Journal of Animal Research: v.8 n.4, p. 719-722. August 2018

DOI: 10.30954/2277-940X.08.2018.27

SHORT COMMUNICATION

Deciphering the Functional Analysis of *Bos taurus* Insulin like Growth Factor 1 Receptor (IGF-1R) Protein through *Insilico* Approaches

Pravas Ranjan Sahoo*

Department of Veterinary Biochemistry, CVSc & A.H. Orissa University of Agriculture and Technology, Bhubaneswar, Odisha, INDIA

**Corresponding author: PR Sahoo; Email: pravasvet86@gmail.com*

Received: 05 April, 2018 **Revised:** 05 July, 2018 **Accepted:** 07 July, 2018

ABSTRACT

The present study was conducted to know the detail functional aspects and molecular interaction of Insulin like growth factor 1 receptor (IGF-1R) of *bos taurus* at Department of Veterinary Biochemistry, College of Veterinary Science & AH, Bhubaneswar from time period between January 2018 to February 2018. IGF1R is one important tyrosine kinase receptor present on the cell surface of bovine as well as human plays a central role in differentiation of the cells and inhibition of apoptosis by mediating IGF1 signaling pathway. Thus, a functional analysis of this protein is required to know the various interactions with other proteins that will give a better platform for designing of drugs against different cancers in bovine. So in this study, the amino acid sequence of the bovine IGF-1R was retrieved from NCBI site, the retrieval of interacting proteins (STRING) platform was used to know the different protein networks for the functional analysis. The conserved domain was determined by using pfam database. It was found there were 11 nodes and 51 edges in its network and having strong interaction with Insulin preproprotein (INS) with score 0.993 but posses' weak interaction with Phosphatidylinositol 3-kinase regulator protein with a score of 0.960. It was observed the Protein tyrosine kinase domain is conserved in this protein at the postion from 999 to1264**,** showing no co expression with other proteins in *bos taurus*.

Keywords: Insulin like growth factor 1 receptor (IGF1R), *insilico*, *Bos taurus*

The insulin like growth factor/ insulin system which comprises of three receptors [insulin receptor (IR), IGF-1 receptor (IGF-1R), and IGF-2/mannose 6-phosphate receptor (M-6-PR)], three ligands (insulin, IGF-1, and IGF-2), and six known types of circulating IGF-binding proteins (IGFBP1–6), plays a crucial role in the growth, development and metabolism of many tissues in human as well as different animals (Pollak, 2008). Among these, the insulin like growth factor 1 receptor (IGF-1R), a tyrosine kinase receptor which is a heterotetrameric glycoprotein composed of two α and two β subunits that controls different intracellular signaling pathway with a vital role in apoptosis, cell growth, and differentiation (Gallagher and LeRoith, 2010). For appropriate activation of the pathway, different proteins are involved in phosphoinositide 3-kinase (PI3K)/Akt signaling pathway as well as the Ras/Raf/MEK/Erk signaling pathway (Denley *et al*., 2003) which are carried out by multiple molecular interactions. The protein protein interaction (PPI) studies have an important role in molecular docking, drug designing and in molecular dynamics field to know different biochemical cascade in signaling pathway (Herce *et al.,* 2013). For this, different bioinformatics tools are extensively used to curb the difficult task of visualizing these molecular interactions exist in the protein networks *(*Kohl *et al*., 2011). Now days, the IGF-1R acts as an attractive drug target against a variety of novel anti-tumor agents for treatment of various human as well as bovine cancer (Arcaro, 2013). So there is need of detail functional analysis of IGF-1R protein with respect to other proteins associated with its network for better development of putative therapeutic target against various cancers in bovine. So, this present study would provide a suitable platform for other researchers to undertake molecular docking research in nearest future.

The amino acid sequence of IGF-1R protein was retrieved from Uniport database with accession number UPI00022754C3 under FASTA format

The STRING 10.5 platform was used to develop the protein interaction network of bovine IGF-1R protein under different *insilico* approaches (Szklarczyk *et al*., 2015). Different nodes and edges are assigned for the interacting protein and the strength of interaction respectively. The proteins which are correlated in the expression of IGF-1R protein were analyzed in the Gene coexpresion viewer.

The conserved domain of the IGF1R protein sequence was determined with using CD Blast (Basic Local Alignment Tool) under pfam database (Marchler-Bauer *et al.,* 2017).

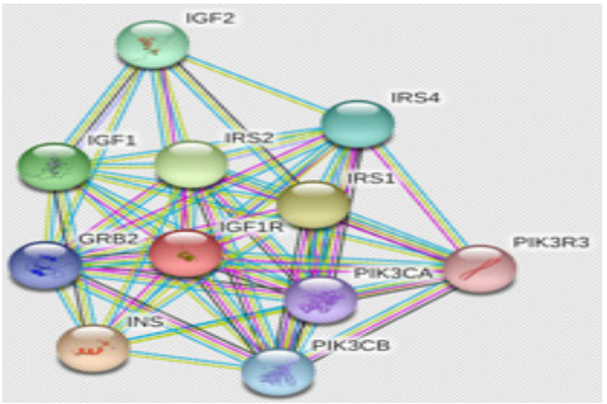

Fig. 1: Showing the interaction network of IGF-1R protein to other proteins

The protein protein interactions are the physical contacts of high specificity, established between two or more protein molecules which are being incorporated in drug designing strategies (Chen *et al*., 2013). The IGF-1R protein interaction network from this study is shown in Fig. 1 and different predicted functional partners are shown in Table 1.

It has been shown that the IGF-1R has ten predicted functional partner with a suitable score. The different interaction networks with INS, IRS1, IRS2, IGF1, IGF2, IRS4, PIK3CB, GRB2, PIK3CA and PIK3R3 were found in this study. The protein IGF1R protein makes a strongest interaction with INS (insulin preprotein) with a highest confidence score of 0.993, but the weakest interaction was observed with PIK3R3 (Phosphatidylinositol 3-kinase regulator protein) having confidence score of 0.960 which is similar finding of that of Breitkopf *et al.,* (2016). It may be due the strong interaction with INS (insulin preproprotein) which accelerates glycolysis, the pentose phosphate cycle, and glycogen synthesis in liver by increasing the cell permeability to monosaccharides, amino acids and fatty acids (Groeneveld *et al.,* 2016) but the PIK3R3 protein which regulates the insulin stimulation, binds to activated protein tyrosine kinase through its SH2 domain, showing weak interaction with IGF1R (Mothe *et al.,* 1997).

The present study showed that there are eleven nodes and fifty one edges found in the current network of the IGFIR protein as shown in Table 2. It may be due to all the eleven interacting protein plays a critical role in IGF signaling pathway and are produced from common encoding gene (Jin *et al*., 2013).

The present study resulted that none of the interacted proteins are co-expressed along with IGF1R in *Bos*

Table 1: The predicted functional partner of IGF1R in *Bos taurus*

Sl. No	Node 1	Node 2	Node 1 annotation	Node 2 annotation	Score
1	IGF1R	INS	Insulin-like growth factor 1 receptor	Insulin preproprotein	0.993
2	IGF1R	IRS1	Insulin-like growth factor 1 receptor	Uncharacterized protein	0.992
3	IGF1R	IRS2	Insulin-like growth factor 1 receptor	Uncharacterized protein	0.992
4	IGF1R	IGF1	Insulin-like growth factor 1 receptor	Insulin-like growth factor I	0.988
5	IGF1R	IGF2	Insulin-like growth factor 1 receptor	Insulin-like growth factor II	0.972
6	IGF1R	IRS4	Insulin-like growth factor 1 receptor	Uncharacterized protein	0.971
7	IGF1R	PIK3CB	Insulin-like growth factor 1 receptor	Phosphatidylinositol 4,5-bisphosphate	0.970
8	IGF1R	GRB2	Insulin-like growth factor 1 receptor	Growth factor receptor-bound protein 2	0.969
9	IGF1R	PIK3CA	Insulin-like growth factor 1 receptor	Phosphatidylinositol 4,5-bisphosphate	0.966
10	IGF1R	PIK3R3	Insulin-like growth factor 1 receptor	Phosphatidylinositol 3-kinase regulator protein	0.960

taurus as shown in Fig. 2. It may be due to the genes are not correlated in expression along a large number of experiments in this species (Chen *et al.,* 2017).

Table 2: Network statistics of IGF-1R protein

Sl. No	Charactestics of Network	Values
1	Number of nodes	11
2	Number of edges	51
3	Average node degree	9.27
4	Avg. local clustering coefficient	0.952
5	Expected number of edges	14
6	PPI enrichment p-value	5.87e-12

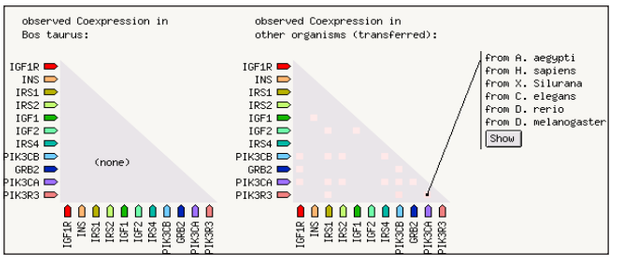

Fig. 2: Showing the co expression of the interacted proteins with IGF-1R

The domains of IGF1R protein was searched in pfam data base as shown in Table 3. It has been seen that the important domains such as Pkinase Tyr, Furin like, Recepo L and fn3 are present in this protein, among these the Insulin Receptor-like Protein Tyrosine Kinases domain helps in autophosphorylation which initiate signaling cascades and biological function mediating cell growth, differentiation, and metabolism in bovine (Samani *et al.,* 2007).

Table 3: Conserved domain present in the IGF1R protein in pfam database

Sl. No	Domain family	Name of Domain	Position
1	Pkinase_Tyr	Protein tyrosine kinase	999-1264
2	Furin like	Funn like cystein rich region	175-330
3	Recepo L domain	Receptor l domain	352-466
4	Recepo L domain	Receptor l domain	51-161
5	fn3	Fibronectin Type III domain	835-917
6	fn3	Fibronectin Type III domain	493-585

CONCLUSION

This study can be concluded that the bovine insulin growth like factor 1 (IGF-1R) plays an important role not only in growth, cell signaling but also acts as major role in tumor genesis. The PPI study can be interpreted that this protein has ten interacted functional partner leaving a suitable therapeutic target against different cancers for drug discovery experiment in bovine as well as human. So this study would provide better information about IGF-1R to other researcher in nearest future.

REFERENCES

Arcaro A. 2013. Targeting the insulin-like growth factor-1 receptor in human cancer. *Front. Pharmacol*., **4**(30): 1-8.

Breitkopf, S.B., Yang, X., Begley, M.J., Kulkarni, M., Chiu, Y., Turke A.B., Lauriol, J., Yuan, M., Qi, J., Engelman, J. A., Hong, P., Kontaridis, M.I., Cantley, L.C., Perrimon, N., Asara, J.M. 2016. A Cross-Species Study of PI3K Protein-Protein Interactions Reveals the Direct Interaction of P85 and SHP2. *Sci. Rep*., **6**: 20471.

Chen, J., Sawyer, N. and Regan, L. 2013. Protein-protein interactions: general trends in the relationship between binding affinity and interfacial buried surface area. *Protein. Sci.*, **22** (4): 510–5.

Chen, Y., Liu, Y., Du, M., Zhang, W., Xu, L., Gao, X., Zhang, L., Gao, H., Xu, L., Li, J. and Zhao, M. 2017. Constructing a comprehensive gene co-expression based interactome in Bos taurus. *Peer J*., **4**: 5:e4107.

Denley, A., Wallace, J.C., Cosgrove, L.J. and Forbes, B.E. 2003. The insulin receptor isoform exon 11-(IR-A) in cancer and other diseases: a review. *Horm. Metab. Res*., **35**: 778–785.

Gallagher, E.J. and LeRoith, D. 2010. The proliferating role of insulin and insulin-like growth factors in cancer. *Trends Endocrinol. Metab*., **21**: 610–618.

Groeneveld, M.P., Brierley, G.V., Rocha, N.M., Siddle, K. and Semple, R.K. 2016. Acute knockdown of the insulin receptor or its substrates Irs1 and 2 in 3T3-L1 adipocytes suppresses adiponectin production. *Sci. Rep*., **6**:21105.

Herce, H.D., Deng, W., Helma, J., Leonhardt, H. and Cardoso, M.C. 2013. Visualization and targeted disruption of protein interactions in living cells. *Nat. Commun.,* **4***: 2660.*

Jin, M., Buck, E. and Mulvihill, M. . 2013. Modulation of insulin-like growth factor-1 receptor and its signaling network for the treatment of cancer: current status and future perspectives. *Onco. Rev*, **7**(1): e3.

Kohl, M., Wiese, S. and Warscheid, B. 2011. Cytoscape: Software for Visualization and Analysis of Biological Networks. Data Mining in Proteomics. *Methods Mol. Biol*., **696**: 291–303.

Marchler-Bauer, A., Bo, Y., Han, L., He, J., Lanczycki, CJ. and Shennan, L. *et al.* 2017. CDD/SPARCLE: functional classification of proteins via subfamily domain architectures. *Nucleic Acids. Res*., **45**(D): 200-3.

Mothe, I., Delahaye, L., Filloux, C., Pons, S., White, M.F. and Van O.E. 1997. Interaction of wild type and dominant-negative p55PIK regulatory subunit of phosphatidylinositol 3-kinase with insulin-like growth factor-1 signaling proteins. *Mol. Endocrinol*. United States., **11**(13): 1911–23.

Pollak, M. 2008. Insulin and insulin like growth factor signalling in neoplasia. *Nat. Rev. Cancer.,* **8**: 915–928.

Samani, A.A., Yakar, S., LeRoith, D. and Brodt, P. 2007. The role of the IGF system in cancer growth and metastasis: overview and recent insights. *Endocr. Rev.*, **28 (**1): 20-47.

Szklarczyk, D., Franceschini, A., Wyder, S., Forslund, K., Heller, D. and Huerta-Cepas, J *et al.* 2015. STRING v10: protein-protein interaction networks, integrated over the tree of life. *Nucleic Acids. Res*., **43**: D447–52.