Using zebrafish CRO to accelerate grant application process

Customer Story

InVivo Biosystems

Overview:
Dr Anita Quintana is an Associate Professor in Biological Sciences at the University of Texas at El Paso. Her lab is focused on understanding the mechanisms underlying multiple congenital anomaly syndrome. They utilize a zebrafish animal model to study gene mutations which they've identified in patients in the clinic.

Challenge:
Dr Quintana approached InVivo Biosystems wanting to collaborate on three independent projects that each targeted a different region or domain of the protein HFC1. HFC1 is of particular interest to Quintana because it is a gene that is associated with intellectual disability and manifests during the developmental period. The end goal of the three projects was to compare how different gene mutations would differ in their disruption of neural precursors.

Solution:
Dr. Quintana chose to leverage InVivo Biosystems' fully validated custom injection mixes to create point mutations that target the protein HFC1 in zebrafish. InVivo Biosystems worked with Dr. Quintana's lab to design the mixes, and provided her lab with the validation protocol. Consequently, Quintana's lab was able to generate F1 heterozygous carriers from the fully validated mixes, and then, used InVivo's screening reagents to identify carriers with the precise germline edit within a matter of weeks.

> Time was really important to me in order to get to a point where we had the mixes and they were validated.
>
> - Dr. Anita Quintana

Benefits:
By working with InVivo Biosystems Dr Quintana was able to overcome their greatest hurdle: the screening, as InVivo Biosystems provided the full protocol used and was available for troubleshooting at any point. Quintana felt confident in InVivo Biosystems' approach, and found great value in the company's validated mixes which provided "higher efficiency." Further, InVivo Biosystems' fully validated injection mix strengthened Quintana's grant application, as it provided proof of concept.

Background:

Dr Anita Quintana's lab utilizes a zebrafish embryo model to identify and characterize the underlying mechanisms associated with congenital human disorders. Congenital disorders are often-inherited conditions that occur before birth, specifically, Quintana's lab focuses on craniofacial (bones of skull and face) abnormalities and intellectual disorders.

Unlike many researchers, Quintana's research actually begins in the clinic - she works with clinicians and geneticists from around the country to find and study patients with these diseases and disorders. After identifying a mutated gene in a patient, Quintana's lab finds its parallel gene in a zebrafish and then conducts in vivo loss of functions studies to better understand how different mutations produce unique disease phenotypes.

One of the genes of interest for Quintana's lab is Hcfc1b. Mutations in the gene has been found to result in X-linked recessive disorder, cblX, which results in craniofacial abnormalities and other developmental defects (Quintana et al., 2014) [Image 1].

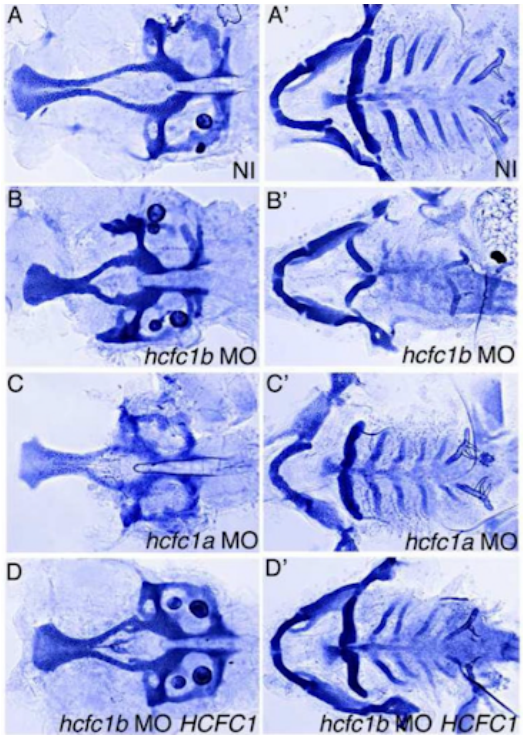

Image 1. Loss of hcfc1b causes defects in craniofacial development (Quintana et al., 2014).

Why zebrafish?

The zebrafish is a particularly beneficial model for Quintana's work as zebrafish embryos are translucent and develop ex-utero, and thus, it is very easy to directly observe cells over the fish's development.

Why Invivo Biosystems?

Quintana explained that InVivo Biosystems has, “the efficiency and the set-up to do it. To do these kinds of assays on your own it takes a lot of optimization.”

Quintana specifically called out the benefit that InVivo provides by having validated mixes, that, “that validation was useful, particularly as preliminary data for some grant proposals that I was in the middle of submitting.” This preliminary data shows that the desired patient variant can be detected in the somatic tissues, and thus, instills grant reviewers with confidence in the ability for a germline carrier to be able to be identified with sufficient screening.

Quintana spoke to how InVivo Biosystems differed from other companies she’s come across, “usually companies just give you the stuff and they don’t tell you how to screen it, they don’t offer the primers and you’re sort of stuck doing that on your own.”

The Data

InVivo Biosystems created mixes for four KI mutations in the hcfc1b loci of zebrafish embryos. These validated mixes were sent to Quintana’s lab, who injected these mixes into their fish with the goal to use CRISPR/Cas9 and gRNA to recode fish genome to mimic the mutations found in humans. InVivo Biosystems was able to send these mixes to Quintana’s lab in a timely manner, which Quintana explained made it, “cheaper in the long run (...) if I had had a student come in and make CRISPR and through go through this process, I couldn’t guarantee that it would work and it could take upwards of a year.”

Eventually, Quintana’s lab is going to conduct single cell RNA sequencing in each mutant to identify subpopulation that would be uniquely disrupted by each individual mutation. For Quintana, the advantage of working with InVivo Biosystems was not only an accelerated process, but “but your company provided the printouts of the validation and they allowed me to use those gels for my grant applications (...) that was exactly what I needed because it was exactly what the reviewers were asking for.” Quintana said that thanks to our collaboration, “right now we’re in a really good position.”

References:

Quintana, A. M., Geiger, E. A., Achilly, N., Rosenblatt, D. S., Maclean, K. N., Stabler, S. P., Artinger, K. B., Appel, B., & Shaikh, T. H. (2014). Hcfc1b, a zebrafish ortholog of HCFC1, regulates craniofacial development by modulating mmachc expression. *Developmental biology*, *396*(1), 94–106. https://doi.org/10.1016/j.ydbio.2014.09.026

About InVivo Biosystems

Founded in Eugene, Oregon in 2011, InVivo Biosystems is working to accelerate deep in-vivo insights into human biology and enable researchers to develop and deliver solutions that improve human health. An expert in CRISPR genome editing, InVivo Biosystems provides a unique capability for creating custom genome edited zebrafish and *C. elegans* that enable therapeutic research on genetic models of aging, developmental, and neurodegenerative disease, uncovering potential cures. The company's *in vivo* analytical testing platforms and technologies provide faster, cost-effective investigations that focus on proof-of-principle experiments for rapid go/no go decision making so that biopharma and nutraceutical companies around the world can better understand aging and aging related diseases and explore potential treatments.

All our projects include on-call project status updates, as well as regularly scheduled communication. We also provide on-call consulting and interpretation with our Ph.D. level, subject-matter experts.

What we do:

- Deliver scientific data on test results in less than 5 months.
- Produce the best outcome measures for anti-aging products.
- Provide information about mechanisms of action (MoA).
- Support your Marketing and IP claims with real science.

Contact us to start a conversation about how our services can support your innovation.

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