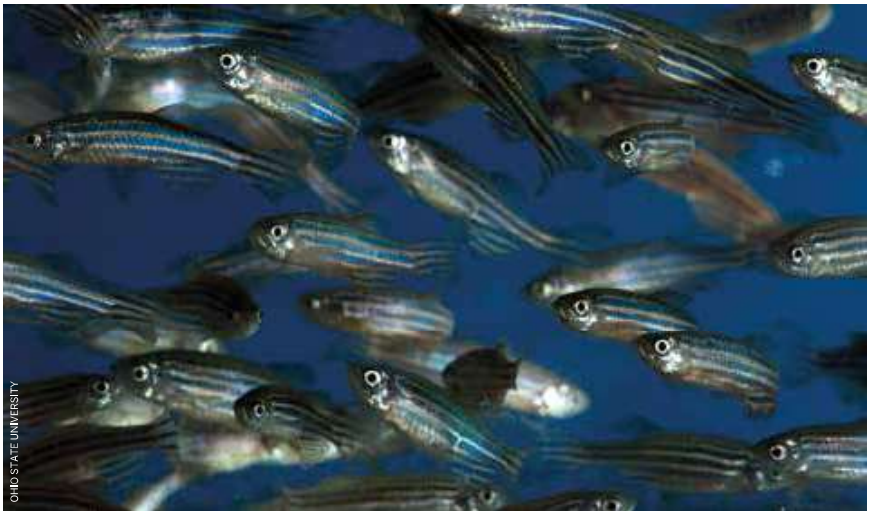
OHIO STATE UNIVERSITY

# Zebrafish steal the show in drug research

*Combining computer algorithms with zebrafish experiments, Rob van Wijk developed a pharmacological model to interpret preclinical data faster and cheaper.*

'In my research project, I develop and improve algorithms to translate research data from in vitro experiments to vertebrates such as animals and humans', says Rob van Wijk. He is a PhD student at the division of Systems Biomedicine and Pharmacology of the Leiden Academic Centre for Drug Research. His research focusses on pharmacokinetic models for uptake, distribution and clearance of drugs. To achieve that, Van Wijk uses zebrafish as a biological model.

For this multidisciplinary research, the former bio-pharmaceutical sciences student collaborates with the Institute of Biology Leiden, and with the Leiden Institute of Advanced Computer Science. Furthermore there are collaborations with the Free University Medical Center Amsterdam (VUmc), Uppsala University in Sweden, as well as with The Dana–Farber/Harvard Cancer Center in Boston, USA.

Conversion of experimental results to vertebrates or between species is a challenge. 'In translational pharmacology it is important to have good quantitative mathematical models', says Van Wijk. 'Systems pharmacology elucidates biological pathways and networks. Systems pharmacology models have great predictive value, but they need to be fuelled by solid experimental input. Therefore, we need lots of high quality data. In our lab we obtain this data by performing laboratory experiments in zebrafish, which is a better model than the traditionally used animal models, which are expensive and time-consuming.'

## Upcoming

Due to the zebrafish's genetic similarity to humans, their high fertility rate, their small size, the presence of major organ systems already at 72–120 hours after fertilisation, and low maintenance costs, zebrafish – already common in biology – are now upcoming in pharmacology. 'We can do high-throughput drug screens with thousands of compounds at the same time. For instance, in antibiotic screens, with the help of fluorescently labelled bacteria, we can easily see in the transparent larvae which compound eradicates the bacteria. This increases experimental speed enormously.'

## Robust

'One of my recent results is the development of a method in which I refined the quantification of paracetamol exposure in the zebrafish. I improved the currently used mathematical model that used measurements from total lysates from 3- to 5-day old zebrafish larvae, and developed a method to draw blood from 5-day old fish, weighing as little as 300 micrograms. I analysed the blood concentrations that were taken at different time points with liquid chromatography / mass spectrometry and modelled these data to determine the clearance of paracetamol. I then compared the data from these experiments with published data on paracetamol clearance. The blood sample data input made the translational model much more robust and improved the predictive value of drug clearance, for the translation to other species.'

Altogether, Van Wijk is pleased with his results so far. 'With my zebrafish model and mathematical algorithms, I obtained pharmacological experimental results faster and with reduced use of rodents as compared to traditional pharmacological research. Therefore, my research not only contributes to better drug development, but it also reflects the ethical guidelines of replacement, reduction and refinement of laboratory animals, which is an important extra.' ●

## *Experimental speed increases enormously*

*Rob van Wijk is participating in the PhD Student Competition at the FIGON Dutch Medicines Days.*