

Expediating CNS drug discovery

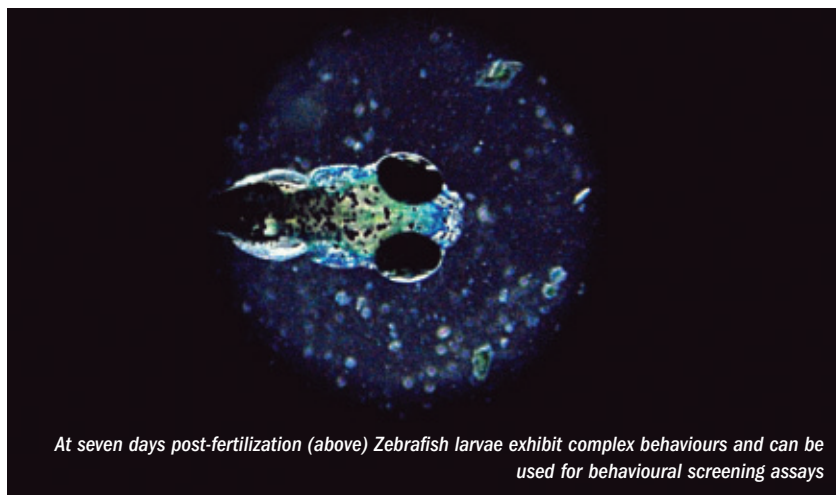
The provision high throughput screening...

Based in Iceland, 3Z is a preclinical drug discovery company that focuses on the discovery of new central nervous system (CNS) active drugs. It provides expert services to pharmaceutical companies involved in high throughput screening of small molecule libraries. The company offers versatile services that can be adapted to fit a wide range of behavioural phenotyping projects.

High throughput screening is an established process for lead discovery and a key provider of novel CNS active agents. While the highly publicised pullout of big pharma from CNS drug development reveals faults that need to be addressed at many fronts, a better selection of chemical entities for the development pipeline is essential for the restoration of CNS drug development.

In recent years, rapid increases in chemical library size and throughput capacity have gone hand-in-hand. Less emphasis has been placed on tailor-made assays and increased result quality. While the appeal of high throughput screening remains high data volume for a low price, CNS drug development and discovery is better served using focused libraries for screening and tailor-made high content assays. 3Z utilises the ultimate readout of the CNS, namely behaviour, to garner tailor-made zebrafish-based assays to reveal novel CNS active molecules.

A unique set of advantages has made zebrafish an increasingly popular vertebrate animal model among researchers. First, their small size and low cost render zebrafish a good laboratory animal. Second, the genome of the zebrafish is close to being completely sequenced, with preliminary sequencing revealing a



At seven days post-fertilization (above) Zebrafish larvae exhibit complex behaviours and can be used for behavioural screening assays

high degree of conservation between zebrafish and humans. Third, fertilisation is external and development rapid, resulting in power to study a wide array of phenomena in the fish. Indeed, many research techniques are unique to zebrafish; for 3Z the most noteworthy is their utility in genetic and chemical screens. Fourth, due to a rich early behavioural repertoire, zebrafish can easily be used for a variety of behavioural screens.

By automatically monitoring behaviour in thousands of zebrafish larvae over 24 hours, and using custom-built data analysis routines, 3Z can quickly and cost-effectively screen thousands of compounds in vivo for CNS effects, significantly increasing the quality of the screen and, thus, reducing the cost and time of CNS drug discovery.

3Z provides state-of-the-art services delivered by professionals in neuroscience

The analyses are behaviourally based. By means of highly developed analysis routines, each screen yields basic parameters for each compound, such as average swim velocity, total activity, sleep percentage, sleep fragmentation, place preference, sleep bout distributions, etc. The customer

receives a compact overview of the effects of all the molecules in the library on larval behaviour. The data is presented in custom-built software with a user-friendly interface. The specific effects of each compound can then be individually visualised and presented in sufficient detail for patent applications.

3Z

3Z was founded in 2008 by Karl Karlsson, Reykjavik University, and Haraldur Thorsteinsson. It springs from RU Neurolab, a Reykjavik University-based neuroscience laboratory, in which a zebrafish model of sleep has been in development since 2006.

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