Use of Integrative Genomic and Systems Biology Approaches to Identify Biomarkers in Donor Cows for *In Vitro* Embryo Production

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The need for increased efficiency of food production calls for widespread implementation of novel precision breeding strategies. Genomic selection (GS) refers to selection decisions on the basis of genomic estimated breeding values (GEBV) and serves as one of the revolutionary breakthroughs in animal breeding to assist in identifying genetically superior animals. *In vitro* fertilization (IVF) is a biotechnological tool which serves as excellent and inexpensive source of embryos for carrying out basic research in developmental physiology [1-9] and can be used in genetic improvement program for hastening traditional breeding programs. The Ovum Pick Up- *In vitro* Production (OPU-IVP) of embryos has greatly advanced our basic understanding of pre-implantation embryonic development and can be used in livestock genetic improvement. Genetic improvement can be speeded up by using the combination of GS with artificial reproductive techniques such as ultrasound-guided ovum pick up (OPU) and subsequent *In vitro* Production (IVP) of embryos. The major drawbacks for implementation of IVP of embryos are reduced oocyte quality after *in vitro* oocyte maturation and lower embryo cryotolerance which leading to reduced pregnancy rates compared to *in vivo*-produced embryos. The large differences between *in vivo* and *in vitro* culture environment can be considered as one of the key reasons which lead to decrease in oocyte quality, survival rate of derived embryo and the viability of the embryos after transfer.

In the recent years, use of next generation sequencing (NGS) has led the scientists to discover a lots of single nucleotide polymorphism (SNP), insertion and deletion (Indel), large structural variation (SVs) involved in trait especially in the field of animal science, and complex trait like double muscling and milk production in dairy cattle [10-11]. For instance to identify the genes involved in milk production by using NGS technology, in one study two groups of Holstein bulls, four animal in each group were sequenced. The groups were separated by estimated breeding value (EBVs) (low EBVs vs. high). Average depth of genome coverage was 10X and over 0.9 million indel were identified in this study. By analyzing about 700 genes with known quantitative trait loci (QTL) and effective SNP which had previously been identified by genome wide association studies (GWAS), associated with milk protein and fat, 11 promising genes that affecting milk production were identified [12].

NGS is promising approach to identify copy number variation (CNV) which is known as variant that is very effective in animal breeding program. In one study to discover some CNV involved in milk production trait, 8 Holstein bulls were selected based on (EBVs) (low EBVs vs. high) and were investigated using WGS [13]. The range of coverage depth per individual was 8.2 - 11.9×. They identified total 14,821 CNVs including 5025 duplications and 9796 deletions. A total of 487 differences were also observed in CNV regions (CNVRs) of the cattle genome between high and low groups. They also identified 10 genes that were significantly enriched for a specific biological function related to protein and lipid metabolism. In another study, to identify genes associated with traits associated with IVP in donor cows, RNA-seq analysis was performed on granulosa cells of some abattoir's ovaries [14]. They identified 56 genes related to blastocyst rate and good IVP outcome was negatively correlated with follicle and positively correlated with early atresia. In another study, the SNPs related to longevity of some Polish Red, Polish Holstein- Friesian, and Hereford breeds were investigated [15]. They concluded that NGS-based RNA-sequencing technology has tremendous potential in identifying genetic variation at many loci, with respect to SNP polymorphisms and understanding the genomic variation in three breeds of cattle that may reflect differences in production traits.

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