

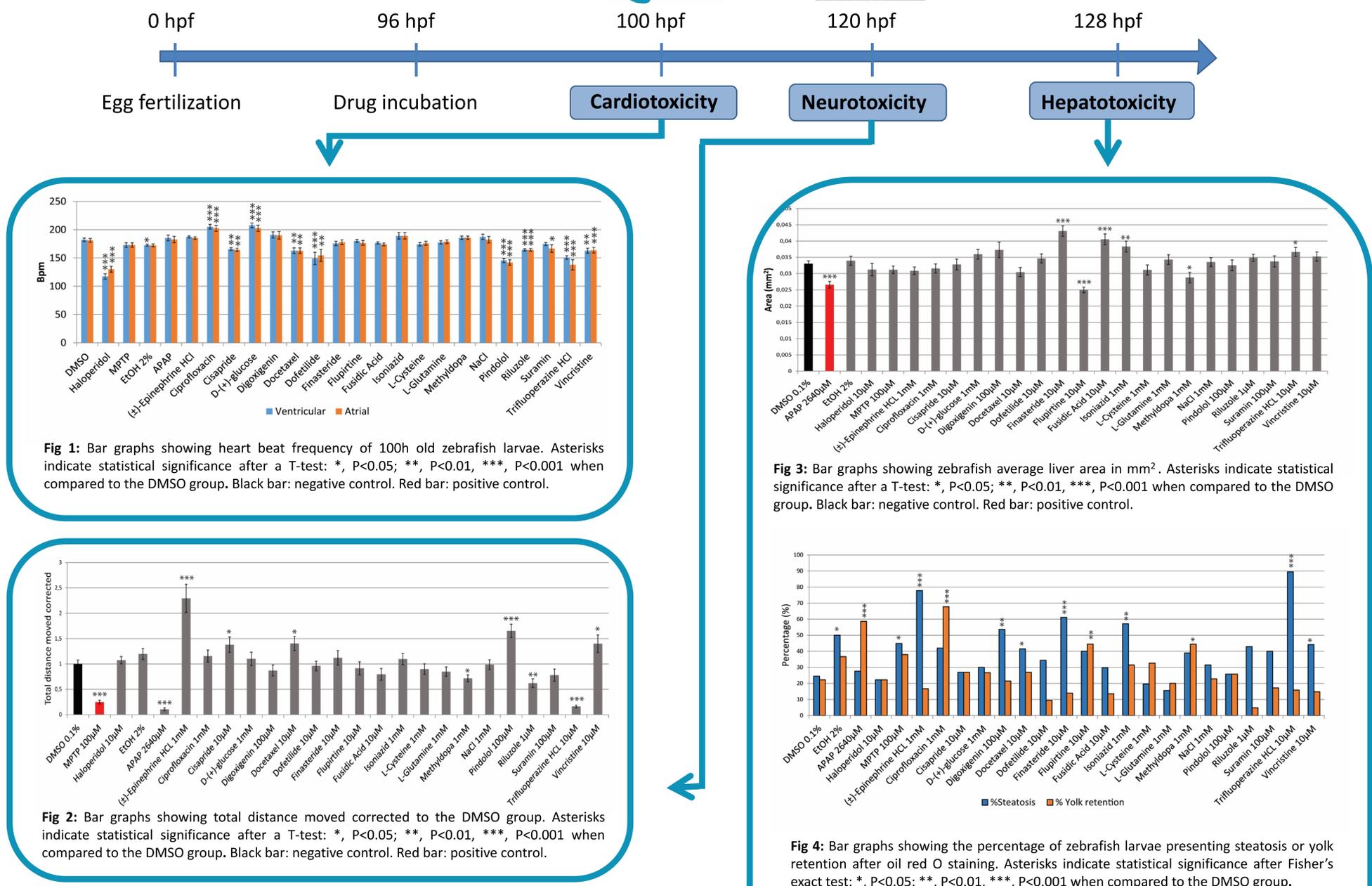
ZeGlobalTox, a new way for global toxicity assessment

Carles Cornet, Rafael Miñana, Simone Calzolari, Davide D'Amico and Javier Terriente.
ZeClinics, PRBB, Barcelona, Spain, www.zeclinics.com.



Zebrafish exploitation for high-throughput drug screening is becoming important for the pharmaceutical industry to assess toxicity and efficacy of novel drugs. Zebrafish has, from early developmental stages, fully functional organs from a physiological point of view. Thus, drug-induced toxicity is easily detected and evaluated, bridging the gap between preclinical *in vitro* and *in vivo* models in a fast and cost-effective manner.

ZeClinics has developed **ZeGlobalTox**, an innovative tool that integrates *in vivo* toxicity assessment for the brain, heart and liver in the same animal, strongly impacting the 3Rs principles. This assay **Reduces**, by up to a third, the number of animals required to assess toxicity in these organ. The new physiological parameters included in the ZeGlobalTox **Refines** the drug toxicity assay. The high predictivity of the ZeGlobalTox (Specificity: 85% and Sensitivity: 76%) allows to **Replace** the use of other classical species, such as rodents or other mammals.



CONCLUSIONS

ZeGlobalTox is highly predictive, demonstrating its validity as an innovative tool for integrated multi-organs toxicity prediction of new drugs during preclinical drug discovery phases and, additionally, for the implementation of 3Rs recommendations.

Zf	Cardiotoxicity		Neurotoxicity		Hepatotoxicity			
	Human		Human		Human			
	-	+	-	+	-	+		
-	TN: 12	FN: 2	-	TN: 13	FN: 2	-	TN: 17	FN: 2
+	FP: 3	TP: 8	+	FP: 2	TP: 8	+	FP: 2	TP: 4

Zf: zebrafish, TN: true negative, TP: true positive, FN: false negative, FP: false positive.

	Specificity TN/(TN+FP)	Sensitivity TP/(TP+FN)	PPV TP/(TP+FP)	NPV TN/(TN+FN)
Cardiotoxicity	80%	80%	73%	86%
Neurotoxicity	87%	80%	80%	87%
Hepatotoxicity	89%	67%	67%	89%
ZeGlobalTox	85%	76%	73%	87%

Zf: zebrafish, PPV: positive predictive value, NPV: negative predictive value, TN: true negative, TP: true positive, FN: false negative, FP: false positive.

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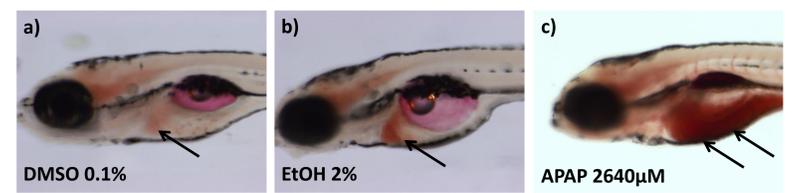


Fig 5: Representative oil red O whole mount staining images of control (DMSO 0.1%), EtOH 2% and APAP 2640µM showing non-affected liver, a), liver with steatosis, b) and yolk retention, c), pointed with black arrows.