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NEWS

The Company of Biologists' Workshop – Fish Muscle Growth and Repair: Models Linking Biomedicine and Aquaculture

In February 2010, The Company of Biologists launched a series of workshops aimed at bringing together and fostering communication between disparate groups of scientists that do not usually have the opportunity to interact. So when Simon Hughes, an MRC Scientist at King's College London, UK, learned of the company's new initiative, he was struck by the opportunity this presented to bring together developmental geneticists studying fish muscle and integrative biologists working in aquaculture. 'The idea behind the workshop was to bring together communities working with the zebrafish as a model organism for basic biological and biomedical research… [and communities of] traditional experimental biologists and technologists working on non-model fish, including aquaculture species, because fish muscle is a food,' says Ian Johnston from St Andrew's University, UK, who co-organised the meeting with Hughes.

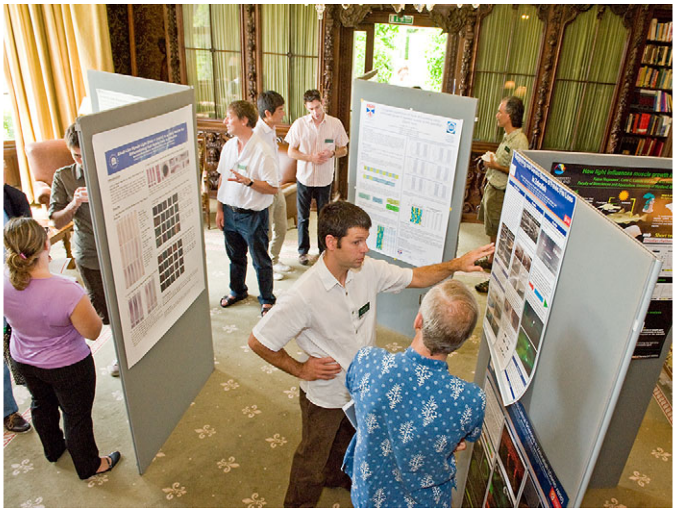
Fascinated by fish muscle development, Hughes is also concerned about the increasing need to improve the efficiency of aquaculture production in the context of declining of global fish stocks and the improving economic situation of people in the developing world increasing the demand for a high protein diet. Hughes says, 'Working on muscle from a basic biomedical point of view I realised I knew next to nothing about the practicalities of translating our findings to the real world of aquaculture; this was one motivation for this meeting.'

Together with Johnston, a fish muscle physiologist, Hughes assembled a program for discussion to address questions such as what controls muscle growth and how growth is integrated between different organ systems. Over three and a half days at the Fish Muscle Growth and Repair; Models Linking Biomedicine and Aquaculture workshop held at Wiston House, Steyning, UK, 31 fish muscle scientists with a wide range of backgrounds from four continents came together to discuss topics ranging from fish muscle development in the zebrafish to the effects of growth hormone in salmonids.

Delegates attending the Fish Muscle Growth and Repair: Models Linking Biomedicine and Aquaculture Company of Biologists Workshop, 26–29 June 2011 at Wiston House, Steyning, UK.

A central theme raised by the conference organisers was how muscle and body growth are coupled. Johnston opened the meeting by speaking about the evolution of dwarfism in Icelandic arctic charr, which is associated with a dramatic loss in muscle fibre number. He showed that differences in the expression of a limited number of mTOR pathway genes, which regulate protein synthesis, were found in multiple dwarf forms compared with large-bodied morphs, supporting the notion that changes in IGF/TOR signalling may be involved in producing the dwarf phenotype. Environmental factors can also have a dramatic effect on fish growth. According to Louisa Valente from CIMAR/ICBAS-UP, Portugal, Senegalese sole raised under higher temperatures grow larger, but also have a greater propensity for deformities. Continuing the theme of temperature effects on fish muscle growth, Peter Steinbacher from the University of Salzburg, Austria, presented a poster showing a somewhat different effect in pearlfish: although fish exposed to lower temperatures during embryonic growth had smaller muscle fibres at hatching, they became larger later in life, potentially because of a shift in the balance between proliferation and differentiation of muscle precursor cells. Focusing more on the mechanistic details underlying muscle growth, Jorge Fernandez found that both light and temperature affect growth with a concomitant change in the expression of microRNAs – small RNA molecules that bind mRNA to regulate gene expression post-transcriptionally. Similarly, Cunming Duan showed that hypoxia inhibits growth by driving the expression of insulin-like growth factor-binding protein 1 (IGFBP1), which in turn inhibits insulin growth factors, which themselves promote muscle growth and differentiation. Joaquin Gutierrez also spoke about IGF signalling, showing that in sea bream, IGFI and IGFII positively regulate myoblast proliferation and differentiation. Shifting to the genetics of early myogenesis, Hughes showed that, in zebrafish, the myogenic transcription factor Myod is necessary for muscle formation and growth. Trina Galloway presented her work on early muscle growth in halibut, which showed that halibut have two paralogues of MyoD. Strikingly, although MyoD1 expression has left–right symmetry, MyoD2 expression is asymmetrical. On the last day, attendees were treated to a pair of talks examining transgenic strategies for enhancing muscle growth in aquaculture. Bob Devlin showed that salmonids overexpressing growth hormone grow larger than their wild-type counterparts, and Terry Bradley blocked TGF-beta signalling in trout and observed resulting increases in muscle growth.

Although muscle growth is of key interest for the aquaculture industry, muscle regeneration after injury and muscle-wasting dystrophic diseases are a major concern for the biomedical community. Although little was known about the mechanisms of muscle regeneration in fish until recently, several groups presented



Poster session where delegates discussed the meeting.

major breakthroughs in our understanding at the workshop. Philip Ingham from the Institute of Molecular and Cell Biology, Singapore, presented the results of experiments on zebrafish embryos, which have shown that after an induced injury to muscle fibres with cardiotoxin, a regenerative process occurs similar to that in mammals. After injury, cells expressing Pax7, a key factor in myogenic progenitor cells, are recruited in the damaged zone and proliferate. These cells also start to express myogenic molecular markers, such as the transcription factor MyoD, which plays a key role in muscle differentiation, and finally develop new muscle fibers. Peter Currie and his group from the Australian Regenerative Medicine Institute support these observations and also found that regeneration in the zebrafish injury model is very rapid, occurring in a matter of hours. Outlining the role of connection problems between muscle fibres and their extracellular matrix in dystrophy diseases, Clarissa Henry from the University of Maine, USA, demonstrated that deficiencies in nicotinamide ribose kinase-2 enzyme, an enzyme involved in NAD^+ biosynthesis, which also binds to cell adhesion structures, cause a severe dystrophy in zebrafish. Moreover, the defect can be partially reverted by NAD^+ treatment, potentially opening the door to new targets for muscle dystrophy research.

Building on Ingham's presentation on the role of transcription factors in muscle regeneration, Hughes and Steven Devoto also discussed their work on specification and formation of muscle in the zebrafish and described how various transcription factors are involved in specifying differentiation of specific muscle lineages. Continuing the theme of building our understanding of the basic mechanisms of muscle differentiation, Derek Stemple discussed his zebrafish TILLING project, where chemically induced gene mutations are introduced and identified by large-scale sequencing in the hope of finding mutants of relevance for in-depth studies of muscle development and growth.

The translation of developmentally based zebrafish research into the more growth-oriented aquaculture questions was one of the most debated issues at the workshop. Genetically modified (GM) aquaculture species with increased growth rates have already been successfully generated and Herve Migaud from the University of Stirling, UK, presented evidence for enhanced growth performance in the sterile triploid salmon in comparison to the diploid. Triploidy is one method of ensuring sterility in aquaculture fish, something essential to prevent the spread of GM genes to wild fish populations. The delegates agreed that environmental factors affecting fish growth, including nutrition and exercise, which had been discussed earlier by Valente and Duan, require further investigation. Also, although great progress has been made in our understanding of early muscle development in zebrafish, the aquaculture community requested more work on muscle development in zebrafish at later stages. This is becoming increasingly tractable with ongoing developments of techniques such as the Cre-lox system in fish, which can be used to control gene expression to address specific mechanistic questions.

Concluding the workshop, Hughes says, 'It did a great job bringing the aquaculture and developmental biology communities together in that most of us had not previously met most people from the other community.' He adds, 'I think that there are many areas in which zebrafish are a good and, most importantly, experimentally tractable model for fish in general. On the other hand, there are specialised aspects of zebrafish biology that, without a broad knowledge of fish diversity, may not be sufficiently understood.' Highlighting muscle growth control, Hughes explains that myostatin seems to work differently in fish than in mammals and that growth control in zebrafish appears to differ markedly from that in larger fish. 'Whether these represent fundamental differences in physiology or just distinct experimental paradigms is unclear as yet,' he says, and hopes that dialogue between the integrative community and developmental biologists can identify areas where the zebrafish model is particularly relevant while developing alternative models to address questions to which the zebrafish is less suited.

Considering the impact of the workshop from the perspective of the integrative community, Johnston says, 'The whole idea is to challenge the JEB community to embrace the power that model systems give to understanding mechanisms, because ultimately we are interested in mechanisms in experimental biology.'

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