



Uncovering the Protein Tyrosine Phosphatome in Cattle

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Table 1. Similarity between homologue PTP genes in humans and cattle

UniProt Prohormone Name	Extended Name	Bos taurus Entrez Number	Bos taurus Entrez Gene Name	E Value ^a	% Identity ^b	% Positive ^c	% Gaps ^d	Predicted?
PTPRD	protein tyrosine phosphatase, receptor type, D	532751	PTPRD	0.00E+00	98	99	0	predicted
PTPRK	protein tyrosine phosphatase, receptor type, K	509657	PTPRK	0.00E+00	98	99	0	predicted
PTPN11	protein tyrosine phosphatase, non-receptor type 11	533590	PTPN11	0.00E+00	98	99	0	predicted

a. Indicator of the statistical probability that the two sequences aligned are true homologues and not similar by chance

b. Alignment locations with the same amino acids in both sequences

c. Alignment locations with similar amino acids in both sequences

d. Insertions or deletions of nucleotides during the evolutionary process that differentiated cattle from humans

Introduction

- Protein tyrosine phosphatases (PTPs), are enzymes involved in signal transduction, cellular signaling, regulation of cellular growth, mitogenesis, motility, cell to cell interactions, metabolism, gene transcription, and the immune response^{1,2}
- Improper functioning of PTPs can play a role in diabetes, obesity, cancers, and immune dysfunctions³
- Due to their association with numerous cellular processes, PTPs have the potential to significantly impact the sustainability of the dairy and beef cattle industries
- The PTP encompasses three evolutionarily unrelated classes of proteins: PTPs, Cdc25, and low molecular weight phosphatases⁴
- The PTP class includes more than 100 genes in humans, and these can be further divided into classical PTPs, which dephosphorylate only tyrosine, and dual specificity phosphatases, which can dephosphorylate tyrosine, serine, and threonine residues⁵
- A total of 38 classical PTP genes have been identified in the human and mouse genomes⁵
- These classical PTPs can be divided into receptor type and non-receptor type⁵

Objectives

- To assemble the first protein tyrosine phosphatome in cattle
- To study the expression patterns of PTP genes across tissues and ages, which will facilitate uncovering potential differences in function and pathways across the PTPs

Materials and Methods

- First, a master list of PTP sequences was created using the human protein tyrosine phosphatome as a guide
- Second, the protein and gene sequences of the human PTPs were retrieved from the NCBI GenBank and UniProt databases (<http://www.ncbi.nlm.nih.gov> <http://www.uniprot.org/uniprot>), and a search for the human PTP protein on cattle was undertaken
- Third, cattle PTP protein sequences that had been automatically annotated as PTPs by GenBank or UniProt were found
- Fourth, the remaining human PTP sequences that were not found in the previous step were searched for in the NCBI Cattle Genome RefSeq repository (<http://www.ncbi.nlm.nih.gov/RefSeq>) using BLASTP, a bioinformatics tool to align sequences to a database of sequences⁶
- Fifth, PTP sequences that were not found in the fourth step were searched against PTP proteins of other livestock mammals available in UniProt to uncover potentially between matches between non-human sequences and the cattle genome
- Sixth, a survey of the Expressed Sequence Tagged and Gene Expression Omnibus profiles summarized in the UniGene database was performed (<http://www.ncbi.nlm.nih.gov/unigene>)

Results

- A total of 37 human PTP protein sequences were found in the GenBank and UniProt searches from the first three search steps
- Of these 37 sequences, only 31 had a counterpart in the cattle genome, and UniProt contained information on only 12 PTPs
- The alignment of the 37 human sequences against the cattle RefSeq sequences using BLASTP uncovered 26 predicted sequences and confirmed 11 known sequences
- The best human-cattle matches were for PTPRD, PTPRK, and PTPN11 – this indicates that they are very-well conserved across these species (Table 1)
- The less reliable human-cattle matches were the sequences for PTPRH, PTPRC, and LOC616515, which may be due to lesser evolutionary conservation or to limitations on the cattle genome sequence
- The search in UniProt for PTPs in other livestock mammals uncovered two sequences in the pig for PTPN11 and PTPRG. For these sequences, the pig genes is more similar than the human to the cattle genes
- The gene expression profiles from the EST and GEO databases indicated that three most common sites of PTP gene expression are the brain, intestine and liver. In terms of development, the calf expresses the most PTP genes, followed by the fetus, and then the adult
- The most commonly expressed PTP genes included PTPN2, PTPRA, and PTPN11

Conclusion

- This comprehensive survey suggests that many PTP genes have been conserved between the human and cattle genomes and provided information describing the various tissues and age groups where PTP genes are expressed in cattle
- Further basic and applied research holds the possibility to improve cattle production and health lies in the application of this information
- The results from this work will help in the design of follow-up functional studies to characterize the role of PTPs in the physiology of cattle

References

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