Contact information

For further information on the project's scientific goals, planned activities and job opportunities please see the project web site (www.zf-models.org) or contact:

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Job opportunities

The participating institutes will continuously provide job opportunities and training for technicians, PhD students and postdocs. To find out about current openings, please see the project web site (www.zf-models.org) or contact the heads of the labs you are interested in directly (contact details are listed on the project's web site).

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Page 3: MPI for Developmental Biology (1, 3), University of Sheffield (2), UCL (4); Page 4: MPI for Developmental Biology; **Layout:** Verena Dreessen

ZF-MODELS

A Sixth Framework Programme Project

Zebrafish Models for Human Development and Disease

SIXTH FRAMEWORK PROGRAMME

Overview

"ZF-MODELS – Zebrafish Models for Human Development and Disease" is an Integrated Project funded by the European Commission as part of its 6th Framework Programme. The aim of this project is to exploit the advantages of the zebrafish as a model organism for vertebrate development and human disease. A total of 29 groups at 15 different institutions in France, Germany, Italy, the Netherlands, Norway, Switzerland and the United Kingdom are working together to achieve this aim. The project, which will run over a period of five years, is funded with € 12,000,000.- from the European Commission and € 400,000.- from the Swiss National Science Foundation.

Scientific goals of the project

The research groups involved in the ZF-MODELS project will produce new insights into how genes control development and ageing in vertebrates, using the zebrafish as a model organism. Apart from gaining fundamental insights into the genetic control of these processes, the results will form a basis for the development of new or improved therapies. Targets of the project will be common pathologies such as cancer, neurodegenerative diseases, muscular dystrophies and eye diseases, as well as resistance to infections, the process of wound healing and behavioural disorders.

The scientific work of the ZF-MODELS project is grouped into five workpackages:

(1) Mutagenesis screening: Two large-scale mutagenesis projects are bringing together scientists from all over Europe to examine zebrafish carrying genetic mutations. In contrast to previous zebrafish mutagenesis screens, the ZF-MODELS project has an emphasis on genes of particular relevance to human diseases. In addition to mutants with defects in early development, there is a focus on mutations that affect the adult fish; these are of special interest for analysis of processes involved in human diseases. New screening assays are being developed to discover such genes. Additionally, fish transgenic for the Green Fluorescent Protein (GFP) is being mutagenised and screened for anomalies in the development of the brain.

(2) Expression patterns: Thousands of fish are being generated, which place GFP under the control of enhancer sequences of specific genes (enhancer detection screening). Under blue light, the tissues of these fish will light up indicating wherever the respective gene is active. In addition, the three-dimensional patterns of gene expression during development is being analysed on a large scale by *in situ* hybridisation.

(3) Expression profiling and proteomics: The activity (expression) of tens of thousands of zebrafish genes is being analysed on gene chips (microarrays) to help understand how genes regulate each other's activity during normal development and how this regulation is disturbed in mutants. In addition, the proteins expressed in normal and mutant zebrafish are analysed to elucidate how protein expression is affected by genetic mutations and to check for post-transcriptional regulation and modifications.

(4) Targeted knock-out: A facility to knock-out genes has been established to provide European researchers with zebrafish mutants for specific genes. These knock-outs are generated on request by three laboratories to make this novel tool available to researchers both within and outside our ZF-MODELS consortium and let them study genes of particular interest for which no mutant is found in the mutagenesis projects. The knock-out fish will be suitable as models for human diseases and the development of therapies.

(5) Bioinformatics: All project data will be integrated into a European zebrafish database. By implementing novel tools to combine quantitative expression data with images of expression patterns and genome annotation, the ZF-MODELS database will provide an unprecedented view of gene expression in the developing vertebrate embryo. A focus will be the establishment of a three-dimensional anatomical atlas of zebrafish brain development linked with the relevant gene activities. The database will be accessible through the project web site (www.zf-models.org) and will be open to scientists and the interested public world-wide.

Information on the zebrafish

The zebrafish (*Danio rerio*), a popular aquarium fish, is ideally suited to study the fundamental processes underlying embryonic development and the genetic basis of diseases. In recent years, it has become one of the favourite model organisms of scientists in academia and the biotech industry.

Picture of an adult zebrafish. The characteristic stripes running along the body and the fins gave this species its name. Adult zebrafish measure only about 4 cm in length.

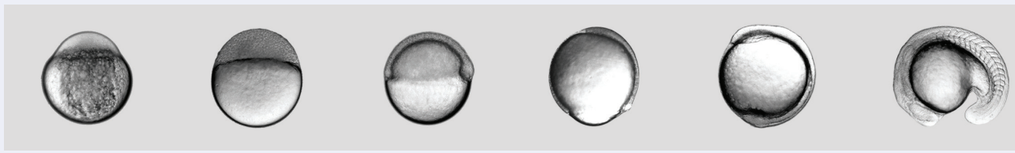
Transparent embryos

The development of the zebrafish is very similar to the embryogenesis in higher vertebrates, including humans. But, unlike mammals, zebrafish develop outside the female body. Moreover, the shell of their eggs is completely see-through. This allows the observation of developing embryos in their "natural environment". Additionally, the embryos themselves are transparent during the first few days of their lives – yielding a unique possibility to examine the formation of internal organs "live" inside the living organism.

Zebrafish larva 24 hours after fertilisation. Internal organs such as the brain, the heart, the inner ear and the muscles of the trunk can be seen.

Rapid development

The embryonic development of zebrafish is very rapid: In the first 24 hours after fertilisation, all major organs form; and by the third day of development, the fish hatch and start looking for food. After three to four months, zebrafish are sexually mature and can generate new offspring. A single female can lay up to 200 eggs per week.



An ideal model organism

These advantages – the large number of offspring, the rapid embryonic development and the transparency of the embryos – make the zebrafish an ideal model organism to study various aspects of development in vertebrates using a genetic approach.

The zebrafish genome

Zebrafish have 25 chromosomes and their genome comprises approx. 1.5 billion base pairs. This is about half the size of mammalian genomes. The zebrafish genome is currently being sequenced by an international consortium that involves the Wellcome Trust Sanger Institute, UK; the Max Planck Institute for Developmental Biology, Germany; the Hubrecht Laboratory, The Netherlands and Harvard Medical School, USA.

Zebrafish embryo stained to reveal the activity of a gene during development. This gene is expressed at the boundaries of the muscles in the trunk as well as in the developing ear and heart.

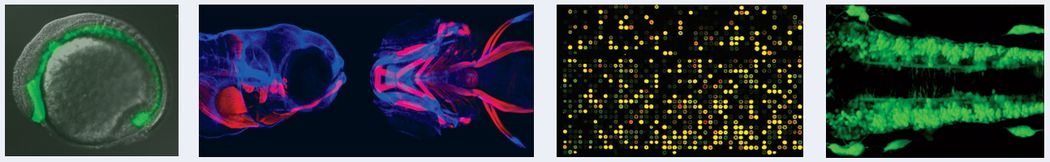
It is currently unknown, how many genes there are in the zebrafish, but it is expected that the total number will be very close to the total found for mammalian genomes. Importantly, the genes in zebrafish are closely related to the ones in humans and often have the same or very similar roles during development, normal body function or disease.

Outreach

The ZF-MODELS project intends to share the knowledge generated during the project with the wider scientific community and the general public as a whole. This is done, for example, by sharing its large-scale resources with scientists outside the consortium on a collaborative basis and by providing an integrative element for all of European zebrafish research (please see www.zf-models.org for details on the projects and resources open to interested parties). Moreover, the ZF-MODELS project will establish a European Working Group on Vertebrate Models by bringing together the leading European research groups who work on other vertebrate model organisms. The aim of this group is to provide a forum for the exchange of expertise, tools and ideas between the different communities.

In addition to reaching out to groups involved in basic research, the ZF-MODELS consortium interacts with clinical researchers and the pharmaceutical industry seeking to address human diseases. This is achieved by, for example, inviting stakeholders from these communities to participate in events (e.g. meetings, symposia, workshops) organised by the ZF-MODELS consortium. Also, visits and placements of staff from these communities to labs of the ZF-MODELS consortium are strongly encouraged. Through this goal, the consortium aims to strengthen existing collaborations and establish new ones.

The ZF-MODELS consortium is strongly committed to furthering the understanding and acceptance of science by the general public. A particular focus of the initiatives aimed at the general public is to get young people interested in taking up a career in science. To support the careers of those already training to be scientists, the ZF-MODELS consortium is establishing training and exchange programmes for students, young researchers as well as junior technical staff.



Background information on the ZF-MODELS project

The project is coordinated by the Max Planck Institute for Developmental Biology in Tübingen, Germany. Dr. Robert Geisler is the project's Scientific Coordinator, Dr. Ralf Dahm is the Project Manager and Nobel Laureate Prof. Christiane Nüsslein-Volhard chairs the project's Executive Committee.
The project officially began on January, 1st 2004 and will end on December, 31st 2008.
The project's website is www.zf-models.org.

Institutions participating in the ZF-MODELS Integrated Project:

- Max Planck Society for the Advancement of Science, Germany
  Participating Max Planck Institutes:
  Max Planck Institute for Developmental Biology, Tübingen, Germany
  Max Planck Institute for Immune Biology, Freiburg, Germany
  Max Planck Institute of Molecular Cell Biology and Genetics, Dresden, Germany
- The Wellcome Trust Sanger Institute, Cambridge, UK
- Institut de Génétique et de Biologie Moléculaire et Cellulaire, Illkirch, France
- Hubrecht Laboratory, Netherlands Institute for Developmental Biology, Utrecht, The Netherlands
- The University of Sheffield, UK
- University College London, UK
- Institut National de la Santé et de la Recherche Médicale, Paris, France
- Albert-Ludwigs-Universität Freiburg, Germany
- University of Bergen, Norway
- Universita' degli Studi di Padova, Italy
- GSF-National Research Center for Environment and Health, Neuherberg, Germany
- Institut Pasteur, Paris, France
- Leiden University, The Netherlands
- ETH – Swiss Federal Institute of Technology, Zurich, Switzerland
- Forschungszentrum Karlsruhe GmbH, Germany

For a full list of participating groups, please see the ZF-MODELS project's website: www.zf-models.org.