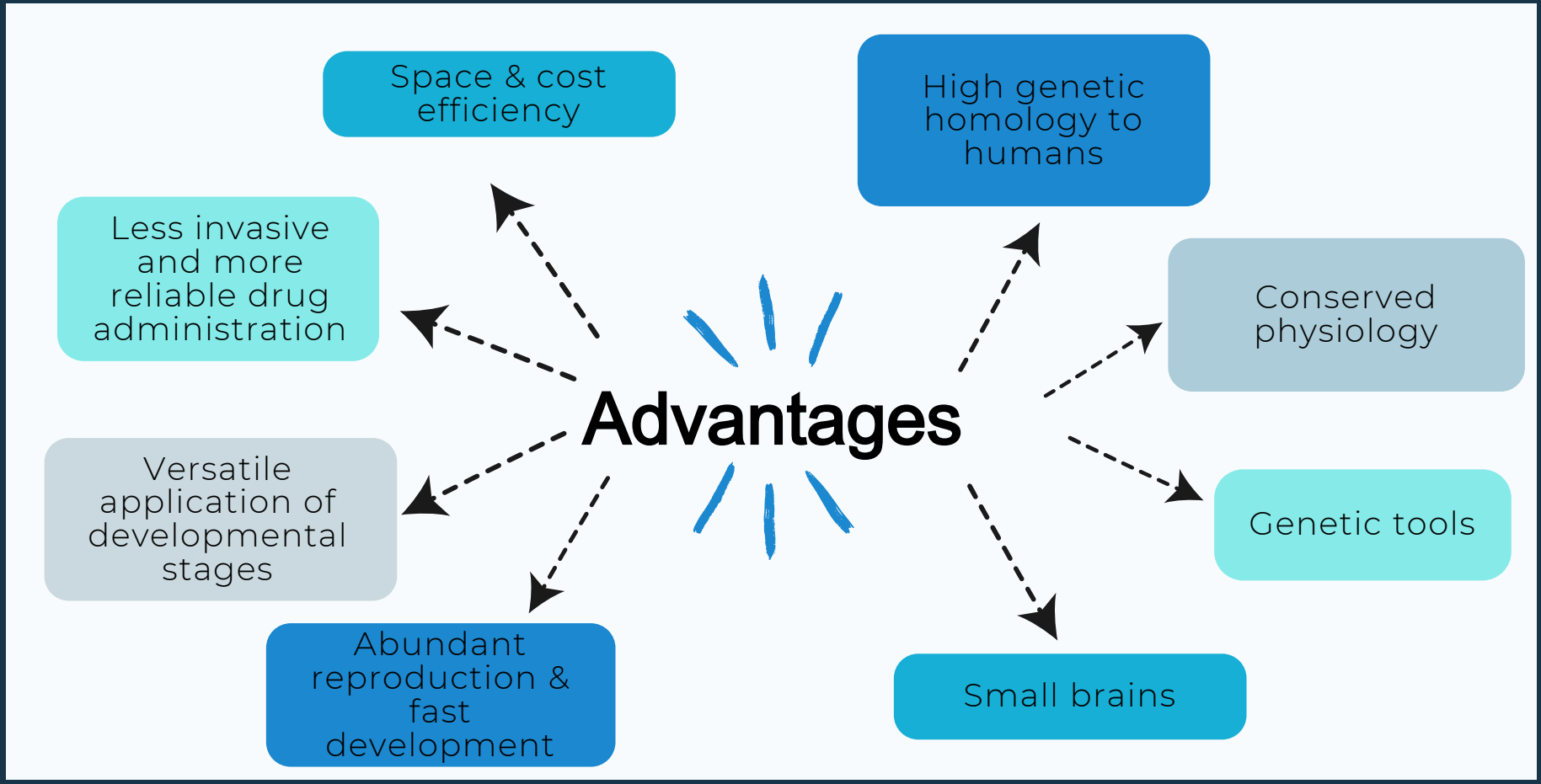
Zebrafish Genome Project was initiated

PRESENT

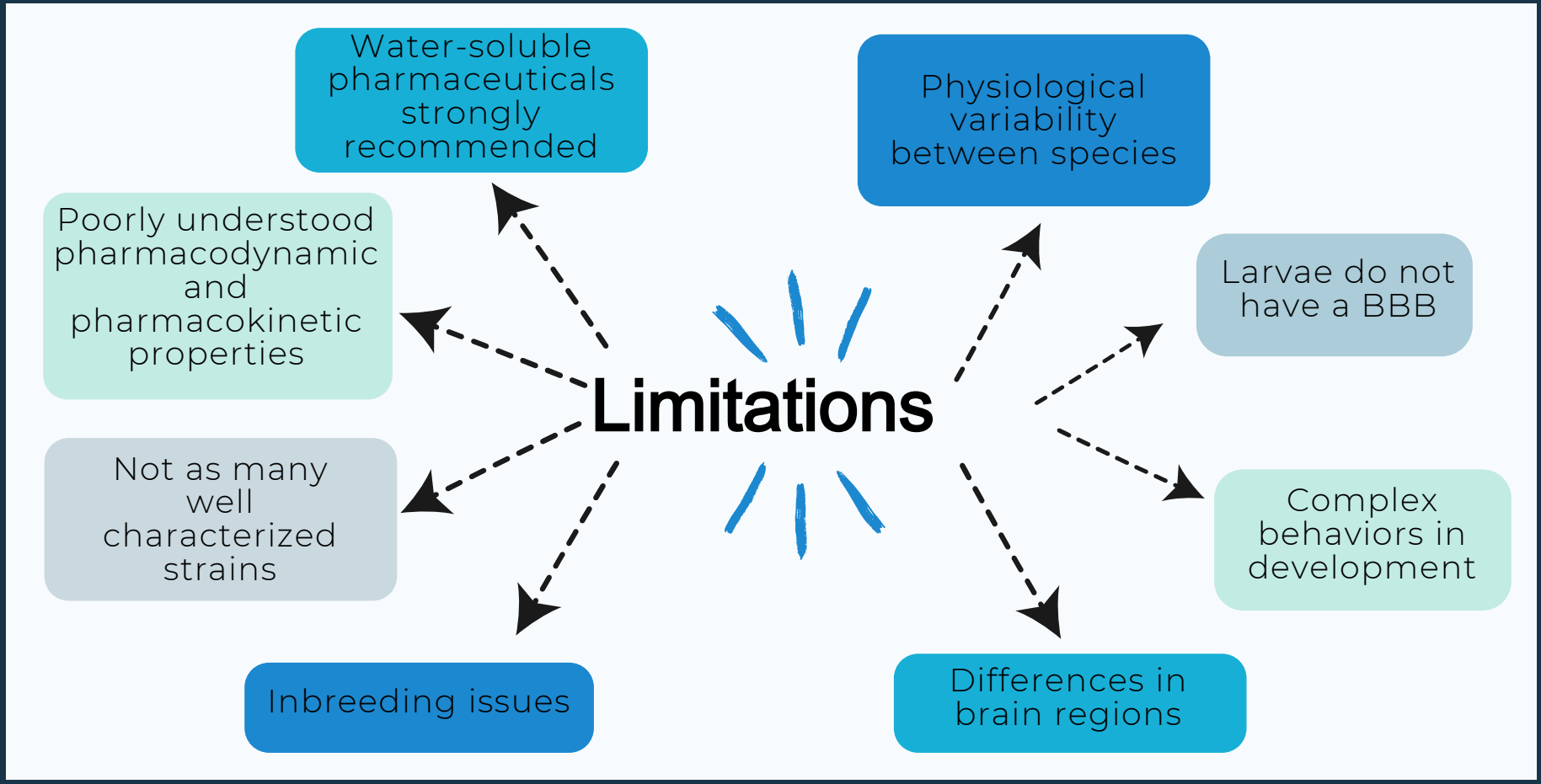
Zebrafish have become a crucial model in human disease research

Ankeny et al., (2012)
Chia et al. (2022)
JP., (2002)

KEY ADVANTAGES & LIMITATIONS



(Chia et al., 2020)
(Stewart et al., 2014)
(Vaz et al., 2018)



(Chia et al., 2020)
(Stewart et al., 2014)
(Vaz et al., 2018)

ZEBRAFISH IN BIOMEDICAL RESEARCH

Genetics & Development

- zebrafish reference genome: GRCz11
- *in vivo* model for studying causal genes and mechanisms underlying human disease pathogenesis
- amenable to genetic manipulations
  - CRISPR/Cas9
  - next-generation sequencing (NGS) & long-read nanopore sequencing
  - functional validation of GWAS findings
- optogenetics and fluorescent markers for tracking cell processes over time
  - non-invasive, real-time imaging of internal structures

The Company of Biologists (2015)

Kar & Subbiah (2013)
Howe et al. (2013)
Choi et al. (2021)
Chernyavskaya et al. (2022)

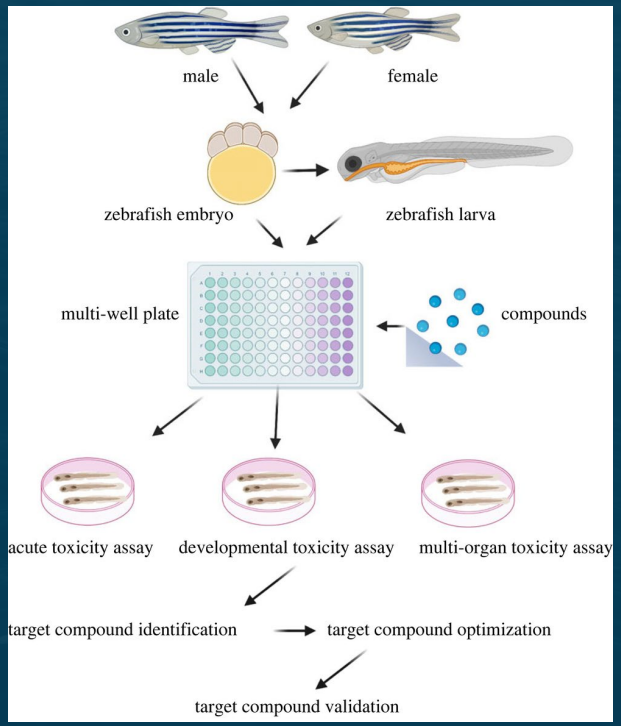
Drug Development & Toxicology

High -throughput Drug Screening

- Zebrafish embryos are permeable to small molecules, enabling rapid compound testing.
- i*n vivo* approaches for phenotype-based screening
  - study signalling cascades using chemical inhibitors
  - assess toxicity and target identification
  - apply AI-driven imaging to track and visualize tagged compounds

Precision Medicine applications:

- new molecular targets for diagnostic and therapeutic strategies



Adapted from: Dash & Patnaik (2023)

Burke (2016)
Choi et al. (2021)
Dash & Patnaik (2023)
Angom & Nakka (2024)

NEUROSCIENCE

NEURODEVELOPMENTAL RESEARCH

Studying Neuronal Development

- Well-conserved nervous system structures with humans
- Model for studying neurogenesis, neuron mapping, and neuroendocrine functions.
- Transparent larval stage allows *in vivo* monitoring of motor neuron pathways and degeneration.

Howard Hughes Medical Institute (2013)

Chia et al. (2022)
Dash & Patnaik (2023)
Angom & Nakka (2024)

NEUROSCIENCE

MODELLING NEURODEGENERATIVE DISEASES

Application in ALS, Parkinson's, Alzheimer's, Huntington's

- Models recreate key pathology features (e.g., protein aggregation, neuron degeneration)

Case Study: ALS and FUS Mutation Studies

- Used to uncover pathological mechanisms like neuron degeneration in ALS (Lebedeva et al., 2016).

Howard Hughes Medical Institute (2013)

Choi et al. (2021)
Chia et al. (2022)

COMPLEX DISEASES

CARDIOVASCULAR RESEARCH

Heart Disease and Regeneration Models

- Zebrafish hearts mimic human cardiac processes, aiding studies in CVD.
- High regenerative capacity of zebrafish cardiomyocytes provides insights into cardiac regeneration.

Doxorubicin Cardiotoxicity Model

- Identification of cardioprotective agents
  - visnagin (VIS) and diphenylurea (DPU)
- found to combat chemotherapy-induced heart damage (Lui et al., 2014)

Nightsea (2014)

Kar & Subbiah (2013)
Dash & Patnaik (2023)
Angom & Nakka (2024)

COMPLEX DISEASES

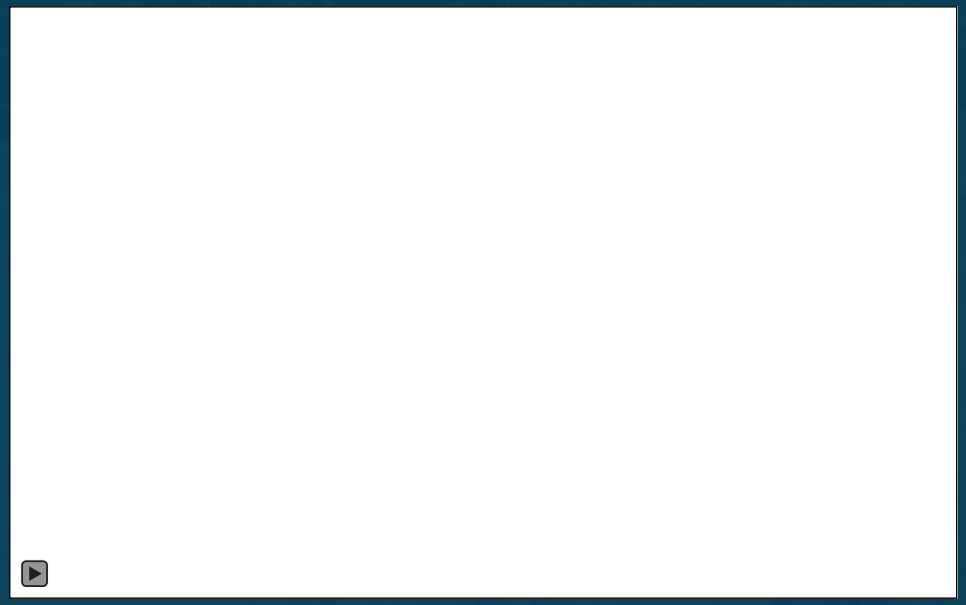
ONCOLOGY RESEARCH

Cancer Modeling and Drug Screening

- Tumour growth visualization, drug screening, and toxicity testing.

Success in Kinase Inhibitor Identification

- Found compounds targeting cell proliferation and migration in melanoma and leukemia (Hason et al., 2023).
- high sensitivity and accuracy for quantifying cancer cell growth
  - valuable model for pre-clinical drug screening.



Cancer Research UK (2014)

Dash & Patnaik (2023)

Conclusions

Zebrafish

A versatile and powerful model organism in biomedical research due to their genetic and physiological similarity to humans.

Advantage

Zebrafish's transparency, high fecundity, and genetic manipulability make them especially useful for developmental biology, genetics, disease modelling, and drug discovery.

Future

CRISPR, NGS, and AI-driven imaging enhance their role in personalized medicine and drug discovery, furthering insights into human diseases, therapeutic targets, and regenerative medicine applications.

THANK YOU

FOR LISTENING

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