ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH



# A COMPARATIVE STUDY OF REPRESSOR ELEMENT 1-SILENCING TRANSCRIPTION FACTOR OF TELEOST FISHES

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#### Received: 18 October 2016, Revised and Accepted: 29 October 2016

# ABSTRACT

**Objective:** Repressor element 1 (RE1)-silencing transcription factor (REST) is a zinc-finger transcription factor or else can be called as neuron-restrictive silencer factor primarily described as a negative regulator of nuclear differentiation at present known to play key function in neuronal cells.

**Methods:** With this initial note the aim of this study was to determination of protein sequence level characteristics of REST of Japanese pufferfish (*Takifugu rubripes*) and channel catfish (*Ictalurus punctatus*) with the help of different bioinformatical research tools.

**Results:** There was no instance of any signal signature present within the amino acid sequence of studied REST molecules. In the present research work protein multiple sequence alignment represented in polarity coloring scheme demonstrates variable sites and as well as conserved sites of proteins in Japanese pufferfish and channel catfish.

**Conclusion:** The current research analysis clearly manifests that protein evolution occurred within the REST of Japanese pufferfish (*Takifugu rubripes*) and channel catfish (*Ictalurus punctatus*).

Keywords: Repressor element 1-silencing transcription factor, Teleost fishes, Japanese pufferfish, Channel catfish, Sequence analysis.

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### INTRODUCTION

In the recent 21st century, the maintenance of cognitive ability throughout the entire lifespan has been emerged as one of the greatest medical challenges. The development of Alzheimer's diseases (AD) was facing some fundamental quest. Why some particular individual's age with an intact cognitive ability, but in others, the cognitive ability decorated and promoted to the development of AD. Previously, a study has been suggested that the neuronal loss was an integral characteristic of senescence brain. In recent advancement of stereological neuronal quantification technique, it became intelligible that neuronal cell volume and neuronal quantity mostly maintained in the hippocampus and neocortex of the aging human brain. The normal status declined in the onset of neurodegenerative disease [1-4]. For preservation of neurons and cognitive function throughout lifetime, resilient stress response mechanisms must have evolved [5,6]. Repressor element 1 (RE1)-silencing transcription factor (REST) is a repressor of neuronal genes. REST throughout embryonic development is downregulated once terminal neuronal differentiation has occurred [7-9].

REST was found in the regulatory regions of target genes, and it was attached with the 17-33 base pair RE1 regulatory regions of target genes [10-12]. About 2000 genes within the mouse and human genomes have been recognized as direct targets of REST [11,13].

Modern state of the art bioinformatics research practices makes it attainable to address complicated research queries in biological science and medical science [14-17]. With this initial note, the aim of this study was to determination of protein sequence level characteristics of REST of Japanese pufferfish (*Takifugu rubripes*) and channel catfish with the help of different bioinformatical tools.

#### METHODS

The primary amino acid sequences of REST proteins were obtained from the National Centre for Biotechnology Information (NCBI) (http://ncbi/nlm/nih.gov) [18]. SignalP 4.1 server was used for the detection of signal peptide within protein sequences (http://www.cbs. dtu.dk/services/SignalP/) [19]. Amino acid sequence characterization of REST including number of amino acids, amino acid composition (%) profile, and a number of positively charged (Arg+Lys) and negatively charged (Asp+Glu) amino acid residues were calculated upon the FASTA sequences of mature protein molecules. Multiple sequence alignment was performed with the help of Clustal X program, followed by manual inspection for errors [20]. Protein aligned sequence sets were represented in polarity coloring scheme using Jalview tool [21].

#### **RESULTS AND DISCUSSION**

REST is a zinc-finger transcription factor or else can be called as neuronrestrictive silencer factor primarily described as a negative regulator of nuclear differentiation at present known to play a key function in neuronal cells [7,22-24].

The factors on which the REST target genes depend are as follows:

- 1. Accessibility of the specific DNA binding sequences
- 2. The binding affinity
- 3. The competition and cooperation with other transcription factors [25,26].

After binding with DNA, REST function is to assemble and position the complex that consists of important enzymes such as demethylase lysine-specific demethylase 1 and histone deacetylases. These complexes are capable to inhibit the transcription of many genes by changing vital sites of DNA and the histones [27,28]. In the entire life span of humans, these neurons are operative; however, the mechanism that protects against degradation of neurons during aging are still unidentified. Chromatin immunoprecipitation with deep sequencing and study of REST show that it promotes cell death and AD pathology which leads to the appearance of nervous tension of gene. In addition to this, REST protects neurons from toxicity of amyloid protein, oxidative stress, and deletion of REST from the brain of mouse leading to age-related neurodegeneration [4]. The activity of REST is lost in small cell lung cancer and colon cancer and is wellknown to initiate anchorage-independent development in human mammary epithelial cells [12].

There was no instance of any signal signature present within the amino acid sequence of studied REST molecules. The amino acid composition of REST present in Japanese pufferfish (*T. rubripes*) was analyzed (Fig. 1).

The amino acid composition (%) was found to be as: Alanine - 7.1%, cysteine - 2.7%, aspartate - 6.7%, glutamate - 6.8%, phenylalanine - 2.1%, glycine - 6.3%, histidine - 4.2%, isoleucine - 2.0%, lysine - 8.5%,

leucine - 5.2%, methionine - 1.7%, asparagine - 5.0%, proline - 8.6%, glutamine - 4.4%, arginine - 6.5%, serine - 8.9%, threonine - 6.2%, valine - 4.7%, tryptophan - 0.1%, and tyrosine - 2.2%. The total number of amino acids that were identified was 954.

The amino acid composition of REST presents in channel catfish (*lctalurus punctatus*) was analyzed (Fig. 1). The amino acid composition (%) was found to be as: Alanine - 5.9%, cysteine - 3.0%, aspartate - 4.9%, glutamate - 13.1%, phenylalanine - 1.7%, glycine - 3.9%, histidine - 3.2%, isoleucine - 2.4%, lysine - 12.1%, leucine - 4.8%, methionine - 1.2%, asparagine - 4.0%, proline - 4.9%, glutamine - 4.8%, arginine - 7.5%, serine - 8.3%, threonine - 5.9%, valine - 5.8%, tryptophan - 0.2%, and tyrosine - 2.2%.

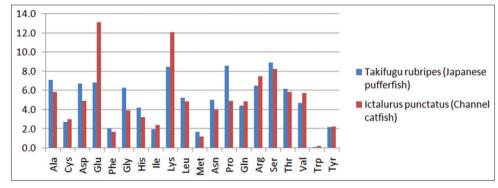


Fig. 1: Amino acid characterization (%) of repressor element 1-silencing transcription factor of teleost fishes

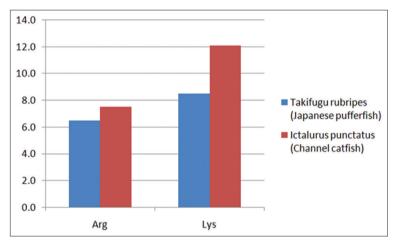


Fig. 2: Positively charged amino acid (%) of repressor element 1-silencing transcription factor of teleost fishes

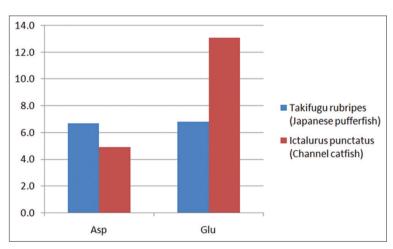


Fig. 3: Negatively charged amino acid (%) of repressor element 1-silencing transcription factor of teleost fishes

Takilugu MAAQTMFSAG PLGMSLMDNS PTLCDLHENA PPPPOLVMLA NVAAVTAADG DGGALDEKEM 60 Istalurus MASQTAFNLC TDDFVTTG-D ASLPEEPGTE LPMPOPVVLA NVALNTESPP E----EDKOM 55 Consensus MAXQTXFXXX XXXXXXXXXX XXXXXXXX XPXPQXVXLA NVAXXTXXXX XGGALXXXXX 120 Takingu MELKTVGSS- YLDSDEDNGS RYTDDNONCK EFCIIEVPES PDPTVQVNPV VTGSGEDDRN 119 ICTAILIUS AELINVGCCG VSDSEDENVV HYGFDD---A AENVDEGTGM GENTVEKVLE TTETMPTDLS 112 Consensus XELXXVGXXG YXDSXXXNXX XYXXDXQNCX XXXXXEXXXX XXXTVXXXXX XTXXXXXDXX Takfugu KAETPPAGAR PRPLASTKPS EODGKVNEGP SGTKKKKPFY CKPCHFGAGN EOOFVEHLRT 179 Ktakrus KKSP-----E TEPSAKPKOS SVAAPIAATE PAKKKKKPFY CKPCHFGAEC EEEFVOHIRV 167 Consensus KXXXPPAGAX XXPXAXXKXS XXXXXXXXX XXXKKKKPFY CKPCHFQAXX EXXFVXHXRX 220 200 Takfugu HSASKMMVVN HVEGRSRNKT RDADAAASGE AENSGGDTGD SKGLIRCERC GYNTNRFDHY 239 Ictalurus HSAKKLIAEK AGSGNSDDES NOAQQKS--- AEN-----C VKGVIRCERC GYNTNRYDHY 218 Consensus HSAXKXXXXX XXXGXSXXXX XXAXXXSGE AENSGGDTGX XKGXIRCERC GYNTNRXDHY 280 260 300 Taktugu IAHLKHHSKE GDDHRVFKCT LCPYTTVSQY HWRKHLRNHF PSKLHTCSQC SYFSDRKSNY 299 ktalurus VAHLRHHKNE GDEGRVFRCT ICPYSTVSQY HWKKHLRNHF PSKLFTCNQC SYFSDRKNNY 278 Consensus XAHLXHHXXE GDXXRVFXCT XCPYXTVSQY HWXKHLRNHF PSKLXTCXQC SYFSDRKXNY 320 340 Takfugu IGHIRTHTGY RPFOCLYCDY SSSGKTHLTR HMRTHSGERP FKCESCNYLA ANGHEVTRHA 359 Ictalurus IGHIRTHTGE RPFOCVYCDY SSSGKTHLTR HMRTHSGERP FKCDSCSYLA ANGHEVTRHA 338 Consensus IOHIRTHTGX RPFQCXYCDY SSSOKTHLTR HMRTHSGERP FKCXSCXYLA ANOHEVTRHA 380 400 420 Takingu ROVHNGPKPL SCPYCDYKTA DRSNYKKHVE LHLNPROFLC PVCKYAASKK CNLOYHIKSR 419 ICTAILURS ROVHNGPKPL SCPYCOYKTA DRSNFKKHVE LHLNPROFLC PVCKYAASKK CNLOYHIKSR 398 Consensus ROVHNGPKPL SCPYCXYKTA DRSNXKKHVE LHLNPRQFLC PVCKYAASKK CNLQYHIKSR 440 Takfugu HAGCN-VAMD ISKVKLRVKK AGPNGAEE-- -NSSVHKRSD TREDFEVDRD NRDKGTDANP 475 Ictalurus HPGCSDISMD VSKVRLRVKK ADGDDSNVGP INLSIKKSGK TNLDGESAKK PTSEPTKEKT 458 Consensus HXGCXDXXMD XSKVXLRVKK AXXXXXXGP INXSXXKXXX TXXDXEXXXX XXXXXXXXXXXX Takfugu INLSIRRSSR PONSOSAGTE APDKVQDKTS RSERE --- KF GKVKEGEKRI TTROKVKRAH 532 Ictalurus CLKRVEKRAA PRNEGNETSS KKARIKETVP CVEKQDGRKD KEVKKAEKVA KSADRVTKSR 518 Consensus XXXXXXXXX PXNXXXXXXX XXXXXXXXX XXEXXDGRKX XXVKXXEKXX XXXXXXXXXX 600 Consensus XKXXEXXXXX XXXXXTKXXD GXXXXXXXX XXXXXXXXX XXXXXXQXQ REEERRERK 620 640 660 Consensus RQEYERLVRA KKEKEQKHRX EXXRXXRXXX XKERLEQEMR EKXQXXRXXX XXXXKXXKXX 680 700 720 Takfugu SONSEKCSRH ADDSOONLSG FOOTPEK ... ....KVAKEK APKRRSAEAP GPTKSLFDMP 667 ICTAILINS SEEEEORKRO RLEKEMRAKE LKOOEEEEER RKSERVEREL REKELKOKOE EEWRERERLE 698 Consensus SXXXEXXXRX XXXXXXXXX XXQXXEXEER RKSEXVXXEX XXKXXXXXXX XXXXXXXXX Takfugu PKTRRTKGAE KLHPIPEGPG KIGDTGSTFT TKOKRSRNVS VNED------NLAVNKI 718 Ictalurus KESKLOKNDV OKREVENVKG SKKALTRKAT KKOAGAVNCD VLEKPPNHEE AKPKMVKRKK 758 820 800 840 Takfugu SGGPAQPQGS TEN.....P DTEPNSSATK EDSPGALG -- LDPRGAQDAP PNPTEPOLSS 770 ACTAURUS AESAPSPOAD KTKRRKVKIA NSOHTSISTS EEVKRSKGNG ROSRKTSKAA VOVEAAKALE 818 Consensus XXXXXXPQXX XXXRRKVKIX XXXXXXXXXX EXXXXXQNG XXXRXXXXAX XXXXXXXX 860 880 900 Takingu DSSLTRVCVT DPONTVEKVP DPSRLPPPEP PPHRPSRPAA PAVPAOPVHG PAEKVADGRL 830 Ictaurus HSSEPKKVGS SPVKVGISTE KVSRTSEELS ITKNPS--EE PSLEDEITSV KTTIEGKGTV 876 Takingu DEDASLMFSH PTSPPTLVLP -VDLAKPADP EDDEGIHSSH EGGSDISDSA SEGSEDSGLN 689 Ictalurus EAGTSSDIDS GTDSPTLDLS KPPCSKSQDG EDDEGIHS-H DGGSDISDCA SEVSYDSGLN 935 Consensus XXXXSXXXXX XTXXPTLXLX KXXXXKXXDX EDDEGIHSSH XGGSDISDXA SEXSXDSGLN 1,000 1,020 Takfugu SNGGSGKLAN DPETPTAELP TPTELKGHMC IFCDRCFPLE AAYRRHLNRH LVNVYYMDTA 949 Ictalurus .....GKLP. ..ETPTEELP SPTOLLSHTC VFCDRTFPLE MDYRRHLNRH LVNVYYLDTA 987 Consensus SNGGSGKLXN DPETPTXELP XPTXLXXHXC XFCDRXFPLE XXYRRHLNRH LVNVYYXDTA Takifugu AGAGR 954 Ictalurus TPGK - 991 Consensus XXXXR

Fig. 4: Multiple sequence analysis of repressor element 1-silencing transcription factor of teleost fishes

The total number of amino acids that were identified was 991. Positively charged amino acid (%) and negatively charged amino acid (%) of REST of teleost fishes were depicted in Figs. 2 and 3.

In the present research work, protein multiple sequence alignment represented in polarity coloring scheme demonstrates variable sites as well as conserved sites of proteins (Fig. 4) in Japanese pufferfish and channel catfish.

## CONCLUSION

Proteins are critical structural building blocks of living organisms. Elucidating the causes of deviation in protein evolutionary rates is fundamental for many disciplines including molecular evolution and structural biology. The current research analysis clearly manifests that protein evolution occurred within the REST of Japanese pufferfish (*T. rubripes*) and channel catfish (*I. punctatus*).

### ACKNOWLEDGMENT

We are very thankful to Prof. Debesh Chandra Majumder, Chairman, Trinity Trust, Asansol, West Bengal, Prof. Kalyan Kumar Sen, Principal, Gupta College of Technological Sciences, Aasnsol, West Bengal, for providing infrastructure facilities for carrying out the research work. The authors are grateful to Late Swami Prameyananda (Ramakrishna Mission, Belur Math), Swami Kripamayananda (Ramakrishna Mission, Belur Math), and Swami Devapriyananda (Ramakrishna Mission, Belur Math) for the motivation and encouragement toward this research work. Authors are greatly indebted to the National Institute of Health and NCBI for providing database support.

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