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Genomics to accelerate genetic improvement in tilapia

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Summary

Selective breeding of tilapia populations started in the early 1990s and over the past three decades tilapia has become one of the most important farmed freshwater species, being produced in more than 125 countries around the globe. Although genome assemblies have been available since 2011, most of the tilapia industry still depends on classical selection techniques using mass spawning or pedigree information to select for growth traits with reported genetic gains of up to 20% per generation. The involvement of international breeding companies and research institutions has resulted in the rapid development and application of genomic resources in the last few years. GWAS and genomic selection are expected to contribute to uncovering the genetic variants involved in economically relevant traits and increasing the genetic gain in selective breeding programs, respectively. Developments over the next few years will probably focus on achieving a deep understanding of genetic architecture of complex traits, as well as accelerating genetic progress in the selection for growth-, quality- and robustness-related traits. Novel phenotyping technologies (i.e. phenomics), lower-cost whole-genome sequencing approaches, functional genomics and gene editing tools will be crucial in future developments for the improvement of tilapia aquaculture.

Keywords domestication, genetic improvement, genomic selection, genomics, GWAS, *Oreochromis niloticus*, sex determination, tilapia

Introduction

Tilapia is the common name of over 70 species of the Cichlidae family native to Africa and the Middle East. The genus *Tilapia* was first described in 1940 by Smith (1940). It consists of three subgenera taxonomically distinguished by reproductive behavior and feeding habits: *Tilapia* (biparental and substrate spawners), *Oreochromis* (female mouthbrooders) and *Sarotherodon* (biparental mouthbrooders). They are primarily herbivores, feeding mainly on phytoplankton and other aquatic vegetation, but readily accept complete artificial feeds that contain plant and/or animal proteins (El-Sayed, 2019).

Tilapia are widely desired for aquaculture across all tropical and subtropical climates owing to their favorable characteristics such as fast growth, tolerance to a wide range of environmental conditions, acceptance of artificial feed, and adaptability for production in different systems (El-Sayed, 2019). Owing to the rapid expansion of aquaculture over recent decades, it has been projected that the global production of tilapia will increase more than double between 2010 and 2030 (FAO, 2018a), which has encouraged the private sector to invest in technological improvements to increase production. Currently, tilapia is one of the most important warm-water species cultivated worldwide and in 2017 it was produced in more than 125 countries (FAO, 2019), reaching an annual global production of 5.88 million tonnes (FAO, 2018b). However, only China (32%), Indonesia (22%), Egypt (15%) and Brazil (7%) dominate world production, with more than 75% of the total. The Nile tilapia (*Oreochromis niloticus*) is the most important farmed tilapia, representing more than 70% of global production, with a value corresponding to US$ 7.6 million in 2017 (FAO, 2019). In addition, *Oreochromis mossambicus* and *Oreochromis* spp. (red tilapia), and hybrid tilapia like *O. aureus* × *O. niloticus* and *O. mossambicus* × *O. aureus*, have also played a significant role in production around the world (El-Sayed, 2019), representing a commercial value of US$ 3.4 million (FAO, 2019).

Tilapia production encompasses the whole spectrum from small farms to larger commercial investments, with all types of semi-intensive and intensive systems (cages, tanks, raceways and recirculation systems). Semi-intensive fish

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production uses natural food or both pond fertilization and supplemental food. This system is considered a low-cost fish production scheme owing to the stimulation of primary productivity through the pond's organic or inorganic fertilization and is commonly adopted for herbivorous and omnivorous species. On the other hand, the intensive system consists of high stock densities, a high rate of water exchange (with temperatures ranging from 20 to 35 °C) and high dependence on artificial food (El-Sayed, 2019). Furthermore, tilapia can be cultured in fresh water in tropical and subtropical climates, but in constrained range of temperatures. In addition, some species, including *O. mossambicuss* and *O. aureus*, have greater tolerance to saline water, whereas the *O. niloticus* have a limited capacity for reproduction, survival and growth in saline conditions (Suresh & Lin, 1992; Ninh *et al.,* 2014).

Domestication and selective breeding

Nile tilapia is one of the aquaculture species for which there is evidence of control of their reproduction early in human history (~3500 years ago; Harache, 2002). It is believed that the ancestors of cichlids had 24 chromosome pairs which eventually became 22 pairs (Majumdar & McAndrew, 1986; Ferreira *et al.,* 2010) during the domestication process. Out of these 22 pairs, three have been categorized into meta-submetacentric and the rest into subtelo-acrocentric chromosomes (Ferreira *et al.,* 2010).

Although tilapia has been farmed for thousands of years, expansion in commercial tilapia farming started in the 1980s, followed by a rapid increase in production (Teletchea, 2019) after the establishment of the first breeding program for Nile tilapia in 1988, by a collaboration between the International Center for Living Aquatic Resources Management (ICLARM, later renamed WorldFish) and AKVAFORSK in Norway. The project was named Genetically Improved Farmed Tilapia (GIFT), generated by crossing four wild strains from Africa and four farmed strains from the Philippines (Eknath *et al.,* 1993). Currently, this strain or some derivative of this strain is farmed in more than 87 countries in Africa, Asia and Latin America, and it has played an important role in tilapia production (Gjedrem *et al.,* 2012; Neira *et al.,* 2016). The selection program of the GIFT strain at the WorldFish Centre is in generation 20 (https://www.worldfishcenter.org/pages/gift/), primarily selected for growth. Meanwhile, another important commercial strain of GIFT (separate breeding program after generation 10 of original GIFT), under the brand name Genomar Supreme Tilapia (GST), is currently in generation 29 of the genetic selection program and fish are primarily selected for growth, fillet yield, disease resistance (*Streptococcus agalactiae* and *Flavobacterium columnare*) and survival, using genomic tools (http://www.genomar.no/).

Mass selection and pedigree-based selection are the most prevalent methods for genetic improvement in tilapias. Marker-assisted selection using microsatellites for parentage assignment has been practiced in Nile tilapia since 2004 in the commercial breeding program of GenoMar Genetics AS. Selection using genome-wide single nucleotide polymorphism (SNPs) is becoming a standard practice in routine selection programs in almost all species, including aquaculture, and is driven by the top international breeding companies. Benchmark Genetics has recently implemented genomic selection to increase resistance against *S. agalactiae*, whereas GenoMar Genetics AS has fully implemented genomic selection for all of the commercial traits in their GST breeding nucleus since 2019. Similarly, AquaBounty has already received genetic modification exemption for gene-edited tilapia (for fillet yield) in the Argentinian market. The different tools and methods that have been sequentially used in selective breeding of tilapias, including past, current and potential approaches, are shown in Fig. 1.

Population genetic studies

Previous studies using microsatellites investigated the genetic changes and characterization of different domesticated strains of tilapia (Rutten *et al.,* 2004; Sukmanomon *et al.,* 2012) or compared the improved strains with wild populations (Bezault *et al.,* 2011). Moderate to great genetic differentiation was reported by Rutten *et al.* (2004) when comparing four different strains from different origins: Chitralada (AIT), International Development Research Centers (IDRC), GIFT and University of Göttingen (GOTT) strains. Sukmanomon *et al.* (2012) reported that three of the four GIFT-derived populations studied retained the purity of GIFT and no reduced genetic variation was observed. McKinna *et al.* (2010) suggested that the decline of genetic diversity of a GIFT strain from Fiji was due to poor management of the genetic resource. In farmed stocks, an adequate level of genetic diversity is important to prevent the accumulation of inbreeding. Different selection and mating allocation strategies have been suggested to be successful in constraining the inbreeding levels and maintaining a sustainable breeding program in the long term in different tilapia breeding programs (Ponzoni *et al.,* 2010; Yoshida *et al.,* 2017c). For instance, Ponzoni *et al.* (2010) estimated an inbreeding rate of 0.37% per generation for a GIFT population established in Malaysia, where Bolivar & Newkirk (2002) estimated an inbreeding coefficient of 6.3% after 12 generations of selection for Nile tilapia.

The estimation of the effective population size (N_e) can be used to quantify how a population could be affected by genetic drift or inbreeding (Falconer & Mackay, 1996) and thus help in the monitoring and control of genetic diversity (Ponzoni *et al.,* 2010). An N_e value ranging from 50 to 200 is recommended to ensure the genetic variability and diversity in breeding programs (Smitherman & Tave, 1987); however, N_e values above 500 are suggested to be necessary in order to retain the evolutionary potential of a

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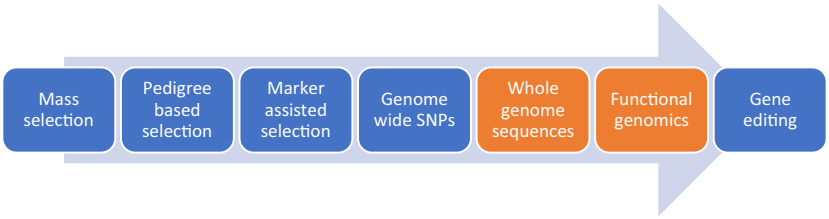

Figure 1 Different tools and methods used in tilapia selective breeding, with the arrow indicating the progressive temporal advancement of the methods. The blue and orange boxes indicate the methods being currently used and those not yet utilized for selection in Nile tilapia, respectively.

population (Franklin & Frankham, 1998). In Nile tilapia, the N_e calculated based on the rate of increase of coancestry was 88 in the GIFT Nile tilapia population (Ponzoni *et al.*, 2010) and 95 in the GST strain (Joshi *et al.*, 2018b), whereas using information from a 50K SNP panel, a contemporary N_e value, ranging from 78 to 159, was calculated for three commercial Nile tilapia populations from Latin America (Yoshida *et al.*, 2019c).

The genomic population structure and linkage disequilibrium (LD) have also been reported using dense SNP panels in different tilapia populations (Xia *et al.*, 2014; Joshi *et al.*, 2018; Conte *et al.*, 2019; Yoshida *et al.*, 2019c). For farmed Nile tilapia, strong admixture among three different farmed populations from Latin America and a rapid decrease in LD with increasing inter-marker distance were observed (Yoshida *et al.*, 2019c), in accordance with Xia *et al.* (2014), who found similar LD patterns for GIFT populations from South Africa, Singapore and China. Most of the linkage groups in Nile tilapia were found to have a sigmoidal pattern of recombination, with wide recombination deserts (areas with no recombination or high LD) stretching up to 5–10 Mb at terminal regions of most of the linkage groups (Joshi *et al.*, 2018a). These patterns have also been observed in the hybrid crosses of Lake Malawi cichlids (Conte *et al.*, 2019) and are opposite to what is seen in other fish species, e.g. channel catfish (Li *et al.*, 2015a, 2015b), salmon (Tsai *et al.*, 2015), Asian seabass (Wang *et al.*, 2015) and stickleback (Roesti *et al.*, 2013), in which the recombination rate is higher in the terminal regions.

Main traits, genetic parameters and genotype by environment interaction

Selective breeding is an effective approach to increase aquaculture production efficiency and profitability (Gjedrem, 2012). Despite the advantages of using improved animals, only a small proportion of global aquaculture is based on genetically improved stocks; nevertheless, most of the operating aquaculture breeding programs in the world were reported for Nile tilapia (Rye, 2012). Although there is a wide variation of culture systems, the main targeted traits included in tilapia breeding programs are associated with growth (e.g. body weight), with only a few breeding programs selecting for fillet yield, survivability and resistance to diseases. The heritability (h^2) for growth-related traits in Nile tilapia is in general diverse, ranging from 0.06 to 0.60 (Ponzoni *et al.*, 2005; Charo-Karisa *et al.*, 2006; Bentsen *et al.*, 2012; Khaw *et al.*, 2009, 2012; Hamzah *et al.*, 2014) (Table 1). Further, significant non-additive genetic effects and maternal effects have been reported for body weight, with inbreeding depression of 0.9% per 1% increase in the individual homozygosity for body weight (Joshi *et al.*, 2018b, 2020a). Genetic studies for resistance against diseases are scarce in Nile tilapia (Table 2), Shoemaker *et al.* (2017) and Suebsong *et al.* (2019) reported heritabilities for resistance to *S. agalactiae* in Nile tilapia, which ranged from 0.22 to 0.38, whereas for *Oreochromis* spp. a heritability of 0.27 was estimated by Sukhavachana *et al.* (2019). Joshi *et al.*, (2020b) reported genomic heritabilities for resistance against *S. agalactiae* in Nile tilapia ranging from 0.15 to 0.26. Significant genetic variation has also been detected for resistance against *Flavobacterium columnare* (Wonmongkol *et al.*, 2018) and *Streptococcus iniae* (LaFrentz *et al.*, 2016; Shoemaker *et al.*, 2017), indicating the potential for improving survival against bacterial outbreaks by using artificial selection.

In aquaculture, fillet yield is a key trait, but difficult to select for (Vandeputte *et al.*, 2020). However, a large phenotypic variation, ranging from 32 to 45%, and low (0.06 ± 0.04) to medium (0.25 ± 0.07) values of heritability have been reported for fillet yield in Nile tilapia, suggesting that this trait can be improved through selection (Rutten *et al.*, 2005; Gjerde *et al.*, 2012; Joshi *et al.*, 2018b, 2020a; Thodesen (Da-Yong Ma) *et al.*, 2011; Yoshida *et al.*, 2019b). However, fillet-related traits are always laborious and costly to measure; furthermore, these traits cannot be recorded on alive breeding candidates (Gjerde *et al.*, 2012a). For this reason, several studies estimated the genetic correlation (Table 3) to identify the feasibility of improving fillet traits through indirect selection for body traits that were recorded on live candidates. If these traits are well correlated, both selection intensity and accuracy may be increased, resulting in a higher genetic gain when compared with sib selection. In general, the genetic correlation between fillet weight and growth traits (e.g. body weight)

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Table 1 Heritabilities (standard error) reported in the literature for body weight, morphological and fillet traits in tilapia.

Traits	Species	Heritability	Mean phenotype	Statement	Reference
BD	*Oreochromis niloticus*	0.14 (0.04) to 0.20 (0.04)	6.7 (1.3) to 7.3 (1.4)	Male, female and all	Nguyen *et al*. (2007)
	Oreochromis niloticus	0.16 (0.04)	8.9 (1.0)	Genomic estimates	Joshi *et al*. (2020a)
	Oreochromis niloticus	0.17 (0.05) to 0.44 (0.1)	8.9 (1.0)	–	Joshi *et al*. (2018b)
	Oreochromis niloticus	0.28 (0.17–0.41)	7.5 (0.7)	–	Reis Neto *et al*. (2014)
	Oreochromis niloticus	0.32 (0.10)	10.3 (1.1)	–	Nguyen *et al*. (2010)
BL	*Oreochromis niloticus*	0.09 (0.03)	22.4 (2.1)	Genomic estimates	Joshi *et al*. (2020a)
	Oreochromis niloticus	0.17 (0.08) to 0.29 (0.08)	22.4 (2.1)	–	Joshi *et al*. (2018b)
	Oreochromis niloticus	0.19 (0.12)	25.9 (3.5)	–	Rutten *et al*. (2005)
	Oreochromis niloticus	0.30 (0.19–0.42)	19.7 (1.5)	–	Reis Neto *et al*. (2014)
	Oreochromis niloticus	0.29 (0.05) to 0.30 (0.05)	16.2 (2.9) to 17.3 (3.0)	Males, females and all	Nguyen *et al*. (2007)
	Oreochromis niloticus	0.31 (0.10)	23.8 (2.0)	–	Nguyen *et al*. (2010)
	Oreochromis niloticus	0.27 (0.19)	18.8 (1.7) to 21.9 (2.3)	Culture in brackish water	Ninh *et al*. (2014)
	Oreochromis spp.	0.13 (0.07)	18.1 (3.4)	–	Hamzah *et al*. (2017)
	Oreochromis spp.	0.07 (0.10) to 0.13 (0.08)	17.6 (2.9) to 18.3 (3.5)	Cage and pound culture	Nguyen *et al*. (2017)
BT	*Oreochromis niloticus*	0.17 (0.04)	4.1 (0.4)	Genomic estimates	Joshi *et al*. (2020a)
	Oreochromis niloticus	0.20 (0.08)	4.7 (0.9)	–	Nguyen *et al*. (2010)
	Oreochromis niloticus	0.21 (0.07)	4.1 (0.4)	–	Joshi *et al*. (2018b)
	Oreochromis niloticus	0.25 (0.13)	5.1 (0.9)	–	Rutten *et al*. (2005)
	Oreochromis niloticus	0.26 (0.05) to 0.29 (0.19–0.41)	3.0 (0.7) to 3.2 (0.7)	Male, female and all	Nguyen *et al*. (2007)
	Oreochromis niloticus	0.29 (0.19–0.41)	3.5 (0.4)	–	Reis Neto *et al*. (2014)
	Oreochromis niloticus	0.10 (0.04)	403.8 (124.8)	Genomic estimates	Joshi *et al*. (2020a)
	Oreochromis niloticus	0.14 (0.07) to 0.43 (0.10)	403.8 (124.8)	–	Joshi *et al*. (2018b)
BWH	*Oreochromis niloticus*	0.19 (0.04)	817.0 (261.1)	Genomic estimates	Joshi *et al*. (2019)
	Oreochromis niloticus	0.06 (0.09) to 0.48 (0.16)	121 (17) to 270 (45)	Five different generations	Bentsen *et al*. (2012)
	Oreochromis niloticus	0.26 (0.12)	787.7 (313.1)	–	Rutten *et al*. (2005)
	Oreochromis niloticus	0.31 (0.05)	166.0 (59.0)	log(BWH)	Khaw *et al*. (2016)
	Oreochromis niloticus	0.31 (0.11)	527 (132.5)	–	Nguyen *et al*. (2010)
	Oreochromis niloticus	0.33 (0.05) to 0.36 (0.05)	168.3 (82.4) to 206.8 (99.7)	Male, female and all	Nguyen *et al*. (2007)
	Oreochromis niloticus	0.34 (0.07)	192.0 (116.1)	–	Ponzoni *et al*. (2005)

Table 1 (Continued)

Traits	Species	Heritability	Mean phenotype	Statement	Reference
	Oreochromis niloticus	0.68 (0.16)	173.0	Cage culture	Bentsen *et al*. (2012)
	Oreochromis niloticus	0.485 (0.05)	262.4 (83.1) to 792.3 (278.3)	Cage culture	de Oliveira *et al*. (2016)
	Oreochromis niloticus	0.38 (0.12) to 0.60 (0.08)	70.0 (23.5) to 130.9 (39.5)	Low-input earthen ponds	Charo-Karisa *et al*. (2006)
	Oreochromis niloticus	0.24 (0.03)	214.9	Cage culture	Hamzah *et al*. (2014)
	Oreochromis niloticus	0.53 (0.12)	217.6 (78.7) to 366.3 (109.2)	Culture in brackish water	Ninh *et al*. (2014)
	Oreochromis niloticus	0.14 (0.06)	73.6 (46.6)	Pond culture	Rezk *et al*. (2009)
	Oreochromis niloticus	0.36 (0.28) to 0.71 (0.26)	53.6 (27.6) to 129.0 (41.0)	Low- and high-input environment	Khaw *et al*. (2009)
	Oreochromis niloticus	0.55 (0.09)	743 (27.7)[1]	Cage culture	Trong *et al*. (2013)
	Oreochromis niloticus	0.10 (0.03)	141.5 (51.4)	Genomic estimates	Joshi *et al*. (2020a)
	Oreochromis niloticus	0.10 (0.05) to 0.45 (0.11)	141.5 (51.4)	–	Joshi *et al*. (2018b)
	Oreochromis niloticus	0.36 (0.05)	953.5 (252.9)	Genomic estimates	Yoshida *et al*. (2019c)
	Oreochromis shiranus	0.14 (0.08)	71.5 (19.4) to 96.1 (24.4)[1]	Pound culture	Maluwa & Gjerde (2007)
	Oreochromis aureus	0.40 (0.04)	142 (61) to 487 (123)	Earthen pond culture	Thodesen Da-Yong Ma *et al*., 2011
	Oreochromis aureus	0.18 (0.09) to 0.55 (0.10)	181.9 (65.2) to 316.2 (125.9)	Pond culture	Zak *et al*. (2014)
	Oreochromis spp.	0.08 (0.08) to 0.22 (0.10)	245.7 (96.7) to 251.4 (138.5)	Cage and pond culture	Nguyen *et al*. (2017)
	Oreochromis spp.	0.38 (0.09)	247.6 (112.5)	–	Hamzah *et al*. (2017)
FW	*Oreochromis niloticus*	0.17 (0.04)	300.0 (107.3)	Genomic estimates	Joshi *et al*. (2019)
	Oreochromis niloticus	0.24 (0.11)	308.1 (152.5)	Tank culture	Rutten *et al*. (2005)
	Oreochromis niloticus	0.33 (0.10)	177.7 (49.9)	–	Nguyen *et al*. (2010)
	Oreochromis niloticus	0.16 (0.05)	197 (22.7) to 537 (25.1)	Net-cages and earthen ponds	Gjerde *et al*., (2012)[1]
	Oreochromis niloticus	0.12 (0.06)	37.3 (5.8)	–	Rutten *et al*. (2005)
	Oreochromis niloticus	0.19 (0.04)	32.6 (3.2)	Genomic estimates	Joshi *et al*. (2020a)
FY	*Oreochromis niloticus*	0.22 (0.04)	36.4 (2.5)	Genomic estimates	Joshi *et al*. (2019)
	Oreochromis niloticus	0.25 (0.07)	33.6 (3.2)	–	Nguyen *et al*. (2010)
	Oreochromis niloticus	0.24 (0.07)	32.6 (3.2)	–	Joshi *et al*. (2018b)
	Oreochromis niloticus	0.23 (0.05)	34.6 (3.0) to 39.7 (3.2)	Cage and ponds culture	Thodesen (Da-Yong Ma) *et al*. (2011)
	Oreochromis niloticus	0.06 (0.04)	41.3 (6.8) to 45.1(4.0)[1]	Net cages and earthen ponds culture	Gjerde *et al*. (2012)
	Oreochromis niloticus	0.12 (0.06)	37.3 (0.16)[1]	Tank culture	Rutten *et al*. (2005)
	Oreochromis niloticus	0.21 (0.04)	31.7 (2.2)	Genomic estimates	Yoshida *et al*. (2019c)

The six morphological traits are: BD, body depth; BL, body length; BT, body thickness; BWH, body weight at harvest; FW, fillet weight; and FY, fillet yield. Units for the mean phenotypes are centimeters for BD, BL and BT; grams for BWH and FW; and percentage for FY.
[1]Coefficient of variation in brackets.

Table 2 Heritabilities for disease resistance traits in tilapia.

Species	Disease	Trait	h^2 (se)	Reference
Nile tilapia	*Streptococcus agalactiae*	Survival	0.15 (0.03)[1] to 0.26 (0.03)[1]	Joshi et al., (2020b)
		Survival	0.27 (0.11)	Lin (2016)
		Survival	0.38 (0.11)	Shoemaker *et al*. 2017)
	Streptococcus iniae	Survival	0.52 (0.12)	Shoemaker *et al*. (2017)
		Survival	0.42 (0.07)	LaFrentz *et al*. (2016)
	Flavobacterium columnare	Survival	0.15 (0.03)	Wonmongkol *et al*. (2018)
		Days to death	0.15 (0.03)	
	TiLV	Survival	0.40 (0.06)	Barría *et al*. (2020)
		Days to death	0.23 (0.05)	
Red tilapia	*Streptococcus agalactiae*	Survival	0.13 (0.02)	Sukhavachana *et al*. (2019)
		Days to death	0.20 (0.03)	
		Survival	0.13 (0.02)	Suebsong *et al*. (2019)
		Days to death	0.20 (0.03)	
		Survival	0.11 (0.19)[1]	Sukhavachana *et al*. (2020)
		Days to death	0.17 (0.03)[1]	

[1]Estimated using genomic matrix.

was close to unity, whereas the genetic association between body weight and fillet yield was generally low (Rutten *et al.,* 2005; Nguyen *et al.,* 2010; Gjerde *et al.,* 2012a; Thodesen (Da-Yong Ma) *et al.,* 2011). Thus, improvement for fillet yield through indirect selection for body weight might be ineffective. In contrast, selection for high growth can result in a significant correlated increase in fillet weight (Nguyen *et al.,* 2010). The use of advanced phenotyping technologies, including computed tomography scan or ultrasound (Vandeputte *et al.,* 2017; Maas *et al.,* 2020; Prchal *et al.,* 2020) and automation of recording procedures (Ventura *et al.,* 2020), will help to effectively measure fillet yield in the future and exploit this information for genetic selection.

To date, genetic evaluations for tilapia breeding programs are primarily based on pedigree and phenotype information, which are well suited for traits that are directly measured in the selection candidates. For instance, high levels of genetic gains have been achieved for growth in Nile tilapia, ranging from 7 to 20% per generation (Bentsen *et al.,* 2017; Eknath *et al.,* 1998; Gjedrem *et al.,* 2012 and Khaw *et al.,* 2008). Nevertheless, pedigree-based genetic evaluations have some limitations for traits which are evaluated via sib-testing. New genomics technologies, including next-generation sequencing and high-performance genotyping methodologies, represent an alternative to disentangle the genetic basis and enhance genetic evaluation methods for important traits which are difficult to measure in selection candidates in tilapia breeding schemes.

The commercial production of tilapia can be done in a wide range of production systems, including cages and excavated ponds subjected to different conditions, whereas the genetic selection is usually conducted in controlled environment, that may result in genotype by environment (G × E) interaction. This means that different genotypes do not respond in the same way in two or more environments, and the same phenotype can represent different traits (Falconer & Mackay, 1996). The G × E interaction can be quantified using the genetic correlation between the trait measured in different environments. For instance, the genetic correlations for growth traits measured in pond and cage environments ranged from 0.73 to 0.99, suggesting that G × E interaction was not important for body traits in Nile tilapia (Khaw *et al.,* 2012; Thodesen (Da-Yong Ma) *et al.,* 2011; Trong *et al.,* 2013). Non-significant G × E interactions have also been reported for body weight and harvest weight of *O. shiranus* (Maluwa *et al.,* 2006) and *Oreochromis* spp. (Nguyen *et al.,* 2017), respectively.

Genomic resources and applications

Reference genome and SNP panels

The use of molecular markers (e.g. SNPs) has allowed the implementation of several applications in aquaculture species, including strain and hybrid traceability, assessment of genetic variability, parentage analyses, pedigree reconstruction, quantitative trait locus (QTL) mapping, genome-wide association study (GWAS), marker assisted selection (MAS) and genomic selection (Liu & Cordes, 2004; Yáñez

Table 3 Genetic correlation and standard error (SE) of body weight at harvest with different traits.

Mean BWH (g)[1]	BD (cm)	BL (cm)	BT (cm)	FW (g)	FY (%)	References
188.9 (94.02)	0.99				(0.01)	0.98 (0.01)
0.93 (0.04)	–	–				Nguyen *et al*. (2007)
527 (132.5)	0.95				(0.02)	0.89 (0.05)
0.82 (0.08)	0.96				(0.02)	0.44 (0.20)
Nguyen *et al*. (2010)						
787.7 (313.1)	–	0.87			(0.08)	0.92 (0.05)
0.99 (0.01)	0.74				(0.18)	Rutten *et al*. (2005)
817 (261.11)	–	–	–	0.96	(0.01)	−0.11 (0.15)
Joshi *et al*. (2019)						
419 (22.4) to 1188 (24.5)	–	–	–	0.99 (ne)	0.21 (0.31)	Gjerde *et al*. (2012)

[1]Standard deviation in brackets.

et al., 2015). By far the most groundbreaking and revolutionary application of dense SNP panels is genomic selection, which has allowed increases in the rate of genetic progress in breeding programs for several species (Meuwissen *et al.,* 2001).

Identifying the molecular basis underlying complex traits at a whole-genome level and implementing genomic selection require a large number of highly informative SNPs, which ideally segregate into several populations. Therefore, discovery and validation of SNPs, which are densely and uniformly distributed across the entire genome, can promote a better understanding of biologically and economically important traits, with a high potential to increase the genetic progress in tilapia. The availability of a reference chromosome-level genome assembly for Nile tilapia (Conte *et al.,* 2017, 2019) has facilitated the development of high-throughput SNP genotyping platforms for this species. The first version of a reference genome assembly for Nile tilapia (Orenil 1.0) was released in January 2011. The most recent Nile tilapia genome assembly (O_niloticus_UMD_NMBU; GenBank assembly accession no. GCA_001858045.3), released in 2018, consists of 1005 Mb of total length sequence across the 22 chromosomes and 2437 unplaced scaffolds, with the minimum contig length needed to cover 50% of the genome (N50) of 2.9 Mb. Besides Nile tilapia there is only one scaffold-level genome assembly for blue tilapia (Tao *et al.,* 2020). A detailed summary of the available genomes is shown in Table 4.

The first SNP array for Nile tilapia was developed in 2018 (Joshi *et al.,* 2018a), which is a 58K Affymetrix (Thermo Fisher) SNP array generated by means of markers discovered based on a whole-genome resequencing experiment in 32 fish from the Genomar farmed strain. A second SNP panel was then developed using a large-scale *de novo* variant discovery effort by whole-genome re-sequencing of 326 Nile tilapias from three different commercial strains (two from Costa Rica and one from Brazil). This information was exploited for the discovery and validation of a 50K SNP panel, which was posteriorly implemented in an Illumina bead chip for routine genotyping (Yáñez *et al.,* 2020). Recently an open access Affymetrix (ThermoFisher) 65K SNP array has been developed by whole-genome re-sequencing of 100 GIFT tilapia and utilizing SNP datasets from wild and several other farmed Nile tilapia strains. The utility of this SNP array has been demonstrated across multiple strains of Nile tilapia (Peñaloza *et al.,* 2020).

At least five linkage maps have been constructed for Nile tilapia using different marker types and densities (Table 5). Low-density maps were constructed using SNPs from Restriction-site Associated DNA (RAD) sequencing experiments (Palaiokostas *et al.,* 2013), microsatellites and/or AFLP markers (Kocher *et al.,* 1998; Lee *et al.,* 2005; Guyon *et al.,* 2012), whereas the genetic map with the highest resolution was recently developed using a dense SNP panel (Joshi *et al.,* 2018a). This linkage map in turn has facilitated the generation of an improved version of the Nile tilapia genome assembly (O_niloticus_UMD to *O_niloticus*_UMD_NMBU assembly). The size of this dense linkage map was 1469.69 cM and consisted of 40,186 SNPs. Further, Nile tilapia, similar to other tilapia species (e.g. blue tilapia; Lee *et al.,* 2004), have a sex-specific pattern of recombination (Joshi *et al.,* 2018a), with females having an approximately 20% higher recombination rate than the males.

QTL mapping, GWAS and genomic selection

Information from SNP markers are being increasingly used to generate a deeper knowledge of the genetic basis of important traits and speed up the genetic progress in aquaculture species by means of GWAS and genomic selection, respectively (Yáñez *et al.,* 2014). GWAS allows the identification of genetic variants associated with complex traits (i.e QTL). When one or few QTL explain a high percentage of genetic variance for a particular trait, it is possible to improve the trait more rapidly by means of MAS. However, the complexity of some traits and the absence of QTL with major effects constrain the successful implementation of MAS. In contrast, genomic selection is the most appropriate way to select for traits that are controlled by several loci of small effects (i.e. polygenic traits) (Meuwissen *et al.,* 2013).

In general, GWAS and genomic selection studies in tilapia are scarce. From previous experience in other aquaculture species, the implementation of genomic selection is expected to speed up the genetic progress for traits that are difficult to measure in selection candidates (Ødegård *et al.,* 2014; Lhorente *et al.,* 2019), including carcass traits (e.g. fillet yield, fat content and composition) and resistance against diseases (e.g. *Streptococcus* spp., *Francisella* spp., viral nervous necrosis and tilapia lake virus).

GWASs have been carried out for several traits in different fish species of commercial interest, including growth traits (Tsai *et al.,* 2015; Gonzalez-Pena *et al.,* 2016; Yoshida *et al.,* 2017b; Garcia *et al.,* 2018; Palaiokostas *et al.,* 2018; Reis Neto *et al.,* 2019) and resistance against bacterial, viral and parasitic diseases traits (Barria *et al.,* 2019, 2018; Cáceres *et al.,* 2019a; Correa *et al.,* 2015; 2017a; Rodríguez *et al.,* 2019; Tsai *et al.,* 2016; Vallejo *et al.,* 2017). Most of these traits are under polygenic control, with several markers explaining a small effect, and thus limiting the implementation of MAS. Therefore, the genomic selection approach has been proposed to effectively accelerate the rate of genetic progress for different traits in important farmed fish species, e.g. salmonids (Tsai *et al.,* 2016; Bangera *et al.,* 2017; Correa *et al.,* 2017b; Barria *et al.,* 2018; Yoshida *et al.,* 2019a, 2018).

Genotyping by sequencing, including RAD-seq and ddRAD-seq approaches, have been applied for QTL and

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Table 4 Available genomes for tilapia.

Species	Versions	Contig N50	Scaffold N50	Number of scaffolds	Percentage on chromosome	Sequencing platform	Genome coverage	Total size (Mb)	Assembly level	References
Oreochromis niloticus	Orenil 1.0	29,493	2,802,423	5,900	87.96	Illumina	269×	928	Scaffold	Brawand *et al.* (2015)
	Orenil 1.1/OreNil2	29,493	2,766,223	5,909	87.97	Illumina	269×	928	Chromosome	
	O_niloticus_UMD1	3,090,215	37,007,722	2,567	99.58	PacBio	44×	1010	Chromosome	Conte *et al.* (2017)
	O_niloticus_UMD_NMBU[1.1]	2,923,640	38,839,487	2,460	99.99	PacBio	44×	1006	Chromosome	Conte *et al.* (2019)
	ONJp	2,651,554	40,346,024	403	97.40	Nanopore	96×	994	Chromosome	Tao *et al.* (2020)
Oreochromis aureus	–	60,338	1,102,239	12,952	89.84	Illumina HiSeq	166×	919	Scaffold	Bian *et al.* (2019)
	OA	4,404,323	40,723,988	303	97.80	Nanopore	85×	1006	Chromosome	Tao *et al.* (2020)

[1]Representative genome.

linkage mapping in tilapia. For instance, using a hybrid population of Mozambique × Red tilapia, Liu *et al.,* (2014) found a major QTL for growth in a sex-determining locus in LG1, explaining more than 65% of phenotypic variation. Lin *et al.* (2016) detected that the phenotypic variation explained by QTL associated with growth-related traits under saline conditions was lower than 3%, with some important genomic regions found in LG12, LG20 and LG22. Evidence of the polygenic nature underlying harvest weight and fillet yield was provided by a GWAS performed using genotypes from a 50K SNP panel in a commercial Nile tilapia population from Costa Rica (Yoshida *et al.,* 2019b), which is in agreement with previous studies for growth-related traits in other fish species (Tsai *et al.,* 2015; Yoshida *et al.,* 2017b; Reis Neto *et al.,* 2019). In addition, the same authors tested the use of genotype imputation from low- to high-density SNP panels, suggesting a reduction of genotyping cost up to 69%, depending on the breeding population size, without considerable losses in accuracy of genomic predictions when compared against the use of true dense SNP genotypes (Yoshida *et al.,* 2019b). Recent studies have also demonstrated the absence of major QTL for resistance against *S. agalactiae*, and also that genomic-based approaches outperform conventional pedigree-based methods for the genetic evaluation of this trait in Nile tilapia (Lu *et al.,* 2020) and hybrid red tilapia (Sukhavachana *et al.,* 2020).

Dense SNP genotypes have also been used for the genomic dissection of additive and non-additive genetic effects for body weight, fillet traits and conformational traits in Nile tilapia, showing non-additive genetic effects, maternal environmental effects and the detrimental effects of inbreeding over these commercially relevant traits (Joshi *et al.,* 2020a). Furthermore, univariate and multivariate genomic selection approaches have also been tested using dense SNP genotypes for growth- and disease resistance-related traits (e.g. *Streptococcus* resistance), showing an increase in prediction accuracy, when compared with conventional pedigree-based genetic evaluation methods (Joshi *et al.,* 2020c, 2019). These results indicate the benefits of genomic evaluations for the genetic improvement of these populations.

Signatures of domestication and selection

The domestication process owing to adaptation to captive conditions and intense selection for desirable traits can result in changes in allele frequencies, LD, haplotype and diversity patterns in farmed populations (Ma *et al.,* 2015). Genomic information allows the identification and characterization of regions underlying selection and adaptation processes, which in turn can help in uncovering the genes involved in domestication and economically important traits (López *et al.,* 2015; Pérez O'Brien *et al.,* 2014).

Table 5 Available linkage maps for tilapia species.

Species/sex		Map length (cM)	Marker number and type	Average marker interval (cM)	References
Oreochromis niloticus	Male	1359.6	40,186 SNPs	0.03	Joshi *et al*. (2018a)
	Female	1632.9		0.04	
	Consensus	1469.69		0.04	
Oreochromis niloticus		704	62 microsatellites + 112 AFLP	–	Kocher *et al*. (1998)
Oreochromis niloticus × *Oreochromis aureus*		1,311	525 microsatellite and 21 gene-based markers	2.4	Lee *et al*., (2005)
Oreochromis niloticus		34,084 cR_{3500} and 937,310 kb	1358 markers – radiation hybrid (RH) map	742 kb	Guyon *et al*. (2012)
Oreochromis niloticus		1,176	3,802 SNPs	0.7	Palaiokostas *et al*. (2013)
Oreochromis mossambicus	Female	514	13 microsatellites and 49 AFLPs	8.3	Agresti *et al*., (2000)
	Male	1632	60 microsatellites and 154 AFLPs	7.6	
Oreochromis mossambicus		1042.5	301 markers		Liu *et al*. (2013)
Oreochromis mossambicus x *Oreochromis* spp.	Consensus	1067.6	401 microsatellites including 282 EST-derived markers	3.3	
	Male	950.8	261 markers	3.6	
	Female	1030.6	261 markers	4	
Red tilapia		984.0	320 markers	3.1	

Few studies have addressed the identification of selection signatures in tilapia. For instance, Hong Xia *et al*. (2015) used next-generation sequencing data from Mozambique, Red and Nile tilapia from South Africa, China and Singapore ($n = 37$) and identified more than 100 putative selection sweep regions for each strain. The gonadotropin-releasing hormone receptor, *Wnt* and integrin signaling pathways were shown to be under positive selection in all of the tilapia lines analyzed. Schomburg and Michal (2012) suggested that these pathways have important roles in animal growth, development and response to diseases. In a recent study, using whole-genome sequences of 326 tilapia from three different strains from Latin America, several candidate genes associated with growth, development, immunity traits, behaviour and reproduction were found to be putatively under selection (Cádiz *et al.,* 2020). The above and future results will be relevant for a deeper knowledge on the genes, functional variants and pathways involved in the complex processes of domestication and selection in tilapia.

Sex determination

In tilapias two types of sex-determining systems have been identified, a male heterogametic XX/XY system in *O. niloticus* and *O. mossambicus*, and a female heterogametic ZZ/ZW system in *O. aureus* (Cnaani *et al.,* 2008). In some of these species, males grow faster and are more uniform in size than females, e.g. the difference in body weight between male and female fish was 15% in *O. niloticus* and 48% in *O. aureus* (Lind *et al.,* 2015). Furthermore, in mixed-sex production uncontrolled reproduction leads to excessive fingerling production and high competition for food (Toguyeni *et al.,* 1997). For this reason, farming all-male populations is desirable in tilapia aquaculture, and is primarily achieved through hormonal treatment in commercial farms. However, in some countries, as in EU member states and the USA, the use of this technique is not fully accepted, owing to potential environmental and public health issues, such as the residual effect on water quality and food security (Baroiller *et al.,* 2009). Therefore, environmentally friendly alternatives to hormonal sex control is practiced to some extent. Baroiller *et al*. (1995) suggested that thermal treatment at 36°C during the critical period of sex differentiation at an early developmental stage increases the proportion of males in Nile tilapia. However, the temperature response is strongly dependent on a parental effect, which can predispose to generate progeny more or less sensitive to temperature (Baroiller & D'Cotta, 2001; Tessema *et al.,* 2006). In order to avoid some of the issues related to mixed-sex production, several studies suggest the hybridization of two different species of *Oreochromis* (e.g. *O. urolepis*, *O. hornorum*, *O. mossambicus* and *O. niloticus*). However, it is difficult to sustain the production of all-male hybrids owing to variable success in generating all-male progenies and also the introduction of hybrids into broodstock (Pruginin *et al.,* 1975; Wohlfarth, 1994; Beardmore *et al.,* 2001). The generation of 'supermales' is another technique to produce mono-sex populations, using a combination of sex reversal and chromosome manipulation techniques (gynogenesis or androgenesis) (Wang & Shen, 2019). In *O. niloticus*, Mair *et al*. (1997) reported a male progeny sex ratio higher than 95% by using estrogen

to induce sex reversal of males to females and a progeny test to generate all-'YY' male genotypes.

Various factors, including tilapia species, genetic background, and environmental conditions (e.g. temperature) have been described to be involved in sex determination in tilapia (Baroiller & D'Cotta, 2001; Cnaani *et al.,* 2008; Palaiokostas *et al.,* 2013; Eshel *et al.,* 2014; Wessels *et al.,* 2014). Thus, the mechanisms involved in sexual dimorphism have been broadly studied, using both quantitative genetics and genomic approaches. From a quantitative genetics viewpoint, the heritability estimated for body weight were not different between the two sexes; furthermore, the high genetic correlation (>0.86) for body traits in males and females suggested no genotype by sex interaction (Nguyen *et al.,* 2007; Bentsen *et al.,* 2012; de Oliveira *et al.,* 2016).

Using information of molecular markers, some studies described several genomic regions involved in sex determination for *O. niloticus*, *O. aureus* and *Oreochromis.* spp., including regions in LG1, LG3, LG20 and LG23 (Lee *et al.,* 2004; Shirak *et al.,* 2006; Cnaani *et al.,* 2008; Eshel *et al.,* 2014; Palaiokostas *et al.,* 2015; Conte *et al.,* 2017; Cáceres *et al.,* 2019a, 2019b). In addition, several genes have been suggested to have a role in sex determination in the tilapia genus, including Wilms tumor suppressor protein 1b (*wt1b*), cytochrome P450 of family 19 subfamily A member 1 (*cyp19a*), the anti-Müllerian hormone (*Amh*) and Doublesex/Mab-3 Related Transcription Factor 2 (*dmrt2*) (Lee *et al.,* 2004; Shirak *et al.,* 2006; Cnaani *et al.,* 2008; Li *et al.,* 2015a, 2015b; Sun *et al.,* 2017; Cáceres *et al.,* 2019a, 2019b). The multiple regions identified to have a role in sex determination in tilapia indicate that this is most likely a complex trait, which can also be modulated from environmental stimulus.

Transcriptome

RNA-seq

RNA sequencing (RNA-seq) is an approach to profiling transcriptomes using deep-sequencing technologies (Marioni *et al.,* 2008). A large quantity of RNA-seq data has been deposited in the NCBI database, derived from different tilapia species and different tissues, indicating that this approach has been widely used and providing a valuable resource to assess gene function and discover genetic variants within genes (Xia *et al.,* 2014).

For instance, RNA-seq has been applied to identify gene transcripts differentially expressed in female and male gonads of Nile tilapia (Tao *et al.,* 2013, 2018), suggesting the importance of classic genes (*Foxl2*, *Cyp19a1a*, *Gsdf*, *Dmrt1* and *Amh*) as well as identifiying new molecules (*Borealin*, *Gtsf1*, *tesk1*, *Zar1*, *Cdn15* and *Rpl*) involved in sex differentiation.

In addition, transcriptomic analysis of the response against infection with *S. agalactiae* (Zhang *et al.,* 2013; Wang *et al.,* 2016b, Zhu et al., 2017) and *S. iniae* (Zhu *et al.,* 2015) have been reported in tilapia, identifying several genes involved in the immune response against bacterial diseases and their interaction with environmental factors (e.g. water temperature). Comparative transcriptomic analyses have also been performed between zebrafish, blue tilapia and Nile tilapia, suggesting positive selection of immune-related genes, such as *notch2* and *nfatc3b*, in tilapia species (Xiao *et al.,* 2015). The transcriptomic response of tilapia has also been evaluated against different abiotic stressors and stimulus including alkalinity (Zhao *et al.,* 2015), hypoxia (Li *et al.,* 2017), salinity (Xu *et al.,* 2015), different concentrations of resveratrol in diet (Zheng *et al.,* 2018) and dietary protein to starch ratio (Xiong *et al.,* 2014).

MicroRNAs (miRNAs) are small non-coding RNA molecules (ranging from 18 to 22 nucleotides), that regulate gene expression, through translational repression and/or transcript cleavage, and protein translation during biological processes (Bartel, 2004). Expression profiles of miRNA related to skeletal muscle growth were analyzed in Nile tilapia (Huang *et al.,* 2012; Yan *et al.,* 2012). For instance, Yan *et al*. (2012) identified 25 conserved miRNAs in tilapia skeletal muscle, some of them differentially expressed in different developmental stages. The inverse correlation between the expression of miRNAs and putative target genes provided evidence of direct regulation of *HDAC4*, *SRF*, *Pax 3* and *Pax 7 in vivo*. Huang *et al*. (2012b) identified significant differences in miRNA expression between fast-growing and control strains of tilapia. Some of these miRNAs are suggested to be involved in the GH/IGF-1 axis signaling pathway.

Nile tilapias infected with *S. agalactiae* were used to investigate immune-related miRNAs by Wang *et al*. (2016a), identifying more than 1000 differentially expressed miRNAs that targeted genes involved in apoptotic processes, signal pathways and immune response. The possible role of miRNAs in the early stages of fish sex differentiation was studied by Tao *et al*. (2016), who found 62 and 49 miRNAs with higher expression in XX and XY gonads, respectively. Some of the genes targeted by these miRNAs included enzymes involved in steroidogenic pathways and molecules involved in vertebrate sex differentiation, such as *Foxl2*, *Amh*, *Star1*, *Sf1*, *Dmrt1* and *Gsdf*.

Despite the increasing number of global gene expression studies in tilapia, it is still unclear how this information can be exploited to accelerate genetic progress in current breeding programs for these species. The integration of transcriptomic data with other sources of information (e.g. GWAS and WGS), will help on the identification of genes and functional variants involved in desirable traits, which in turn could be used to accelerate tilapia breeding.

Perspectives and final considerations

Some studies have used WGS data for genome scans, showing some advantages over genotypes from SNP panels, because the causative mutations (i.e. quantitative trait nucleotides or QTNs) are most likely to be included among the analyzed variants. Identifying causative mutations will lead to a better understanding of biological mechanisms behind QTL (Meuwissen *et al.,* 2013). Previous studies used WGS information to understand the evolutionary diversification of African cichlid fish (Brawand *et al.,* 2015), identify signatures of selection (Hong Xia *et al.,* 2015; Cádiz *et al.,* 2020) and sex determination regions through GWAS in tilapia (Cáceres *et al.,* 2019a, 2019b). In contrast, genomic prediction studies using WGS in tilapia are still not avaliable. Nevertheless, examples in cattle show that only a slight increase in reliability is observed when using 777K chip or sequence data compared with a 54K SNP panel (Su *et al.,* 2012; van Binsbergen *et al.,* 2015). In the next few years, it is expected that WGS data will be widely available for several applications, owing to rapidly decreasing costs. Despite this, it is still expensive to sequence large numbers of individuals. Nevertheless, genotype imputation can reduce the costs of testing the usefulness of WGS data in GWAS and genomic selection in tilapia (Marchini *et al.,* 2007; Howie *et al.,* 2009).

The identification of specific polymorphisms responsible for observed variation, also called QTNs, will help to maximize the accuracy of genomic predictions in livestock and aquaculture species (Pérez-Enciso *et al.,* 2015), through their incorporation on genomic selection approaches or direct selection based on QTNs (Weller & Ron, 2011). Using simulated data, Fragomeni *et al.* (2017) estimated an accuracy of breeding values close to the unity when using a single-step genomic evaluation approach fitted including QTN information. When the selection is based on QTN the efficiency of selection does not decrease owing to changes in LD between the QTL and SNPs, and once the QTN is detected and validated, the selection based on this information can be efficiently applied across different populations (Weller & Ron, 2011). Until now, QTNs have been identified and validated only for dairy cattle, swine and sheep (Grisart *et al.,* 2002; Van Laere *et al.,* 2003; Cohen-Zinder *et al.,* 2005; Clop *et al.,* 2006; Nishimura *et al.,* 2012); however, we believe that in the near future, causative polymorphisms will be identified for relevant traits in tilapia populations.

Gene editing methods have already been developed for Nile tilapia (Feng *et al.,* 2015a; Li *et al.,* 2015a, 2015b; Xie *et al.,* 2016; Wu *et al.,* 2016a, 2016b; Jiang *et al.,* 2017; Li & Wang, 2017; Li *et al.,* 2014, 2019). Targeted mutagenesis using TALENs and CRISPR/Cas9 technology have been successfully applied to understand the genetic basis of sex determination and sex differentiation in Nile tilapias. Jiang *et al.* (2016) and Li *et al.* (2015a) reported that the homozygous mutation of genes *amhy*, *amhrII* and *gsdf* resulted in sex reversal from male (XY) to female, whereas the homozygous mutation in the genes *foxl2* or *cyp19a1a* resulted in a reversal of female (XX) to male (Zhang *et al.,* 2017). In addition, mutations in other genes such as *dmrt1*, *dmrt6*, *cyp26a1*, *aldh1a2*, *sf-1andigf3*, *nanos2* and *nanos3* have been efficiently bred to the F_1 generation (Li *et al.,* 2013, 2014; Feng *et al.,* 2015; Jiang *et al.,* 2016; Xie *et al.,* 2016), suggesting that gene editing is a powerful tool for genetic engineering in tilapia. Nevertheless, regulation of genetically engineered organisms in tilapia-producing countries and the main markets have to be accounted for in the final application and commercialization of these promising biotechnologies to improve tilapia aquaculture.

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Competing interests

RJ was hired by a commercial institution (GenoMar Genetics AS) during the period of the study. The remaining authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

Agresti J.J., Seki S., Cnaani A., Poompuang S., Hallerman E.M., Umiel N., Hulata G., Gall G.A.E., May B. (2000) Breeding new strains of tilapia: Development of an artificial center of origin and linkage map based on AFLP and microsatellite loci. *Aquaculture* **185**, 43–56.

Bangera R., Correa K., Lhorente J.P., Figueroa R., Yáñez J.M. (2017) Genomic predictions can accelerate selection for resistance against *Piscirickettsia salmonis* in Atlantic salmon (Salmo salar). *BMC Genomics* **18**, 121.

Baroiller J.F., Chourrout D., Fostier A., Jalabert B. (1995) Temperature and sex chromosomes govern sex ratios of the mouthbrooding Cichlid fishOreochromis niloticus. *Journal of Experimental Zoology* **273**, 216–23.

Baroiller J.F., D'Cotta H. (2001) Environment and sex determination in farmed fish. *Comparative Biochemistry and Physiology - C Toxicology and Pharmacology* **130**, 399–409. https://doi.org/10.1016/S1532-0456(01)00267-8.

Baroiller J.F., D'Cotta H., Bezault E., Wessels S., Hoerstgen-Schwark G. (2009) Tilapia sex determination: Where temperature and genetics meet. *Comparative Biochemistry and Physiology Part A: Molecular & Integrative Physiology* **153**, 30–8.

Barria A., Christensen K.A., Yoshida G.M., Correa K., Jedlicki A., Lhorente J.P., Davidson W.S., Yáñez J.M. (2018) Genomic

predictions and genome-wide association study of resistance against *Piscirickettsia salmonis* in Coho Salmon (*Oncorhynchus kisutch*) using ddRAD Sequencing. *G3 Genes/Genomes/Genetics* **8**, 1183–94. https://doi.org/10.1534/g3.118.200053.

Barria A., Marín-Nahuelpi R., Cáceres P., López M.E., Bassini L.N., Lhorente J.P., Yáñez J.M. (2019) Single-Step Genome-wide association study for resistance to *Piscirickettsia salmonis* in rainbow trout (*Oncorhynchus mykiss*). *G3; Genes/Genomes/Genetics* **9**, 3833–3841. http://dx.doi.org/10.1534/g3.119.400204

Barría A., Trinh T.Q., Mahmuddin M., Benzie J.A.H., Chadag V.M., Houston R.D. (2020) Genetic parameters for resistance to Tilapia Lake Virus (TiLV) in Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **522**, 735126.

Bartel D.P. (2004) MicroRNAs: genomics, biogenesis, mechanism, and function. *Cell* **116**, 281–97.

Beardmore J., Mair G., Lewis R. (2001) Monosex male production in finfish as exemplified by tilapia: applications, problems, and prospects. *Aquaculture* **197**, 283–301.

Bentsen H.B., Gjerde B., Eknath A.E. *et al*. (2017) Genetic improvement of farmed tilapias: Response to five generations of selection for increased body weight at harvest in *Oreochromis niloticus* and the further impact of the project. *Aquaculture* **468**, 206–17.

Bentsen H.B., Gjerde B., Nguyen N.H. *et al*. (2012) Genetic improvement of farmed tilapias: Genetic parameters for body weight at harvest in Nile tilapia (*Oreochromis niloticus*) during five generations of testing in multiple environments. *Aquaculture* **338–341**, 56–65.

Bezault E., Balaresque P., Toguyeni A., Fermon Y., Araki H., Baroiller J.F., Rognon X. (2011) Spatial and temporal variation in population genetic structure of wild *Nile tilapia* (*Oreochromis niloticus*) across Africa. *BMC Genetics* **12**, 102.

Bian C., Li J., Lin X., Chen X., Yi Y., You X., Zhang Y., Lv Y., Shi Q. (2019) Whole Genome Sequencing of the Blue Tilapia (*Oreochromis aureus*) Provides a Valuable Genetic Resource for Biomedical Research on Tilapias. *Marine Drugs* **17**, 386.

Bolivar R.B., Newkirk G.F. (2002) Response to within family selection for body weight in Nile tilapia (*Oreochromis niloticus*) using a single-trait animal model. *Aquaculture* **204**, 371–81.

Brawand D., Wagner C.E., Li Y.I. *et al*. (2015) The genomic substrate for adaptive radiation in African cichlid fish. *Nature* **513**, 375–81.

Cáceres G., López M.E., Cádiz M.I., Yoshida G.M., Jedlicki A., Palma-Véjares R., Travisany D., Díaz-Domínguez D., Maass A., Lhorente J.P., Soto J., Salas D., Yáñez J.M. (2019a) Fine mapping using whole-genome sequencing Confirms anti-müllerian hormone as a major gene for sex determination in farmed Nile Tilapia (*Oreochromis niloticus* L.). *G3; Genes/Genomes/Genetics* **9**, 3213–3223. http://dx.doi.org/10.1534/g3.119.400297.

Cáceres P., Barría A., Christensen K.A., Bassini L.N., Correa K., Lhorente J.P., Yáñez J.M. (2019b) *Genome-scale comparative analysis for host resistance against sea lice between Atlantic salmon and rainbow trout*. https://doi.org/10.1101/624031.

Cádiz M.I., López M.E., Díaz-Domínguez D., Cáceres G., Yoshida G.M., Gomez-Uchida D., Yáñez J.M. (2020) Whole genome re-sequencing reveals recent signatures of selection in three strains of farmed *Nile tilapia* (*Oreochromis niloticus*). *Scientific Reports*, **10**, 11514. https://doi.org/10.1038/s41598-020-68064-5

Charo-Karisa H., Komen H., Rezk M.A., Ponzoni R.W., van Arendonk J.A.M., Bovenhuis H. (2006) Heritability estimates and response to selection for growth of Nile tilapia (*Oreochromis niloticus*) in low-input earthen ponds. *Aquaculture* **261**, 479–86.

Clop A., Marcq F., Takeda H. *et al*. (2006) A mutation creating a potential illegitimate microRNA target site in the myostatin gene affects muscularity in sheep. *Nature Genetics* **38**, 813–8.

Cnaani A., Lee B.Y., Zilberman N. *et al*. (2008) Genetics of sex determination in tilapiine species. *Sexual Development* **2**, 43–54.

Cohen-Zinder M., Seroussi E., Larkin D.M. *et al*. (2005) Identification of a missense mutation in the bovine ABCG2 gene with a major effect on the QTL on chromosome 6 affecting milk yield and composition in Holstein cattle. *Genome Research* **15**, 936–44. https://doi.org/10.1101/gr.3806705.

Conte M.A., Gammerdinger W.J., Bartie K.L., Penman D.J., Kocher T.D (2017) A high quality assembly of the Nile Tilapia (Oreochromis niloticus) genome reveals the structure of two sex determination regions. *BMC Genomics* **18**, 341.

Conte M.A., Joshi R., Moore EC., Nandamuri S.P., Gammerdinger W.J., Roberts R.B., Carleton K.L., Lien S., Kocher T.D. (2019) Chromosome-scale assemblies reveal the structural evolution of African cichlid genomes. *Gigascience* **8**, giz030.

Correa K., Bangera R., Figueroa R., Lhorente J.P, Yáñez J.M. (2017b) The use of genomic information increases the accuracy of breeding value predictions for sea louse (*Caligus rogercresseyi*) resistance in Atlantic salmon (*Salmo salar*). *Genetics Selection Evolution* **49**, 15.

Correa K., Lhorente J.P., López M.E., Bassini L., Naswa S., Deeb N., Di Genova A., Maass A., Davidson W.S., Yáñez J.M. (2015) Genome-wide association analysis reveals loci associated with resistance against Piscirickettsia salmonis in two Atlantic salmon (*Salmo salar* L.) chromosomes. *BMC Genomics* **16**, 854.

Correa K., Lhorente J.P., Bassini L., López M.E., Di Genova A., Maass Al., Davidson W.S., Yáñez J.M. (2017a) Genome wide association study for resistance to *Caligus rogercresseyi* in Atlantic salmon (*Salmo salar* L.) using a 50K SNP genotyping array. *Aquaculture* **472** 61–65. http://dx.doi.org/10.1016/j.aquaculture.2016.04.008

de Oliveira C.A.L., Ribeiro R.P., Yoshida G.M., Kunita N.M., Rizzato G.S., de Oliveira S.N., dos Santos A.I., Nguyen N.H. (2016) Correlated changes in body shape after five generations of selection to improve growth rate in a breeding program for Nile tilapia *Oreochromis niloticus* in Brazil. *Journal of Applied Genetics* **57**, 487–93.

Eknath A.E., Acosta B.O., Eknath A.E., Acosta B.O. 1998. *Genetic Improvement of Farmed Tilapias (GIFT) Project: final report, March 1988 to December 1997*.

Eknath A.E., Tayamen M.M., Palada-de Vera M.S. *et al*. (1993) Genetic improvement of farmed tilapias: the growth performance of eight strains of *Oreochromis niloticus* tested in different farm environments. *Aquaculture* **111**, 171–88.

El-Sayed A.-F.M. (2019) *Tilapia Culture*. Amsterdam, Netherlands: Elsevier Science & Technology.

Eshel O., Shirak A., Dor L. *et al*. (2014) Identification of male-specific amh duplication, sexually differentially expressed genes and microRNAs at early embryonic development of Nile tilapia (*Oreochromis niloticus*). *BMC Genomics* **15**, 774.

Falconer D.S., Mackay T.F.C., eds. (1996) *Introduction to Quantitative Genetics.*, 4th Editio. ed. Harlow.

FAO (2019) *Fisheries and aquaculture software*. FishStatJ - Software for Fishery and Aquaculture Statistical Time Series.

FAO, 2018a. *The State of Fisheries and Aquaculture in the world 2018, fao.org*.

FAO (2018b) *The State of World Fisheries and Aquaculture 2018 - Meeting the sustainable development goals*. Rome.

Feng R., Fang L., Cheng Y., He X., Jiang W., Dong R., Shi H., Jiang D., Sun L., Wang D. (2015) Retinoic acid homeostasis through aldh1a2 and cyp26a1 mediates meiotic entry in Nile tilapia (*Oreochromis niloticus*). *Scientific Reports* **5**, 1–12.

Ferreira I.A., Poletto A.B., Kocher T.D., Mota-Velasco J.C., Penman D.J., Martins C. (2010) Chromosome evolution in African cichlid fish: contributions from the physical mapping of repeated DNAs. *Cytogenetic and Genome Research* **129**, 314–22.

Fragomeni B.O., Lourenco D.A.L., Masuda Y., Legarra A., Misztal I. (2017) Incorporation of causative quantitative trait nucleotides in single-step GBLUP. *Genetics Selection Evolution* **49**, 59.

Franklin I.R., Frankham R. (1998) How large must populations be to retain evolutionary potential? *Animal Conservation* **1**, 69–70.

Garcia A.L.S., Bosworth B., Waldbieser G., Misztal I., Tsuruta S., Lourenco D.A.L. (2018) Development of genomic predictions for harvest and carcass weight in channel catfish. *Genetics Selection Evolution* **50**, 66.

Gjedrem T. (2012) Genetic improvement for the development of efficient global aquaculture: A personal opinion review. *Aquaculture* **344–349**, 12–22.

Gjedrem T., Robinson N., Rye M. (2012) The importance of selective breeding in aquaculture to meet future demands for animal protein: A review. *Aquaculture* **350–353**, 117–29.

Gjerde B., Mengistu S.B., Ødegård J., Johansen H., Altamirano D.S. (2012a) Quantitative genetics of body weight, fillet weight and fillet yield in Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **342–343**, 117–24.

Gonzalez-Pena D., Gao G., Baranski M., Moen T., Cleveland B.M., Kenney P.B., Vallejo R.L., Palti Y., Leeds T.D. (2016) Genome-wide association study for identifying loci that affect fillet yield, carcass, and body weight traits in rainbow trout (*Oncorhynchus mykiss*). *Frontiers in Genetics* **7**, 203.

Grisart B., Coppieters W., Farnir F. *et al.* (2002) Positional candidate cloning of a QTL in dairy cattle: Identification of a missense mutation in the bovine DGAT1 gene with major effect on milk yield and composition. *Genome Research* **12**, 222–31.

Guyon R., Rakotomanga M., Azzouzi N. *et al.* (2012) A high-resolution map of the Nile tilapia genome: a resource for studying cichlids and other percomorphs. *BMC Genomics* **13**, 222.

Hamzah A., Ponzoni R., Nguyen N., Khaw H., Yee H., Nor S. (2014) Performance of the genetically improved tilapia (GIFT) strain over ten generations of selection in Malaysia. *Pertanika Journal of Tropical Agricultural Scienc* **37**, 411–29.

Hamzah A., Thoa N.P., Nguyen N.H. (2017) Genetic analysis of a red tilapia (*Oreochromis* spp.) population undergoing three generations of selection for increased body weight at harvest. *Journal of Applied Genetics* **58**, 509–19.

Harache Y. (2002) *Development and diversification issues in aquaculture*. A historical and dynamic view of fish culture diversification. CIHEAM - Options Méditerranéennes 15–23.

Hong Xia J., Bai Z., Meng Z. *et al.* (2015) Signatures of selection in tilapia revealed by whole genome resequencing. *Scientific Reports* **5**, 14168.

Howie B.N., Donnelly P., Marchini J. (2009) A flexible and accurate genotype imputation method for the next generation of genome-wide association studies. *PLoS Genetics* **5**, e1000529.

Huang C.W., Li Y.H., Hu S.Y. *et al.* (2012) Differential expression patterns of growth-related microRNAs in the skeletal muscle of Nile tilapia (*Oreochromis niloticus*)1. *Journal of Animal Science* **90**, 4266–79.

Huang Y., Hickey J.M., Cleveland M.A., Maltecca C. (2012) Assessment of alternative genotyping strategies to maximize imputation accuracy at minimal cost. *Genetics Selection Evolution* **44**, 25.

Jiang D., Chen J., Fan Z., Tan D., Zhao J., Shi H., Liu Z., Tao W., Li M., Wang D. (2017) CRISPR/Cas9-induced disruption of wt1a and wt1b reveals their different roles in kidney and gonad development in Nile tilapia. *Developmental Biology* **428**, 63–73.

Jiang D.N., Yang H.H., Li M.H., Shi H.J., Zhang X.B., Wang D.S. (2016) gsdf is a downstream gene of dmrt1 that functions in the male sex determination pathway of the Nile tilapia. *Molecular Reproduction and Development* **83**, 497–508.

Joshi R., Árnyasi M., Lien S., Gjøen H.M., Alvarez A.T., Kent M. (2018a) Development and Validation of 58K SNP-Array and High-Density Linkage Map in Nile Tilapia (O. niloticus). *Frontiers in Genetics* **9**, 472.

Joshi R., Meuwissen T.H.E., Woolliams J.A., Gjøen H.M. (2020a) Genomic dissection of maternal, additive and non-additive genetic effects for growth and carcass traits in Nile tilapia. *Genetics Selection Evolution* **52**, 1.

Joshi R., Skaarud A., Alvarez A.T., Moen T., Odegard J. 2020b. *Bayesian genomic models boost prediction accuracy for resistance against Streptococcus agalactiae in Nile tilapia (Oreochromus niliotic-us)*. bioRxiv.

Joshi R., Skaarud A., de Vera M., Alvarez A.T., Odegard J. (2019) Genomic prediction for commercial traits using univariate and multivariate approaches in Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **516**, 734641.

Joshi R., Skaaurd A., Alvarez A.T., Moen T., Ødegård J. 2020c. *Bayesian genomic models boost prediction accuracy for resistance against Streptococcus agalactiae in Nile tilapia (Oreochromus niliotic-us)*. bioRxiv 2020.01.09.900134. doi: 10.1101/2020.01.09.900134.

Joshi R., Woolliams J., Meuwissen T., Gjøen H. (2018b) Maternal, dominance and additive genetic effects in Nile tilapia; influence on growth, fillet yield and body size traits. *Heredity* **120**, 452–62.

Khaw H.L., Bovenhuis H., Ponzoni R.W., Rezk M.A., Charo-Karisa H., Komen H. (2009) Genetic analysis of Nile tilapia (*Oreochromis niloticus*) selection line reared in two input environments. *Aquaculture* **294**, 37–42.

Khaw H.L., Ponzoni R.W., Danting M.J.C. (2008) Estimation of genetic change in the GIFT strain of Nile tilapia (*Oreochromis niloticus*) by comparing contemporary progeny produced by males born in 1991 or in 2003. *Aquaculture* **275**, 64–9.

Khaw H.L., Ponzoni R.W., Hamzah A., Abu-Bakar K.R., Bijma P. (2012) Genotype by production environment interaction in the GIFT strain of Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **326–329**, 53–60.

Khaw H.L., Ponzoni R.W., Yee H.Y., Aziz M.Ab, Bijma P. (2016) Genetic and non-genetic indirect effects for harvest weight in the GIFT strain of Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **450**, 154–61.

Kocher T.D., Lee W.J., Sobolewska H., Penman D., McAndrew B. (1998) A genetic linkage map of a cichlid fish, the tilapia (*Oreochromis niloticus*). *Genetics* **148**, 1225–32.

LaFrentz B.R., Lozano C.A., Shoemaker C.A., García J.C., Xu D.H., Løvoll M., Rye M. (2016) Controlled challenge experiment demonstrates substantial additive genetic variation in resistance of Nile tilapia (*Oreochromis niloticus*) to Streptococcus iniae. *Aquaculture* **458**, 134–39.

Lee B.Y., Hulata G., Kocher T.D. (2004) Two unlinked loci controlling the sex of blue tilapia (*Oreochromis aureus*). *Heredity (Edinb)*. **92**, 543–49.

Lee B.Y., Lee W.J., Streelman J.T., Carleton K.L., Howe A.E., Hulata G., Slettan A., Stern J.E., Terai Y., Kocher T.D. (2005) A second-generation genetic linkage map of tilapia (*Oreochromis* spp.). *Genetics* **170**, 237–44.

Lhorente J.P., Araneda M., Neira R., Yáñez J.M. (2019) Advances in genetic improvement for salmon and trout aquaculture: the Chilean situation and prospects. *Reviews in Aquaculture* **11**, 340–53.

Li H.L., Lin H.R., Xia J.H. (2017) Differential Gene expression profiles and alternative isoform regulations in gill of nile tilapia in response to acute hypoxia. *Marine Biotechnology* **19**, 551–62.

Li M.-H., Yang H.-H., Li M.-R. *et al*. (2013) Antagonistic roles of Dmrt1 and Foxl2 in sex differentiation via estrogen production in tilapia as demonstrated by TALENs. *Endocrinology* **154**, 4814–25.

Li M., Liu X., Dai S., Xiao H., Wang D. (2019) High efficiency targeting of non-coding sequences using CRISPR/Cas9 system in Tilapia. G3 Genes. *G3: Genes/Genomes/Genetics* **9**, 287–95.

Li M., Sun Y., Zhao J. *et al*. (2015a) A Tandem Duplicate of Anti-Müllerian Hormone with a Missense SNP on the Y Chromosome Is Essential for Male Sex Determination in Nile Tilapia, Oreochromis niloticus. *PLOS Genetics* **11**, e1005678.

Li M., Wang D. (2017) Gene editing nuclease and its application in tilapia. *Science Bulletin* **62**, 165–73.

Li M., Yang H., Zhao J. *et al*. (2014) Efficient and heritable gene targeting in tilapia by CRISPR/Cas9. *Genetics* **197**, 591–9.

Li Y., Liu S., Qin Z., Waldbieser G., Wang R., Sun L., Bao L., Danzmann R., Dunham R., Liu Z. (2015b) Construction of a high-density, high-resolution genetic map and its integration with BAC-based physical map in channel catfish. *DNA Research* **22**, 39–52.

Lin G., Chua E., Orban L., Yue G.H. (2016) Mapping QTL for sex and growth traits in salt-tolerant Tilapia (*Oreochromis* spp. X *O. mossambicus*). *PLoS One* **11**, e0166723.

Lin M. 2016. *Statistical model comparison in genetic analysis of challenge test data on Streptococcus agalactiae resistance in Nile tilapia (*Oreochromis niloticus*)*.

Lind C.E., Safari A., Agyakwah S.K. *et al*. (2015) Differences in sexual size dimorphism among farmed tilapia species and strains undergoing genetic improvement for body weight. *Aquaculture Reports* **1**, 20–7.

Liu F., Sun F., Li J., Xia J.H., Lin G., Tu R.J., Yue G.H. (2013) A microsatellite-based linkage map of salt tolerant tilapia (*Oreochromis mossambicus* x *Oreochromis* spp.) and mapping of sex-determining loci. *BMC Genomics* **14**, 58.

Liu F., Sun F., Xia J.H., Li J., Fu G.H., Lin G., Tu R.J., Wan Z.Y., Quek D., Yue G.H. (2014) A genome scan revealed significant associations of growth traits with a major QTL and GHR2 in tilapia. *Scientific Reports* **4**. https://doi.org/10.1038/srep07256

Liu Z.J., Cordes J.F. (2004) DNA marker technologies and their applications in aquaculture genetics. *Aquaculture* **238**, 1–37.

López M.E., Neira R., Yáñez J.M. (2015) Applications in the search for genomic selection signatures in fish. *Frontiers in Genetics* **5**, 458. http://dx.doi.org/10.3389/fgene.2014.00458

Lu S., Zhu J., Du X., Sun S., Meng L., Liu S., Fan G., Wang J., Chen S. (2020) Genomic selection for resistance to Streptococcus agalactiae in GIFT strain of Oreochromis niloticus by GBLUP, wGBLUP, and BayesCπ. *Aquaculture* **523**, 735212.

Ma Y., Ding X., Qanbari S,. Weigend S., Zhang Q., Simianer H. (2015) Properties of different selection signature statistics and a new strategy for combining them. *Heredity (Edinb)* **115**, 426–36.

Maas P., Grzegrzółka B., Kreß P., Oberle M., Judas M., Kremer-Rücker P.V. (2020) Prediction of body composition in mirror carp (*Cyprinus carpio*) by using linear measurements in vivo and computed tomography post-mortem. *Archives Animal Breeding* **63**, 69–80.

Mair G.C., Abucay U.S., Skibinski D.O.F., Abella T.A., Beardmore J.A. (1997) Genetic manipulation of sex ratio for the large-scale production of all-male tilapia, Oreochromis niloticus. *Canadian Journal of Fisheries and Aquatic Science* **54**, 396–404.

Majumdar K.C., McAndrew B.J. (1986) Relative DNA content of somatic nuclei and chromosomal studies in three genera, Tilapia, Sarotherodon, and Oreochromis of the tribe Tilapiini (Pisces, Cichlidae). *Genetica* **68**, 175–88.

Maluwa A.O., Gjerde B. (2007) Response to selection for harvest body weight of Oreochromis shiranus. *Aquaculture* **273**, 33–41.

Maluwa A.O., Gjerde B., Ponzoni R.W. (2006) Genetic parameters and genotype by environment interaction for body weight of Oreochromis shiranus. *Aquaculture* **259**, 47–55.

Marchini J., Howie B., Myers S., McVean G., Donnelly P. (2007) A new multipoint method for genome-wide association studies by imputation of genotypes. *Nature Genetics* **39**, 906–13.

Marioni J.C., Mason C.E., Mane S.M., Stephens M., Gilad Y. (2008) RNA-seq: An assessment of technical reproducibility and comparison with gene expression arrays. *Genome Research* **18**, 1509–17.

McKinna E.M., Nandlal S., Mather P.B., Hurwood D.A. (2010) An investigation of the possible causes for the loss of productivity in genetically improved farmed tilapia strain in Fiji: inbreeding versus wild stock introgression. *Aquaculture Research* **41**, e730–e42.

Meuwissen T., Hayes B., Goddard M. 2013. Accelerating improvement of livestock with genomic selection. *Annual Review of Animal Biosciences* **1**, 221–37.

Meuwissen T.H.E., Hayes B.J., Goddard M.E. (2001) Prediction of total genetic value using genome-wide dense marker maps. *Genetics* **157**, 1819–29.

Neira R., García X., Lhorente J.P., Filp M., Yáñez J.M., Cascante A.M. (2016) Evaluation of the growth and carcass quality of diallel crosses of four strains of Nile tilapia (Oerochromis niloticus). *Aquaculture* **451**, 213–22.

Nguyen N.H., Hamzah A., Thoa N.P. (2017) Effects of genotype by environment interaction on genetic gain and genetic parameter estimates in Red Tilapia (*Oreochromis* spp.). *Frontiers in Genetics* **8**. https://doi.org/10.3389/fgene.2017.00082

Nguyen N.H., Khaw H.L., Ponzoni R.W., Hamzah A., Kamaruzzaman N. (2007) Can sexual dimorphism and body shape be altered in Nile tilapia (*Oreochromis niloticus*) by genetic means? *Aquaculture* **272**, S38–46.

Nguyen N.H., Ponzoni R.W., Abu-Bakar K.R., Hamzah A., Khaw H.L., Yee H.Y. (2010) Correlated response in fillet weight and yield to selection for increased harvest weight in genetically improved farmed tilapia (GIFT strain), Oreochromis niloticus. *Aquaculture* **305**, 1–5.

Ninh N.H., Thoa N.P., Knibb W., Nguyen N.H. (2014) Selection for enhanced growth performance of Nile tilapia (Oreochromis niloticus) in brackish water (15–20 ppt) in Vietnam. *Aquaculture* **428–429**, 1–6.

Nishimura S., Watanabe T., Mizoshita K., Tatsuda K., Fujita T., Watanabe N., Sugimoto Y., Takasuga A. (2012) Genome-wide association study identified three major QTL for carcass weight including the PLAG1-CHCHD7 QTN for stature in Japanese Black cattle. *BMC Genetics* **13**, 1–11.

Ødegård J, Moen T, Santi N, Korsvoll SA, Kjøglum S, Meuwisse THE (2014) Genomic prediction in an admixed population of Atlantic salmon (*Salmo salar*). *Frontiers in Genetics* **5**, 1–8.

Palaiokostas C., Bekaert M., Khan M.G.Q., Taggart J.B., Gharbi K., McAndrew B.J., Penman D.J. (2015) A novel sex-determining QTL in Nile tilapia (*Oreochromis niloticus*). *BMC Genomics* **16**, 171.

Palaiokostas C., Bekaert M., Khan M.G.Q., Taggart J.B., Gharbi K., McAndrew B.J., Penman D.J. (2013) Mapping and validation of the major sex-determining Region in Nile Tilapia (Oreochromis niloticus L.) using RAD sequencing. *PLoS One* **8**, e68389.

Palaiokostas C., Kocour M., Prchal M., Houston R.D. (2018) Accuracy of genomic evaluations of juvenile growth rate in common carp (*Cyprinus carpio*) using genotyping by sequencing. *Frontiers in Genetics* **9**, 82.

Peñaloza C., Robledo D., Barría A., Trịnh T.Q., Mahmuddin M., Wiener P., Benzie J.A.H., Houston R.D. (2020) *Development and Validation of an Open Access Snp Array for Nile Tilapia (Oreochromis niloticus)*. G3: Genes/Genomes/Genetics g3.401343.2020. https://doi.org/10.1534/g3.120.401343.

Pérez-Enciso M., Rincón J.C., Legarra A. (2015) Sequence- vs. chip-assisted genomic selection: Accurate biological information is advised. *Genetics Selection Evolution* **47**, https://doi.org/10.1186/s12711-015-0117-5.

Pérez O'Brien A.M., Utsunomiya Y.T., Mészáros G., Bickhart D.M., Liu G.E., Van Tassell C.P., Sonstegard T.S., Da Silva M.V., Garcia J.F., Sölkner J. (2014) Assessing signatures of selection through variation in linkage disequilibrium between taurine and indicine cattle. *Genetics Selection Evolution* **46**, 19.

Ponzoni R.W., Hamzah A., Tan S., Kamaruzzaman N. (2005) Genetic parameters and response to selection for live weight in the GIFT strain of Nile Tilapia (*Oreochromis niloticus*). *Aquaculture* **247**, 203–10.

Ponzoni R.W., Khaw H.L., Nguyen N.H., Hamzah A. (2010) Inbreeding and effective population size in the Malaysian nucleus of the GIFT strain of Nile tilapia (*Oreochromis niloticus*). *Aquaculture* **302**, 42–8.

Prchal M., Kocour M., Vandeputte M. *et al.* (2020) Morphological predictors of slaughter yields using 3D digitizer and their use in a common carp breeding program. *Aquaculture* **520**, 734993.

Pruginin Y., Rothbard S., Wohlfarth G., Halevy A., Moav R., Hulata G. (1975) All-male broods of *Tilapia nilotica* × *T. aurea* hybrids. *Aquaculture* **6**, 11–21.

Reis Neto R.V., de Oliveira C.A.L., Ribeiro R.P., de Freitas R.T.F., Allaman I.B., de Oliveira S.N. (2014) Genetic parameters and trends of morphometric traits of GIFT tilapia under selection for weight gain. *Science in Agriculture* **71**, 259–65.

Reis Neto R.V., Yoshida G.M., Lhorente J.P., Yáñez J.M. (2019) Genome-wide association analysis for body weight identifies candidate genes related to development and metabolism in rainbow trout (*Oncorhynchus mykiss*). *Molecular Genetics and Genomics* **294**, 563–71.

Rezk M.A., Ponzoni R.W., Khaw H.L., Kamel E., Dawood T., John G. (2009) Selective breeding for increased body weight in a synthetic breed of Egyptian Nile tilapia, Oreochromis niloticus: Response to selection and genetic parameters. *Aquaculture* **293**, 187–94.

Rodríguez F.H., Flores-Mara R., Yoshida G.M., Barría A., Jedlicki A.M., Lhorente J.P., Reyes-López F., Yáñez J.M. (2019) Genome-wide association analysis for resistance to infectious pancreatic necrosis virus identifies candidate genes involved in viral replication and immune response in rainbow trout (*Oncorhynchus mykiss*). *G3; Genes/Genomes/Genetics* **9**, 2897–2904. http://dx.doi.org/10.1534/g3.119.400463

Roesti M., Moser D., Berner D. (2013) Recombination in the threespine stickleback genome - Patterns and consequences. *Molecular Ecology* **22**, 3014–27.

Rutten M.J.M., Bovenhuis H., Komen H. (2005) Genetic parameters for fillet traits and body measurements in Nile tilapia (*Oreochromis niloticus* L.). *Aquaculture* **246**, 125–32.

Rutten M.J.M., Komen H., Deerenberg R.M., Siwek M., Bovenhuis H. (2004) Genetic characterization of four strains of Nile tilapia (*Oreochromis niloticus* L.) using microsatellite markers. *Animal Genetics* **35**, 93–7.

Rye M. (2012) *Current status and prospects for the application of genetic improvement in aquaculture species*. 9th Bienn. Symp. Brazilian Soc. Anim. Breed. 11. https://doi.org/10.13140/RG.2.1.3138.2884.

Schomburg D. (Dietmar), Michal G. (2012) *Biochemical pathways: an atlas of biochemistry and molecular biology*. Heidelberg, Germany: John Wiley & Sons.

Shirak A., Seroussi E., Cnaani A., Howe A.E., Domokhovsky R., Zilberman N., Kocher T.D., Hulata G., Ron M. (2006) Amh and Dmrta2 genes map to tilapia (*Oreochromis* spp.) linkage group 23 within quantitative trait locus regions for sex determination. *Genetics* **174**, 1573–81.

Shoemaker C.A., Lozano C.A., LaFrentz B.R., García J.C., Soto E., Xu D.H., Beck B.H., Rye M. (2017) Additive genetic variation in resistance of Nile tilapia (Oreochromis niloticus) to Streptococcus iniae and S. agalactiae capsular type Ib: Is genetic resistance correlated? *Aquaculture* **468**, 193–8.

Smith A. (1940) *Illustration of the Zoology of South Africa*, Volume 4. ed. London.

Smitherman R.O., Tave D. (1987) Maintenance of genetic quality in cultured tilapia. *Asian Fisheries Science* **1**, 75–82.

Su G., Brøndum R.F., Ma P., Guldbrandtsen B., Aamand G.P., Lund M.S. (2012) Comparison of genomic predictions using medium-density (~54,000) and high-density (~777,000) single

nucleotide polymorphism marker panels in Nordic Holstein and Red Dairy Cattle populations. *Journal of Dairy Science* **95**, 4657–65.

Suebsong W., Poompuang S., Srisapoome P., Koonawootrittriron S., Luengnaruemitchai A., Johansen H., Rye M. (2019) Selection response for *Streptococcus agalactiae* resistance in Nile tilapia *Oreochromis niloticus*. *Journal of Fish Diseases* **42**, 1553–62.

Sukhavachana S., Poompuang S., Onming S., Luengnaruemitchai A. (2019) Heritability estimates and selection response for resistance to Streptococcus agalactiae in red tilapia *Oreochromis* spp. *Aquaculture* **502**, 384–90.

Sukhavachana S., Tongyoo P., Massault C., McMillan N., Leungnaruemitchai A., Poompuang S. (2020) Genome-wide association study and genomic prediction for resistance against Streptococcus agalactiae in hybrid red tilapia (*Oreochromis* spp.). *Aquaculture* **525**, 735297.

Sukmanomon S., Kamonrat W., Poompuang S., Nguyen T.T.T., Bartley D.M., May B., Na-Nakorn U. (2012) Genetic changes, intra- and inter-specific introgression in farmed Nile tilapia (*Oreochromis niloticus*) in Thailand. *Aquaculture* **324–325**, 44–54.

Sun C., Niu Y., Ye X., Dong J., Hu W., Zeng Q., Chen Z., Tian Y., Zhang J., Lu M. (2017) Construction of a high-density linkage map and mapping of sex determination and growth-related loci in the mandarin fish (*Siniperca chuatsi*). *BMC Genomics* **18**, 1–10.

Suresh A.V., Lin C.K. (1992) Tilapia culture in saline waters: a review. *Aquaculture* **106**, 201–26.

Tao W., Chen J., Tan D., Yang J., Sun L., Wei J., Conte M.A., Kocher T.D., Wang D. (2018) Transcriptome display during tilapia sex determination and differentiation as revealed by RNA-Seq analysis. *BMC Genomics* **19**, 1–12.

Tao W., Sun L., Shi H., Cheng Y., Jiang D., Fu B., Conte M.A., Gammerdinger W.J., Kocher T.D., Wang D. (2016) Integrated analysis of miRNA and mRNA expression profiles in tilapia gonads at an early stage of sex differentiation. *BMC Genomics* **17**, 328.

Tao W., Xu L., Zhao L., Zhu Z., Wu X., Min Q., Zhou Q., Wang D., Zhou Q. 2020. *High-quality chromosome-level genomes of two tilapia species reveal their evolution of repeat sequences and sex chromosomes*. bioRxiv 2020.03.30.016618. https://doi.org/10.1101/2020.03.30.016618.

Tao W., Yuan J., Zhou L., Sun L., Sun Y., Yang S., Li M., Zeng S., Huang B., Wang D. (2013) Characterization of Gonadal Transcriptomes from Nile Tilapia (*Oreochromis niloticus*) Reveals Differentially Expressed Genes. *PLoS One* **8**, e63604.

Teletchea F. 2019. *Fish Domestication: An Overview, in: Animal Domestication*. IntechOpen. https://doi.org/10.5772/intechopen.79628.

Tessema M., Müller-Belecke A., Hörstgen-Schwark G. (2006) Effect of rearing temperatures on the sex ratios of *Oreochromis niloticus* populations. *Aquaculture* **258**, 270–7.

Thodesen (Da-Yong Ma) J., Rye M., Wang Y.-X., Yang K.-S., Bentsen H.B., Gjedrem T. (2011) Genetic improvement of tilapias in China: Genetic parameters and selection responses in growth of Nile tilapia (*Oreochromis niloticus*) after six generations of multi-trait selection for growth and fillet yield. *Aquaculture* **322–323**, 51–64.

Toguyeni A., Fauconneau B., Fostier A., Abucay J., Mair G., Baroiller J.-F. (1997) *Influence of genotype and social behaviour on growth performances in tilapia, Oreochromis niloticus, in: Proceedings of the Fourth International Symposium on Tilapia in Aquaculture = [Actes Du 4ème Congrès International Sur Tilapia En Aquaculture]*. *s.n.*

Trong T.Q., Mulder H.A., van Arendonk J.A.M., Komen H. (2013) Heritability and genotype by environment interaction estimates for harvest weight, Growth rate, And shape of Nile tilapia (*Oreochromis niloticus*) grown in river cage and VAC in Vietnam. *Aquaculture* **384–387**, 119–27.

Tsai H.-Y., Hamilton A., Tinch A.E. *et al*. (2016) Genomic prediction of host resistance to sea lice in farmed Atlantic salmon populations. *Genetics Selection Evolution* **48**, 47.

Tsai H.Y., Hamilton A., Tinch A.E., Guy D.R., Gharbi K., Stear M.J., Matika O., Bishop S.C., Houston R.D. (2015) Genome wide association and genomic prediction for growth traits in juvenile farmed Atlantic salmon using a high density SNP array. *BMC Genomics* **16**, 1–9.

Vallejo R., Liu S., Gao G. *et al*. (2017) Similar genetic architecture with shared and unique quantitative trait loci for bacterial cold water disease resistance in two rainbow trout breeding populations. *Frontiers in Genetics* **8**, 1–15.

van Binsbergen R., Calus M.P.L., Bink M.C.A.M., van Eeuwijk F.A., Schrooten C., Veerkamp R.F. (2015) Genomic prediction using imputed whole-genome sequence data in Holstein Friesian cattle. *Genetics Selection Evolution* **47**, 71.

Van Laere A.S., Nguyen M., Braunschweig M. *et al*. (2003) A regulatory mutation in IGF2 causes a major QTL effect on muscle growth in the pig. *Nature* **425**, 832–6.

Vandeputte M., Fraslin C., Haffray P., Bestin A., Allal F., Kocour M., Prchal M., Dupont-Nivet M. (2020) How to genetically increase fillet yield in fish: Relevant genetic parameters and methods to predict genetic gain. *Aquaculture* **519**, 734877.

Vandeputte M., Puledda A., Tyran A.S. *et al*. (2017) Investigation of morphological predictors of fillet and carcass yield in European sea bass (Dicentrarchus labrax) for application in selective breeding. *Aquaculture* **470**, 40–9.

Vieira Ventura R., Fonseca e Silva F., Manuel Yáñez J., Brito L.F. (2020) Opportunities and challenges of phenomics applied to livestock and aquaculture breeding in South America. *Anim. Front.* **10**, 45–52.

Wang B., Gan Z., Cai S., Wang Z., Yu D., Lin Z., Lu Y., Wu Z., Jian J. (2016) Comprehensive identification and profiling of Nile tilapia (*Oreochromis niloticus*) microRNAs response to Streptococcus agalactiae infection through high-throughput sequencing. *Fish & Shellfish Immunology* **54**, 93–106.

Wang H.-P., Shen Z.-G. 2019. Sex Control in Aquaculture: Concept to Practice, in: Wang H, Piferrer F, Chen S, Shen Z-G (Eds.), *Sex Control in Aquaculture*. Hoboken, New Jersey: Wiley-Blackwell, pp. 3–34.

Wang L., Liu P., Wan Z.Y., Huang S.Q., Wen Y.F., Lin G., Yue G.H. (2016) RNA-Seq revealed the impairment of immune defence of tilapia against the infection of *Streptococcus agalactiae* with simulated climate warming. *Fish & Shellfish Immunology* **55**, 679–89.

Wang L., Wan Z.Y., Bai B. *et al*. (2015) Construction of a high-density linkage map and fine mapping of QTL for growth in Asian seabass. *Scientific Reports* **5**, 1–10.

Weller J.I., Ron M. (2011) Invited review: Quantitative trait nucleotide determination in the era of genomic selection. *Journal of Dairy Science* **94**, 1082–90.

Wessels S., Sharifi R.A., Luehmann L.M., Rueangsri S., Krause I., Pach S., Hoerstgen-Schwark G., Knorr C. (2014) Allelic variant in the anti-müllerian hormone gene leads to autosomal and temperature-dependent sex reversal in a selected nile tilapia line. *PLoS One* **9**, e104795.

Wohlfarth G.W. (1994) The unexploited potential of tilapia hybrids in aquaculture. *Aquaculture Research* **25**, 781–8.

Wonmongkol P., Sukhavachana S., Ampolsak K., Srisapoome P., Suwanasopee T., Poompuang S. (2018) Genetic parameters for resistance against *Flavobacterium columnare* in Nile tilapia *Oreochromis niloticus* (Linnaeus, 1758). *Journal of Fish Diseases* **41**, 321–8.

Wu L., Wu F., Xie L., Wang D., Zhou L. (2016a) Synergistic role of β-catenin1 and 2 in ovarian differentiation and maintenance of female pathway in Nile tilapia. *Molecular and Cellular Endocrinology* **427**, 33–44.

Wu L., Yang P., Luo F., Wang D., Zhou L. (2016b) R-spondin1 signaling pathway is required for both the ovarian and testicular development in a teleosts, Nile tilapia (Oreochromis niloticus). *General and Comparative Endocrinology* **230–231**, 177–85.

Xia J.H., Wan Z.Y., Ng Z.L., Wang L., Fu G.H., Lin G., Liu F., Yue G.H. (2014) Genome-wide discovery and in silico mapping of gene-associated SNPs in Nile tilapia. *Aquaculture* **432**, 67–73.

Xiao J., Zhong H., Liu Z., Yu F., Luo Y., Gan X., Zhou Y. (2015) Transcriptome analysis revealed positive selection of immune-related genes in tilapia. *Fish & Shellfish Immunology* **44**, 60–5.

Xie Q.-P., He X., Sui Y.-N., Chen L.-L., Sun L.-N., Wang D.-S. (2016) Haploinsufficiency of SF-1 Causes Female to Male Sex Reversal in Nile Tilapia, *Oreochromis niloticus*. *Endocrinology* **157**, 2500–14.

Xiong Y., Huang J., Li X., Zhou L., Dong F., Ye H., Gan L. (2014) Deep sequencing of the tilapia (*Oreochromis niloticus*) liver transcriptome response to dietary protein to starch ratio. *Aquaculture* **433**, 299–306.

Xu Z., Gan L., Li T., Xu C., Chen K., Wang X., Qin J.G., Chen L., Li E. (2015) Transcriptome Profiling and Molecular Pathway Analysis of Genes in Association with Salinity Adaptation in Nile Tilapia Oreochromis niloticus. *PLoS One* **10**, e0136506.

Yan B., Guo J.T., Zhao L.H., Zhao J.L. (2012) MicroRNA expression signature in skeletal muscle of Nile tilapia. *Aquaculture* **364–365**, 240–6.

Yáñez J.M., Houston R.D., Newman S. (2014) Genetics and genomics of disease resistance in salmonid species. *Frontiers in Genetics* **5**, 1–13.

Yáñez J.M., Newman S., Houston R.D. (2015) Genomics in aquaculture to better understand species biology and accelerate genetic progress. *Frontiers in Genetics* **6**, 1–3.

Yáñez J.M., Yoshida G., Barria A. *et al.* (2020) High-Throughput Single Nucleotide Polymorphism (SNP) Discovery and Validation Through Whole-Genome Resequencing in Nile Tilapia (*Oreochromis niloticus*). *Marine Biotechnology* **22**, 109–17.

Yoshida G., Carvalheiro R., Rodríguez F.H., Lhorente J.P., Yáñez J.M. (2019a) Single-step genomic evaluation improves accuracy of breeding value predictions for resistance to infectious pancreatic necrosis virus in rainbow trout. *Genomics* **111**, 127–32.

Yoshida G.M., Lhorente J.P., Correa K., Soto J., Salas D., Yáñez J.M. (2019) Genome-wide association study and cost-efficient genomic predictions for growth and fillet yield in Nile Tilapia (*Oreochromis niloticus*). *G3; Genes/Genomes/Genetics* **9**, 2597–2607. http://dx.doi.org/10.1534/g3.119.400116

Yoshida G.M., Bangera R., Carvalheiro R., Correa K., Figueroa R., Lhorente J.P., Yáñez J.M. (2018) Genomic prediction accuracy for resistance against Piscirickettsia salmonis in farmed rainbow trout. *G3; Genes/Genomes/Genetics* **8**, 719–726. http://dx.doi.org/10.1534/g3.117.300499

Yoshida G.M., Barria A., Cáceres G., Correa K., Jedlicki A., Cadiz M.I., Lhorente J.P., Yáñez J.M. (2019c) Genome-wide patterns of population structure and linkage disequilibrium in farmed Nile tilapia (*Oreochromis niloticus*). *Frontiers in Genetics* **10**, 745.

Yoshida G.M., Lhorente J.P., Carvalheiro R., Yáñez J.M. (2017b) Bayesian genome-wide association analysis for body weight in farmed Atlantic salmon (*Salmo salar* L.). *Animal Genetics* **48**, 698–703.

Yoshida G.M., Yáñez J.M., de Oliveira C.A.L., Ribeiro R.P., Lhorente J.P., de Queiroz S.A., Carvalheiro R. (2017c) Mate selection in aquaculture breeding using differential evolution algorithm. *Aquaculture Research* **48**, 5490–7.

Zak T., Deshev R., Benet-Perlberg A., Naor A., Magen I., Shapira Y., Ponzoni R.W., Hulata G (2014) Genetic improvement of Israeli blue (Jordan) tilapia, *Oreochromis aureus* (Steindachner), through selective breeding for harvest weight. *Aquaculture Research* **45**, 546–57.

Zhang R., Zhang L.L., Ye X., Tian Y.Y., Sun C.F., Lu M.X., Bai J.J. (2013) Transcriptome profiling and digital gene expression analysis of Nile tilapia (Oreochromis niloticus) infected by Streptococcus agalactiae. *Molecular Biology Reports* **40**, 5657–68.

Zhang X., Li M., Ma H., Liu X., Shi H., Li M., Wang D. (2017) Mutation of foxl2 or cyp19a1a results in female to male sex reversal in XX nile tilapia. *Endocrinology* **158**, 2634–47.

Zhao Y., Wang J., Thammaratsuntorn J., Wu J.W., Wei J.H., Wang Y., Xu J.W., Zhao J.L. (2015) Comparative transcriptome analysis of Nile tilapia (*Oreochromis niloticus*) in response to alkalinity stress. *Genetics and Molecular Research* **14**, 17916–26.

Zheng Y., Wu W., Hu G., Zhao Z., Meng S., Fan L., Song C., Qiu L., Chen J. (2018) Hepatic transcriptome analysis of juvenile GIFT tilapia (*Oreochromis niloticus*), fed diets supplemented with different concentrations of resveratrol. *Ecotoxicology and Environmental Safety* **147**, 447–54.

Zhu J., Li C., Ao Q., Tan Y., Luo Y., Guo Y., Lan G., Jiang H., Gan X. (2015) Trancriptomic profiling revealed the signatures of acute immune response in tilapia (*Oreochromis niloticus*) following Streptococcus iniae challenge. *Fish & Shellfish Immunology* **46**, 346–53.