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Mini Review

Study on the relationship between silent mutations and quantitative trait Loci genes in cattle

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ABSTRACT:

Silent mutation is one among the mutations that occurs in coding and non-coding regions of different genes which governs the protein function. Often the sequences lead to variance in one of the amino acids because of the triplet code therefore with low percentages and non-significantly changing genetic code expressions they influence on protein function and folding. Mostly, the secondary structure for mRNA will be altered and correlated with Quantitative Trait Loci (QTL) which are a part of DNA and associated with phenotype, quantitative trait variance and can be identified by SNPs and AFLPs. These are related polygenic genes found on different chromosomes that are responsible for quantitative traits and change continuously. This review explains the importance of silent mutations and their relation with quantitative characteristics such as productivity as well as performance of the cattle.

Keywords:
Silent mutation, QTL, Genes, Cattle.

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INTRODUCTION

Over twenty years, it has been discovered that QTLs are found in the genes of Diacylglycerol O – Acyl Transferase (DGAT), ATP binding cassette subfamily G member 2 (ABCG2), Insulin like Growth Factor 2 (IGF2) and Growth Hormone Receptor (GHR) which were linked with health, growth traits and immunity (Al -Samaraai and Ali, 2018). Occasionally, changes occur in some regions of genes that are referred as silent mutations which alter DNA significantly in the non-coding regions of genes or within introns or exons. Mostly, this mutation is the same as synonymous mutation but the opposite is untrue altering amino acid sequences, transcription splicing, mRNA transcription and translation to change the phenotypes (Shabalina *et al*., 2006). Genetic differences influences hormone production and protein building resulting in the damage of some organs (Nayyef, 2018).

Silent mutation produced due to additive, deletion or insertion causing difference in reading the code of mRNA which reflects on t-RNA code during translation (Mueller *et al*., 2009) which break down protein code and will be altered to produce amino acid with similar function like lysine instead of iso-leucine. This mutation does not influence protein function, however through several codes, many of the amino acids could be changed during mRNA translation (Komar *et al.*, 2007). For example, when codon alter AAA to AAG, the same amino acids will be formed in the peptide chain (Czech *et al*., 2010). Polymorphism at 348 position as a silent mutation does not even change the amino acid aspargine (i.e.) AAT>AAC within exon 4 for integrin beta chain – 2 (CD18) gene which correlates with milk production (Patel *et al*., 2015). Whereas, base pairs at CD18 gene that alter aspartic to glycine (Patel *et al*., 2012) causes another silent mutation which replaces cytosine to thiamine at 775 position. At 383 bp position and 880 bp cDNA position, silent mutations remove 105 bp within exon 4 for CD18 gene (Patel *et al.*, 2011). Silent mutations are correlated with diseases or negative effects but there are advances because of creating genetic variation among different individuals; so, some of the infections didn't appear without one available lethal gene (Komar *et al*., 2007).

If m-RNA moves to the ribosome late, translation will be slowed down due to the depression of gene expression which contains this mutation inside exon while ribosome waits for a long time to pick up amino acid as well as may be translated earlier with difference in one of the three letters in the triplet codon that has similar biological and chemical features (Calero *et al.*, 2016). In the same side, triplet codon modifications impact on protein translation (Brooker, 2017). Replacement of one amino acid in a protein may alter the function and the tertiary structure or may not be affected depending on traits. Correlated amino acids may be entering codon before limited time for stopping codon UGA, thus, this mutation perform to produce incomplete protein and functional folding depending upon the area of stop codon in the same hand. If mRNA is unstable relatively, it will effect in cytoplasm by enzymes (Mueller *et al*., 2015).

However, when mRNA is stable with strong bands, gene may be under expression Dopamine receptor D2 gene is less stable and can be analyzed quickly resulting in the reduction of gene activity. On the other hand, silent mutation in Multi Drug Resistant gene (MDR) enabled cell membrane to resist a set of drugs and reduced translation performance by abnormal folding of the proteins (Brooker, 2017). Variance of mRNA splicing in cells were influenced by mutations and does not alter protein codon which appeared *via* changing of gene expression throughout splicing, translation during mutation in exon 7 of Survival Motor Neuron 1 (SMN1) gene (Czech *et al.*, 2010). This influence on accuracy of splicing, stability of mRNA structure and its function, whereas, there is a mutation beside splicing area of intron flanking exon 10 for

microtubule associated protein tau (MAPT) gene (Stylianos *et al*., 2013),

There are 36,693 positions of quantitative traits for 492 traits in cattle including 5815 regions for milk fat, 3157 for milk protein, 1824 for milk production, 550 for fatty acids contents and 1246 for mastitis (Albengha *et al.*, 2016). Silent mutation of C>T at 775 bp position for CD1 gene codon is an indicator for higher milk production. However, association between polymorphism of T<C 775 and milk yield performance is a parameter to QTL (Czarnik *et al*., 2007); this mutation localized at 775 bp area for integrin beta - 2 precusor (ITGB2) gene was associated with protein contents, while there are three regions for QTL on Betaine lipid synthase 1 (BTA_1) gene that are coupled with milk production (Czarnik *et al*., 2004). On the same hand, D128G mutation is a QTL index found within coding genes which is related with lactation (Czarnik, 2000). Silent mutation revealed in exon 6 for pituitary – specific positive transcription factor 1 (POUIFI) gene have polymorphisms acting on body contents, milk production, body weight at an early age as well as carcass traits and furthermore growth in beef cattle (Xue *et al*., 2006). However Zhao *et al*. (2004) found SNPs within 3, 4 and 5 introns of bovine gene POUIF1 as a silent mutation.

On the other hand, Diacylglycerol O– Acyltransferase 1 (DGAT1) gene was responsible for milk yield, fat contents, in addition to intra muscular fat composition. Also, a SNP in 5' UTR area for this gene was related with high fat ratio in milk (Yang *et al*., 2011). Silent mutation from GCC-Ala 487 to GCT Ala 487 available in exon 17 at 8539 bp in Chinese sheep (Xu *et al*., 2008) and on the same direction, SNP 15 (9258C>T) for calcium dependent protease (CAPN1) gene was considered a silent mutation in exon 4 on chromosome 29 which correlated significantly with meat quality (Liu *et al*., 2015). In a study done by Uijan *et al*. (2011), QTL for growth traits and meat quality was founded at 0 – 30, 55 – 70 and 70 – 80 cμ on chromosome 5 including SNPs for myogenic genes in these regions.

On the other hand, there are three silent mutations for bovine GL1 family, zinc finger 3 (GL 13) gene is associated with body weight at birth and six months age in Nanyang cattle. Also, silent mutation in INGI gene is linked with growth in Qinchuan cattle. Furthermore, Non – SMC Condensin in complex I subunit G (NCAPG) gene coding condensin1 protein has important role in mitosis both in the division and organization (Duan *et al*., 2015). Moreover, primary effect of NCAPG mutation on progenitor cells was correlated with phenotype and daily body weight in Germany Holstein. Proud and Roberts (2007) also correlated with total body weight, hip width and carcass weight so that significant differences was found between NCAPG, Ligand Dependent Nuclear Receptor Corepressor Like (LCORL) and DDB1 and CuL4 associated factor 16 (DCAF 16) with body muscular development in addition to the embryonic growth (Peters and Sian, 2004). Silent mutation in Apoptotic Peptidase Activating Factor 1 (APAF1) (Adems *et al*., 2016), is an active element of cytochrome that modulated apoptotic cascade that was related with infections. Also, this factor contributed in the development of central nerve system (Ghanem and Nishibori, 2018).

However, a silent mutation at 240 bp within exon 3 and 5 for ASS1 gene does not affect the amino acids in Holstein cattle (Kolikalapudi *et al*., 2014), while two silent mutations in Melanocortin Receptor l (MC1R) gene on chromosome 14, was significant in skin colour in Chinese sheep. These mutations are found to be c.218 T>A.P.73 met>Lys. C.361 G>A, P.121 Asp>Asn (Yang *et al*., 2013).

CONCLUSION

From the above data, it can be concluded that silent mutation that happened within genes correlated with quantitative traits were not affected by these changes sometimes. Anyway, these mutations could be dependent upon them as an active marker for the selection and keeping of productivity balance in cattle.

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