

# *ELF3* and *FOXA2* Loci, Probable Putative Trans-QTL for Abnormal Sperm Percentage in Cattle: An *In-silico* Analysis

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# Outline

**Goal for Animal Genomics**

**Need for *In-Silico* Trans QTL Identification**

**Methodology**

**Results**

**Conclusion & Future Directions**

# A Goal of Farm Animal Genomics

**“To select the farm animals for better Semen quality traits by genetic markers”**

**Low to moderate heritability traits can be improved by marker assisted selection**

**Heritabilities (0.15-0.30<sup>1</sup>)**

**QTLs or chromosomal regions that explain the variation in phenotypes**

**Breeding strategies**

**Evaluation of selection response**

# Identified QTL for Semen Quality Traits in Cattle

	No. of QTL	Chromosomes
Percentage of abnormal sperm (ABSP)	3	20, 21, 23
Percentage of live sperm after osmotic stress	1	23

**Need to identify Further possible QTL & Functional annotation of genes in the QTL**

Percentage of average path velocity	1	23
Sperm counts	3	4,11, 27
Sperm motility	6	4,7, 11, 27

**A total of only 21 QTL in AnimalQTLdb**

# Methodology: *In-Silico* Analysis for Cattle ABSP

Selected QTL (n = 3)  
from AnimalQTLdb

Extraction of chromosomal coordinates  
for the QTL from Cattle tracks from  
UMD3.1 Genome

Extraction of annotated  
genes from Ensembl Cattle UMD3.1  
genome

Gene name if  
no homology

NCBI BLAST for the Protein/  
nucleotide sequence

NO

Gene names known

YES

Total Gene List (n = 134)

Functional annotation  
from Panther 9.0 based  
on cattle database

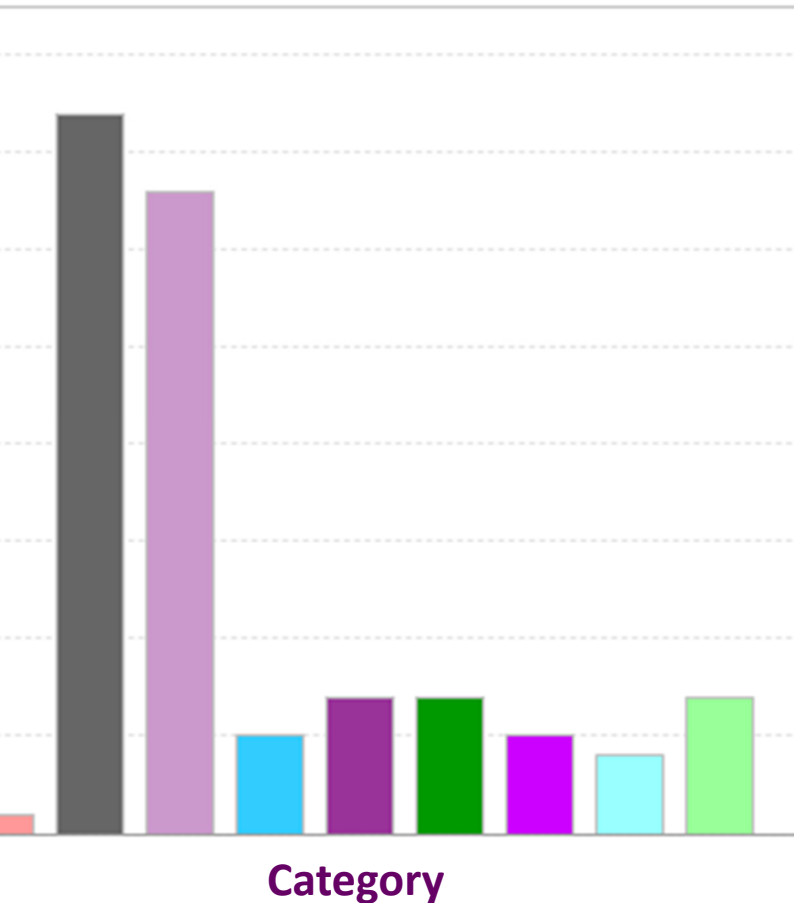
Single Site Analysis (SSA) by oPPOSUM 3.0  
for common orthologous transcription factors (oTF)  
based on human genome (Z score > 10; Fisher score > 10)

Alternative regulative (Trans) QTL based on significant oTF gene co-ordinates in cattle genome

# Results: Molecular Functions of Genes at reported QT Cattle ABSP

## GO Molecular Function

Total # Genes: 101 Total # function hits: 106

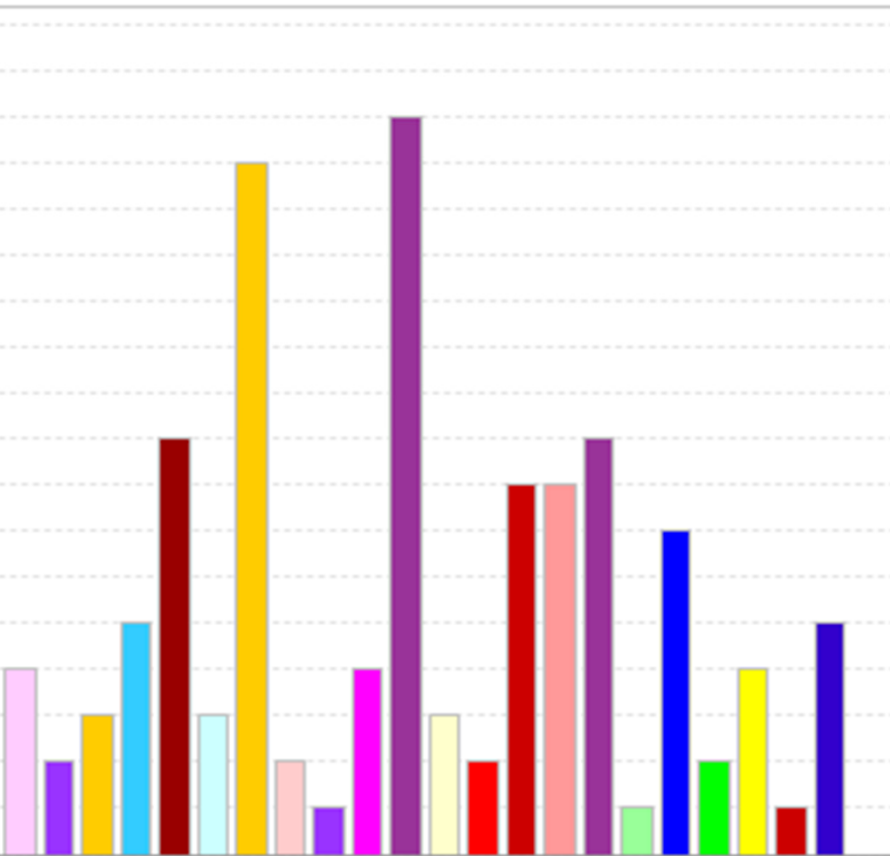


- antioxidant activity (GO:0016209) 1%
- binding (GO:0005488) 36.6%
- catalytic activity (GO:0003824) 32.7%
- enzyme regulator activity (GO:0030234) 5.0%
- nucleic acid binding transcription factor activity (GO:0001071) 6.9%
- receptor activity (GO:0004872) 6.9%
- structural molecule activity (GO:0005198) 5.0%
- translation regulator activity (GO:0045182) 4.0%
- transporter activity (GO:0005215) 6.9%

# Results: Protein Class of Genes at reported QTL for Ca ABSP

## PANTHER Protein Class

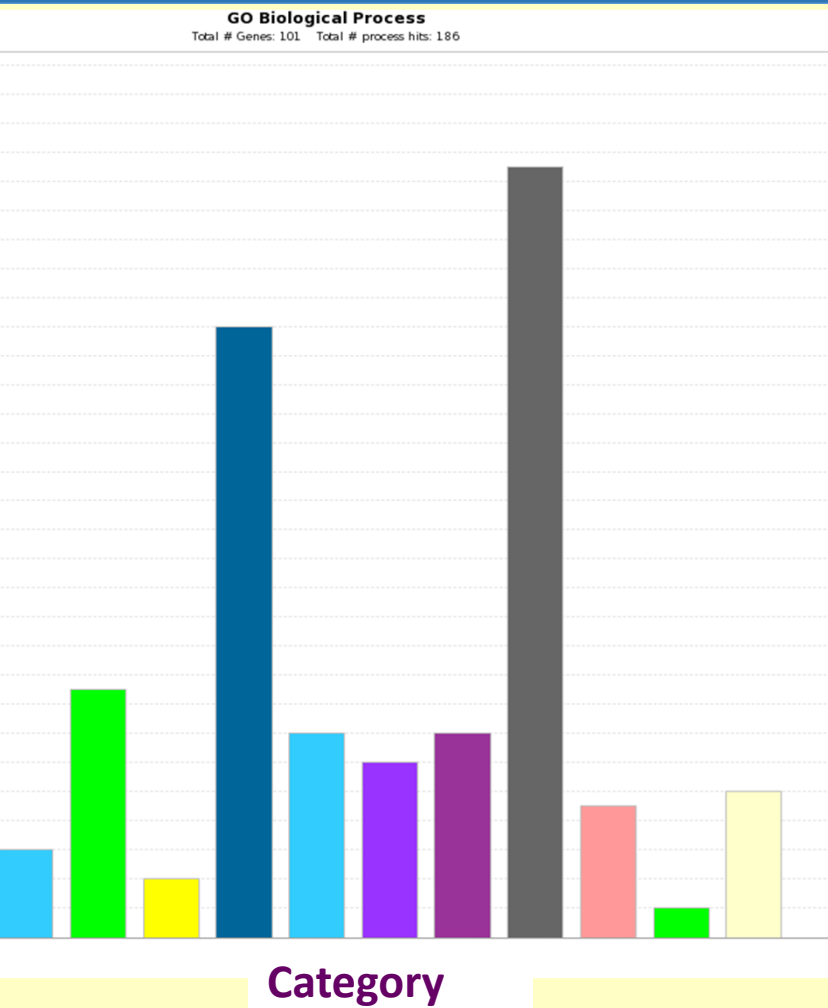
Total # Genes: 101 Total # protein class hits: 115















Category

- [calcium-binding protein \(PC00060\)](#) 1.0%
- [cell adhesion molecule \(PC00069\)](#) 4.0%
- [chaperone \(PC00072\)](#) 2.0%
- [cytoskeletal protein \(PC00085\)](#) 3.0%
- [defense/immunity protein \(PC00090\)](#) 5.0%
- [enzyme modulator \(PC00095\)](#) 8.9%
- [extracellular matrix protein \(PC00102\)](#) 3.0%
- [hydrolase \(PC00121\)](#) 14.9%
- [kinase \(PC00137\)](#) 2.0%
- [lyase \(PC00144\)](#) 1.0%
- [membrane traffic protein \(PC00150\)](#) 4.0%
- [nucleic acid binding \(PC00171\)](#) 15.8%
- [oxidoreductase \(PC00176\)](#) 3.0%
- [phosphatase \(PC00181\)](#) 2.0%
- [protease \(PC00190\)](#) 7.9%
- [receptor \(PC00197\)](#) 7.9%
- [signaling molecule \(PC00207\)](#) 8.9%
- [structural protein \(PC00211\)](#) 1.0%
- [transcription factor \(PC00218\)](#) 6.9%
- [transfer/carrier protein \(PC00219\)](#) 2.0%
- [transferase \(PC00220\)](#) 4.0%
- [transmembrane receptor regulatory/adaptor protein \(PC00226\)](#) 5.0%
- [transporter \(PC00227\)](#) 5.0%

# Results: Biological Functions of Genes at Reported QT Cattle ABSP



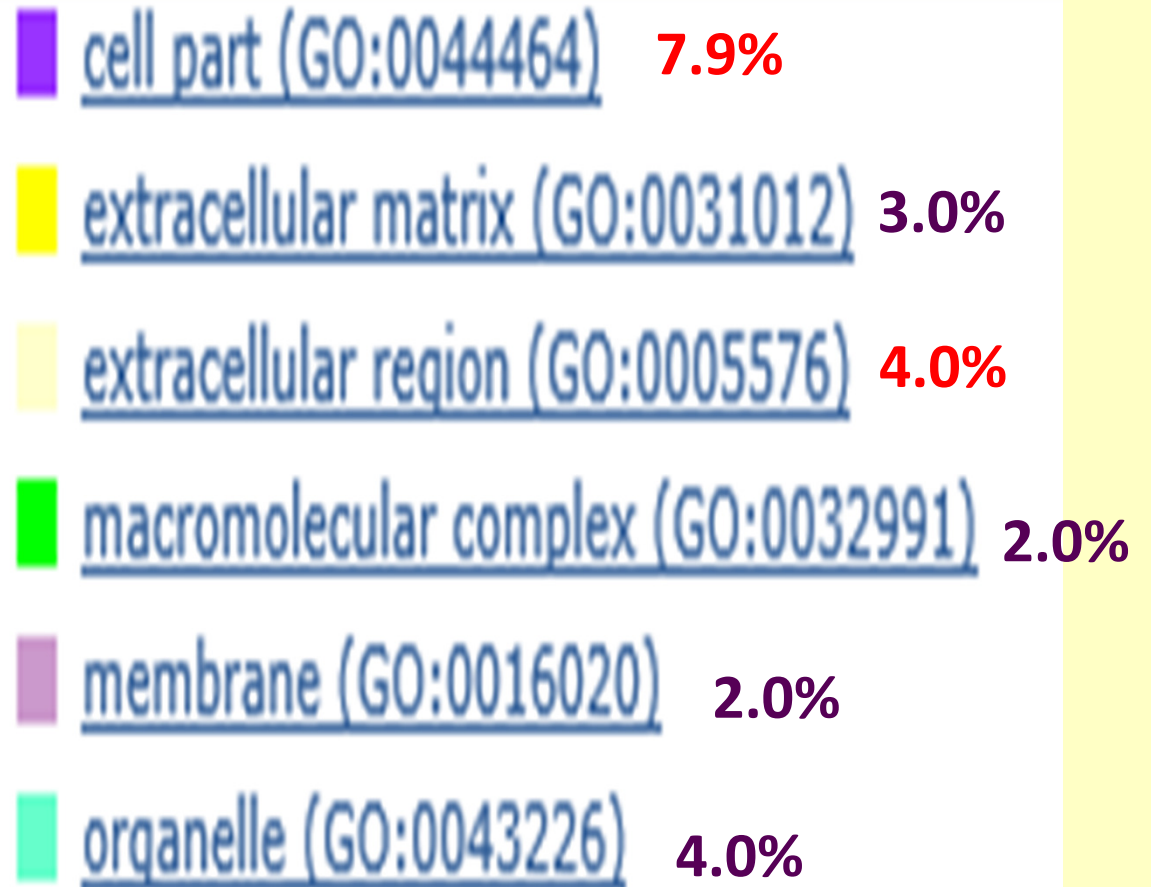
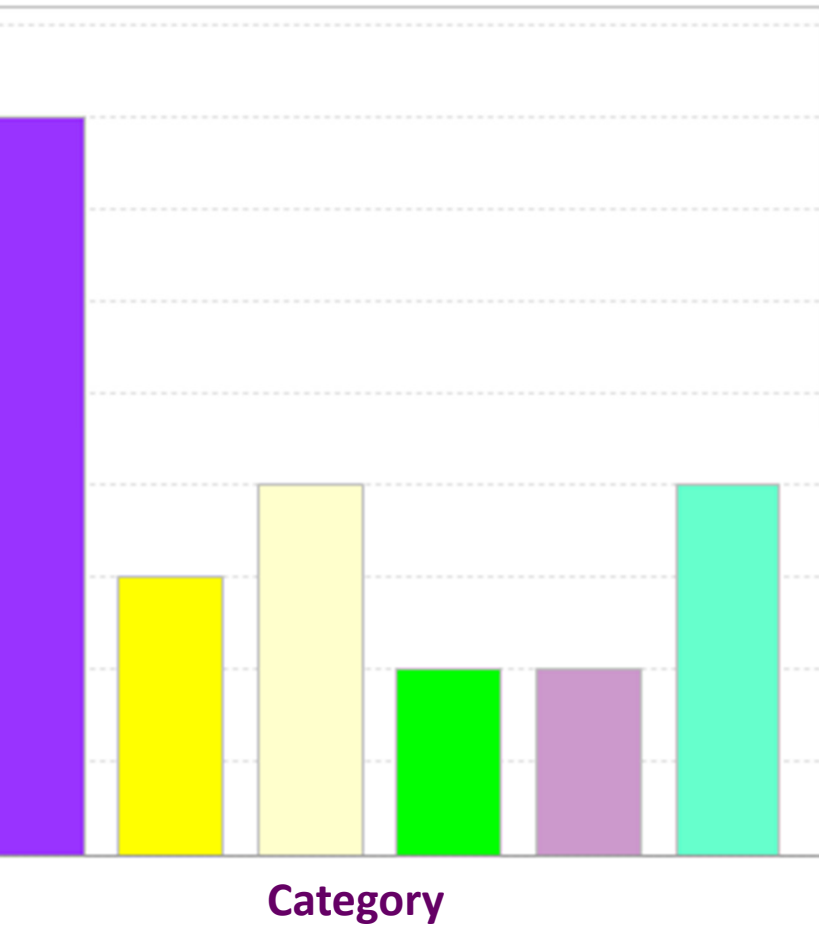
	<a href="#">apoptotic process (GO:0006915)</a>	3.0%
	<a href="#">biological adhesion (GO:0022610)</a>	5.9%
	<a href="#">biological regulation (GO:0065007)</a>	16.8%
	<a href="#">cellular component organization or biogenesis (GO:0071)</a>	3.6%
	<a href="#">cellular process (GO:0009987)</a>	41.6%
	<a href="#">developmental process (GO:0032502)</a>	13.9%
	<a href="#">immune system process (GO:0002376)</a>	11.9%
	<a href="#">localization (GO:0051179)</a>	13.9%
	<a href="#">metabolic process (GO:0008152)</a>	52.5%
	<a href="#">multicellular organismal process (GO:0032501)</a>	8.9%
	<a href="#">reproduction (GO:0000003)</a>	2.0%
	<a href="#">response to stimulus (GO:0050896)</a>	9.9%



# Results: Cellular Locations of Genes at reported QTL Cattle ABSP

## GO Cellular Component

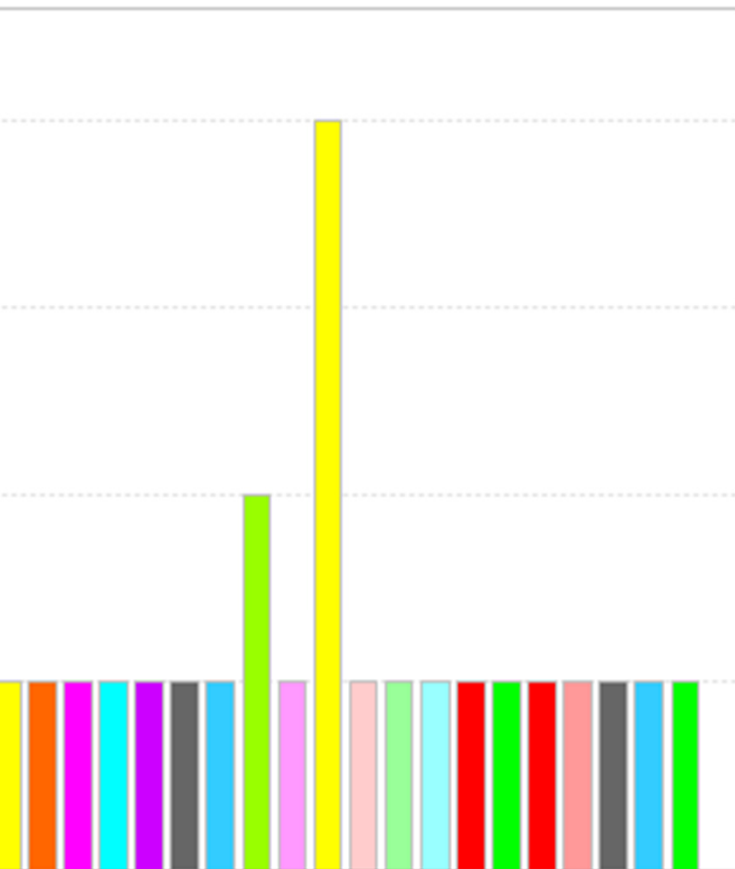
Total # Genes: 101 Total # component hits: 23



# Results: Pathway Analysis of Genes at reported QTL Cattle ABSP

## PANTHER Pathway

Total # Genes: 101 Total # pathway hits: 25



Category

- [Alzheimer disease-amyloid secretase pathway \(P00003\)](#)
  - [Alzheimer disease-presenilin pathway \(P00004\)](#)
  - [Angiogenesis \(P00005\)](#)
  - [Apoptosis signaling pathway \(P00006\)](#)
  - [Axon guidance mediated by semaphorins \(P00007\)](#)
  - [Cholesterol biosynthesis \(P00014\)](#)
  - [Cytoskeletal regulation by Rho GTPase \(P00016\)](#)
  - [EGF receptor signaling pathway \(P00018\)](#)
  - [Endothelin signaling pathway \(P00019\)](#)
  - [FGF signaling pathway \(P00021\)](#)
  - [Gonadotropin releasing hormone receptor pathway \(P06664\)](#) **4.0%**
  - [Huntington disease \(P00029\)](#)
  - [Inflammation mediated by chemokine and cytokine signaling pathway \(P00031\)](#)
  - [Integrin signalling pathway \(P00034\)](#)
  - [Ionotropic glutamate receptor pathway \(P00037\)](#)
  - [Metabotropic glutamate receptor group III pathway \(P00039\)](#)
  - [Ras Pathway \(P04393\)](#)
  - [T cell activation \(P00053\)](#)
  - [TGF-beta signaling pathway \(P00052\)](#)
  - [Toll receptor signaling pathway \(P00054\)](#)
  - [Vasopressin synthesis \(P04395\)](#)
- 2.0%**
- 1.0%**

# Results: Orthologous Transcription Factors for Genes Reported QTL for Cattle ABSP

A total of 178 TF were predicted to be regulating at least 2 genes within 5000 bp up- or down-stream of a gene.

	Target gene hits	Target gene non hits	Background gene hits	Background gene non hits	Target TFBS hits	Target TFBS nucleotide rate	Background TFBS hits	Background TFBS nucleotide rate	Z-Score
	<b>66</b>	33	12278	12474	246	0.0186	40428	0.0146	<b>13.93</b>
<b>2</b>	<b>45</b>	54	6534	18218	94	0.00931	14127	0.0067	<b>13.42</b>

# Results: Functional Role of *ELF3*

r Location

Molecular Function

Biological Function

- Sequence-specific DNA Binding

- Blastocyst Development

*First in-silico report for possible role of  
ELF3 in abnormal sperm percentage in  
cattle*

- Positive Regulation Of Transcription, I
- Positive Regulation Of Transcription F
- RNA Polymerase II Promoter
- Mammary Gland Involution

# Results: Functional Role of *FOXA2*

er Location

Molecular Function

Biological Function

IS  
ription  
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- RNA Polymerase II Core Promoter Proximal

lyonic

***First in-silico report for possible role of  
FOXA2 in abnormal sperm percentage in  
cattle***

- Transcription Factor Binding
- DNA Binding, Bending
- Protein Domain Specific Binding
- Transcription Regulatory Region DNA Binding

- Regulation Of Blood Coagulation
- Glucose Homeostasis

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omotory Beha

# Results: Orthologous Transcription Factors for Genes Reported QTL for Cattle ABSP

## Gene: **ELF3** ENSBTAG00000008756

Description: Bos taurus E74-like factor 3 (ets domain transcription factor, epithelial-specific ) (ELF3), mRNA. [Source:RefSeq;Acc:NM\_001098909]

Location: [Chromosome 16: 70,826,736-70,830,809](#) forward strand.

Genomic coordinates: chromosome:UMD3.1:GK000016.2:70826736:70830809:1

Transcripts: This gene has 1 transcript (splice variant) [Show transcript table](#)

## Gene: **FOXA2** ENSBTAG00000012407

Description: forkhead box A2 [Source:HGNC Symbol;Acc:HGNC:5022]

Synonyms: HNF3B

Location: [Chromosome 13: 41,910,591-41,911,910](#) reverse strand.

Genomic coordinates: chromosome:UMD3.1:GK000013.2:41910591:41911910:1

Transcripts: This gene has 1 transcript (splice variant) [Show transcript table](#)

Earlier reported QTL for ABSP were on Chr 20, 21 and 27

# Conclusions

*Many genes in the reported QTL for ABSP are involved in cellular (42), metabolic (53), binding (37) and catalytic (33) activities.*

*Pathway analysis found that 25 genes are involved in 21 pathways with a major contribution of GnRH pathway members (follistatin, PTGER4, ISL1 and MAP3K1)*

*ELF3 (Chr 16 at 70.8 Mb) and FOXA2 (Chr 13 at 41.9 Mb) loci could be probable putative trans QTL for abnormal sperm percentage in cattle. In-silico analysis.*

# Future Directions

***“Association studies have to be conducted for abnormal sperm percentage by using the genetic markers located at the ELF3 and FOXA2 gene loci to confirm their possible association with this ABSP in cattle.”***





**Thank you!!**