Completion of the zebrafish reference genome yields strong comparisons with the human genome

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Researchers demonstrate today that 70 per cent of protein-coding human genes are related to genes found in the zebrafish and that 84 per cent of genes known to be associated with human disease have a zebrafish counterpart. Their study highlights the importance of zebrafish as a model organism for human disease research.

The team developed a high-quality annotated zebrafish genome sequence to compare with the human reference genome. Only two other large genomes have been sequenced to this high standard: the human genome and the mouse genome. The completed zebrafish genome will be an essential resource that drives the study of gene function and disease in people.

At first glance, Zebrafish may seem to be a strange comparator to humans, but like us they are vertebrates and we share a common ancestor. They are remarkably biologically similar to people and share the majority of the same genes as humans, making them an important model for understanding how genes work in health and disease.

"Our aim with this project, like with all biomedical research, is to improve human health," says Dr Derek Stemple, senior author from the Wellcome Trust Sanger Institute. "This genome will allow researchers to understand how our genes work and how genetic variants can cause disease in ways that cannot be easily studied in humans or other

organisms."

Zebrafish research has already led to biological advances in cancer and heart disease research, and is advancing our understanding of muscle and organ development. Zebrafish have been used to verify the causal gene in muscular dystrophy disorders and also to understand the evolution and formation of melanomas or skin cancers.

"The vast majority of human genes have counterparts in the zebrafish, especially genes related to human disease," says Professor Jane Rogers, senior author formerly at The Genome Analysis Centre. "This high quality genome is testament to the many scientists who worked on this project and will spur biological research for years to come.

"By modeling these human disease genes in zebrafish, we hope that resources worldwide will produce important biological information regarding the function of these genes and possibly find new targets for drug development."

The zebrafish genome has some unique features, not seen in other vertebrates. They have the highest repeat content in their genome sequences so far reported in any vertebrate species: almost twice as much as seen in their closest relative, the common carp. Also unique to the zebrafish, the team identified chromosomal regions that influence sex determination.

The zebrafish genome contains few pseudogenes - genes thought to have lost their function through evolution - compared to the human genome. The team identified 154 pseudogenes in the zebrafish genome, a fraction of the 13,000 or so pseudogenes found in the human genome.

"To realize the benefits the zebrafish can make to human health, we need to understand the genome in its entirety – both the similarities to

the human genome and the differences," says Professor Christiane Nüsslein-Volhard, author and Nobel laureate from the Max Planck Institute for Developmental Biology. "Armed with the zebrafish genome, we can now better understand how changes to our genomes result in disease."

"This genome will help to uncover the biological processes responsible for common and rare disease and opens up exciting new avenues for disease screening and drug development," adds Dr Stemple.

More information: Kerstin Howe, Matthew D. Clark, et al (2013) "The Zebrafish Reference Genome Sequence and its Relationship to the Human Genome" Advanced online publication in *Nature*, 17 April - DOI: 10.1038/nature12111

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