Supplementary Figure 2. **Bioinformatic analysis of functional domains conservation in primary IGF-IR sequence**. IGF-IR sequence conservation was analyzed using *ConSurf* server, based on alignment of 24 homologues as described in *Experimental procedures*. Residues colored magenta are highly conserved, while residues colored turquoise are not conserved.

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1               11            21          31            41
MKSGSGG S   TSLWGLLFLS   AAL LWPTSG   IC PGIDIR   NDYQQLKRLE
51              61            71          81            91
NCTVIECYLH  ILLISKAEDY   RSYRFPKLTV  ITEYLLLFRV  ACLESLG LF
101             111           121         131           141
PNLTVIRGWK  LFYNYALVI    YTNLKDIGL   YNLRNITRGA  IRI KNA LC
151             161           171         181           191
YLSTVDWSLI   DAVSNNYIV   GN PP   C     CP  M E P  MCEK TIN E
201             211           221         231           241
YNYRCWTTNR  CCK CPSTCG   KRAC ENN C   CHPECLGSCS   PDNDTAC A
251             261           271         281           291
CRHYY AGVC   VP CIPNTY    EG RCVDRD   FCANI  AE  S SEGFVIH
301             311           321         331           341
GEQMQECPSG  FIRNGSQSMY  C PCEGPCPK   VCEEEK    T  IDSVTSAQML
351             361           371         381           391
QGCTIFKGNL  LINIRRGNNI  ASELENFM L   IEVVTGYVKI  RHS ALVSLS
401             411           421         431           441
FLKNLRLILG  EE LEGNYSF  YVLDNQNLQQ  L D  HRNLT  I AC MYFAF
451             461           471         481           491
SPKLCV EIY  RMEEVTGTKG  RQSKGDINTR  NXG  ASC    DVI   ST T
501             511           521         531           541
 KNR IITWH     P DYRDL  ISF VYYKEA  PF NVT YDG  QDACGSNSWN
551             561           571         581           591
  D     NK  DVE  ILLHG  LKPWTQYAVY  VKAVTL MVE  NDHIR AKSE
601             611           621         631           641
ILYIRGNASV  PSIP DV S   S SSSQLIVK  WNPPSLPNGN  LS YIVR Q
651             661           671         681           691
QPQDGY YRH  NYCS    PI   KY  GTI I  E VTENPK E  VCGGEKGPCC
701             711           721         731           741
ACPKTEAEKQ  AEK    EY    VFENFLHNSI   PR  RKRR   VMQVANTTM
751             761           771         781           791
SSR RNTT A  D  N TDPEE  LETEY  FES  RVDNK  TVI  SN RPFTLYR
801             811           821         831           841
IDIHSCNHEA  EKLGCSA       RTMPAEG  AD IP PV W  EPRPE  IFL
851             861           871         881           891
KWP PENPYG  LILMYEIKYG  QV DQRECV   SRQEYR  GG  A LNRLN GN
901             911           921         931           941
YT RI ATS   SGNGSWTDP  F YVQA TGY  E FIHLIIAL  PV VLLI GG
951             961           971         981           991
 VIMLYVFHR  KRNNSRLGNG  VLYASVNPEY  FSAA  YVPC  EWEVAREKIT
1001            1011          1021        1031          1041
MSRELGQGSF  GMVYEGVAKG  V KD PETRV  AIKTVNEAAS  MRERIEFLNE
1051            1061          1071        1081          1091
ASVMKEFNCH  HVVRLLGVVS  QGQPTLVIME  LMT CDLKSY  LRSLRPE EN
1101            1111          1121        1131          1141
 P L PPSLS  KMIQMAGEIA  DGMAYLNANK  FVHRDLAARN  CMVAED TVK
1151            1161          1171        1181          1191
IGDFGMTRDI   ETDYYRKGG  KGLLPVRWMS  PESLKDGVFT  TYSDVWSFGV
1201            1211          1221        1231          1241
VLWEIATLAE  QPYQGLSNEQ  VLRFVMEGGL  LDKPDNCPDM  LFELMRMCWQ
1251            1261          1271        1281          1291
YNP MRESIL  EHISSIKEEM  EPGF EVSFY  YSEE KLPEP  EELDLE ENM
1301            1311          1321        1331          1341
ESVPLDPS S  SS LPLP RH  SGH A   P  PGVLV RASF  DERQ YAHMN
1351            1361
G RKNERA    L QSST
```

The conservation scale:

| 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 |
|---|---|---|---|---|---|---|---|---|

Variable          Average          Conserved