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Review

Advances in European sea bass genomics and future perspectives

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ABSTRACT

Only recently available sequenced and annotated teleost fish genomes were restricted to a few model species, none of which were for aquaculture. The application of marker assisted selection for improved production traits had been largely restricted to the salmon industry and genetic and Quantitative Trait Loci (QTL) maps were available for only a few species. With the advent of next generation sequencing the landscape is rapidly changing and today the genomes of several aquaculture species have been sequenced. The European sea bass, *Dicentrarchus labrax*, is a good example of a commercially important aquaculture species in Europe for which in the last decade a wealth of genomic resources, including a chromosomal scale genome assembly, physical and linkage maps as well as relevant QTL have been generated. The current challenge is to stimulate the uptake of the resources by the industry so that the full potential of this scientific endeavor can be exploited and produce benefits for producers and the public alike.

Contents

1. Introduction

As little as a decade ago the only available fish genomes were from model fish species: *Fugu rubripes* (Aparicio et al., 2002), *Tetraodon nigroviridis* (Jaillon et al., 2004), *Danio rerio* (Howe et al., 2013), *Oryzias latipes* (Kasahara et al., 2007) and *Gasterosteus aculeatus* (Jones et al., 2012). With the "next generation sequencing" revolution, the flood of genomic and genetic data has grown exponentially and recently several genetics and genomics resources, including transcriptomes and genomes of economically relevant fish species have been published, e.g. Chen et al. (2014); Star et al. (2011); Guyon et al. (2012); Wang et al. (2014) and Canario et al. (2008) for a review. Despite these advances, so far the impact on aquaculture of new technologies in genome analysis coupled to a parsimonious breeding program is still limited (Gjedrem, 2010). This is particularly true in the Mediterranean area where intensive models of production have only recently been adopted and few documented examples of structured selective breeding programs exist. The objective of the present review is to evaluate the status of genomic and genetic tools for the European sea bass, *Dicentrarchus labrax*, and discuss a conceptual approach for the efficient application by industry of genomic information into selective breeding programs for this species. The strategy proposed for implementation of genomic data in a production setting may also be applicable to newly adopted aquaculture species of interest for which available resources may be limited.

2. European sea bass aquaculture history and genetics resources

The European sea bass is a gonochoristic marine teleost fish, distributed in temperate European coastal areas of the Northeast Atlantic Ocean and Mediterranean Sea. Its intensive exploitation as an aquaculture species is relatively recent and production is concentrated predominantly in the Mediterranean basin. It was initially cultivated in

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semi-intensive lagoon systems but since the 1980's production has become progressively more intensive due to its high commercial value. The total production of European sea bass was 126 thousand tonnes in 2010, with a market value of 500 million Euro (FAO, 2012). The expansion of European sea bass aquaculture production throughout Europe and the associated increase in its commercial importance have been the catalyst that has led in a relatively short space of time to a significant body of scientific and technical knowledge about this species. The bulk of the research carried out on the European sea bass has largely occurred over the past twenty years and encompasses basic biology through to modern day genetics and genomics.

The European sea bass has in the last 10 years moved to the forefront of aquaculture species in terms of availability of genetic and genomic resources. The production of genomics and genetics tools for this species has been a community wide effort that has involved numerous scientists in Europe and in a large part has been driven by European Commission funded consortia. Outputs from such European projects include high density linkage and synteny maps, a radiation hybrid map, transcriptome data (Chistiakov et al., 2005, 2008; Massault et al., 2010; Volckaert et al., 2012; Guyon et al., 2010; Louro et al., 2010; Kuhl et al., 2010, 2011a), a high quality draft genome sequence (NCBI bioproject accession: PRJEA39865) (Kuhl et al., 2010; Tine et al., submitted for publication; Kuhl et al., 2011b) and mapped QTLs for economic traits (Massault et al., 2010; Volckaert et al., 2012; Chatziplis et al., 2007; Dupont-Nivet et al., 2008; Saillant et al., 2006). Table 1 lists publicly available genetic, genomic and/or transcriptomics resources for European sea bass and the source reference. Clearly the next important step is to apply these tools to a long-term and sustainable breeding program for European sea bass analogous to what has been developed for terrestrial farm animal production (de Koning et al., 2007; Sellner et al., 2007).

3. Genetics & genomics trends in research & industry

Selective breeding in aquaculture is mostly done by mass selection of the previous generation, or through family based selection. While mass selection is based only on selected parentage phenotypic values to identify the best individuals (selection candidates) in terms of their genetic potential for the desired traits, within family selection is based on breeding values (calculated through phenotype measurements and pedigree information) of the fish that is the target of selection and incorporating information on its relatives (Falconer and Mackay, 1996; Gjedrem, 2005). Selection based on genomic information is still a novelty in aquaculture, and there are relatively few examples of marker assisted selection (MAS) (Fernando and Grossman, 1989; Sonesson, 2007). One example of successful application of MAS is in salmonids, in which a major quantitative trait locus (QTL) affecting resistance to infectious pancreatic necrosis was selected by incorporating marker information in the selective breeding program (Houston et al., 2008).

Alternative or complimentary approaches and strategies are required to MAS, which despite its utility has inherent weaknesses linked to the limited number of QTL flanking markers used which means only a fraction of the total genetic variance is captured (Dekkers, 2004). An alternative approach to tracing a limited number of QTLs with markers is to trace all the QTL genome wide. This can be done by dividing the entire genome into chromosome segments, by adjacent markers with such density that the population-wide linkage disequilibrium between markers and QTL is utilized to generate the predicted genetic merit of the individual. This method has been termed genomic selection (GS) (Meuwissen et al., 2001), but needs a dense set of markers across the genome. Thus, genomic selection integrated with next-generation-sequencing (NGS) promises to be of great potential to create genomic information of added value for the accuracy of genomic prediction and genome wide association studies (e.g. finding causal mutations). The GS approach can potentially be done either by genotyping with Restriction site Associated DNA (RAD) (Miller et al., 2007), Genotyping-by-Sequencing (GBS) (Elshire et al., 2011), or by whole genome re-sequencing (Stratton, 2008) methodologies as illustrated by the 1000 bull genome project (http://www.1000bullgenomes.com/). Simulations based upon the standard aquaculture breeding practices of the gains (improved growth, disease resistance, etc.) suggest that genome-wide selection will result in high genetic gain for a typical family (Sonesson and Meuwissen, 2009).

3.1. Genomic selection approach

GS can be seen as a new form of scale-up MAS with genetic markers densely covering the whole genome identifying the full suite of QTLs of a given trait genome-wide. With the ease of production of large single nucleotide polymorphism (SNP) marker data and lower genotyping costs, the limitation today may be in the initial steps, namely of obtaining a reference population with robust phenotype data (and posterior prediction tuning) for the genomic prediction of phenotypes and breeding values with higher accuracies and better control of inbreeding (Daetwyler et al., 2013). To calculate the genomic estimated breeding value (gEBV), a reference population is genotyped and phenotyped in order to obtain a prediction equation which basically is the sum of the substitution effects over all SNPs. Selection candidates can then be screened through genotyping to choose the breeders by and obtain predictions of the phenotypes (Meuwissen et al., 2001). This approach

Table 1
Genetic, genomic and transcriptomics publicly available resources.

Resource type	Resource description	Year	Reference	Accession #
Genomic	Genome project	2011, 2014	Tine et al. (2014) and Kuhl et al. (2011b)	PRJEA39865
Genomic	Comparative BAC end mapping	2010	Kuhl et al. (2010)	FN436279 to FN538968
Genomic	Radiation hybrid map	2010	Guyon et al. (2010)	–
Transcriptomics	ESTs and de-novo RNA-seq assemblies	2010, 2012, 2014	Louro et al. (2010), Magnanou et al. (2014) and Sarropoulou et al. (2012)	FM000001 to FM029260, SRA050000, E-MTAB-1867
Transcriptomics	Oligo DNA microarray	2008, 2010, 2011	Ferraresso et al. (2010), Geay et al. (2011) and Darias et al. (2008)	PRJNA120433 PRJNA120529 PRJNA138507
Genetic	Growth and stress related QTLs	2007, 2010	Massault et al. (2010) and Chatziplis et al. (2007)	–
Genetic	Growth and stress related heritability's estimations	2006, 2008, 2012	Volckaert et al. (2012), Dupont-Nivet et al. (2008) and Saillant et al. (2006)	–
Genetic	1st and 2nd generation linkage maps	2005, 2008	Chistiakov et al. (2005 2008)	Notes at PMC1449790
Genetic	SNV calling	2011, 2012	Kuhl et al. (2011a) and Molecular Ecology Resources Primer Development et al. (2012)	FQ310506 to FQ310508, JM497134 to JM497249
Transcriptomics	Oligo DNA microarray. Immune response to stressor	2011	–	PRJNA138797
Transcriptomics	RNA-seq/de novo assembly	2014	–	PRJEB4602
Metagenomics	Gut metagenome	2012	–	PRJNA171730