N-terminus αN β1 α1 αA

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Gai1-human  M---------GC---T----------LSA-----------------EDKAAVERSKMIDRNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEAGYSEEECKQ--------------YKAVVYSNTIQSIIAIIRAMGRLK- 92
Gai2-human  M---------GC---T----------VSA-----------------EDKAAAERSKMIDKNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEDGYSEEECRQ--------------YRAVVYSNTIQSIMAIVKAMGNLQ- 92
Gai3-human  M---------GC---T----------LSA-----------------EDKAAVERSKMIDRNLREDGEKAAREVKLLLLGAGESGKSTIVKQMKIIHEDGYSEDECKQ--------------YKVVVYSNTIQSIIAIIRAMGRLK- 92
Gat-bovine  M---------GA---G----------ASA-----------------EEK----HSRELEKKLKEDAEKDARTVKLLLLGAGESGKSTIVKQMKIIHQDGYSLEECLE--------------FIAIIYGNTLQSILAIVRAMTTLN- 88
Gas-human   M---------GC--LGNS-K-TEDQRN-------------------EEKAQREANKKIEKQLQKDKQVYRATHRLLLLLGAGESGKSTIVKQMRILHVNGFNGEGGEEDPQAARSNSDGEKATKVQDIKNNLKEAIETIVAAMSNLVP 115
Gao-human   M---------GC---T----------LSA-----------------EERAALERSKAIEKNLKEDGISAAKDVKLLLLGAGESGKSTIVKQMKIIHEDGFSGEDVKQ--------------YKPVVYSNTIQSLAAIVRAMDTLG- 92
Golf-human  M---------GC--LGGNSKTTEDQGV-------------------DEKERREANKKIEKQLQKERLAYKATHRLLLLLGAGESGKSTIVKQMRILHVNGFNPEEKKQ--------------KILDIRKNVKDAIVTIVSAMSTIIP 102
Gaq-human   MTLES-----I----MAC---C--------LSE-------------EAKEARRINDEIERQLRRDKRDARRELKLLLLGTGESGKSTFIKQMRIIHGSGYSDEDKRG--------------FTKLVYQNIFTAMQAMIRAMDTLK- 98
Gaz-human   M---------GC---R----------QSS-----------------EEKEAARSRRIDRHLRSESQRQRREIKLLLLGTSNSGKSTIVKQMKIIHSGGFNLEACKE--------------YKPLIIYNAIDSLTRIIRALAALR- 92
Ga11-human  MTLES-----M----MAC---C--------LSD-------------EVKKESKRINAEIEKQLRRDKRDARRELKLLLLGTGESGKSTFIKQMRIIHGAGYSEEDKRG--------------FTKLVYQNIFTAMQAMIRAMETLK- 98
Ga12-human  MSGVVR----T----LSRC---L--------LPAEAGGARERRAGSGARDAERRARRRSRDIDALLARERRAVRLVKILLLLGAGESGKSTFLKQMRIIHGREFDQKALLE-----------FRDTIFDNILKGSRVLVDARDKLG- 116
Ga13-human  MADFLPSRSVLSVCFPGC---L--------LT-------------SGEAEQQRKSKEIDKCLSREKTYVKRLVKILLLLGAGESGKSTFLKQMRIIHGQDFDQRAREE------------FRPTIYSNVIKGMRVLVDAREKLH- 107
Ga14-human  MA--------GCC---C----------LSA-----------------EEKESQRISAEIERQLRRDKKDARRELKLLLLGTGESGKSTFIKQMRIIHGSGYSDEDRKG--------------FTKLVYQNIFTAMQAMIRAMDTLR- 94
Ga15-human  MARSL-----T----WRCCPWC--------LTE-------------DEKAAARVDQEINRILLEQKKQDRGELKLLLLGAGESGKSTFIKQMRIIHGAGYSEEERKG--------------FRPLVYQNIFVSMRAMIEAMERLQ- 101
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αB αC αD αE αF β2 β3 α2 β4

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Gai1-human  -IDFGDSARADDARQLFVLAGAAE--------EGFMTAELAGVIKRLWKDSGVQACFNRSREYQLNDSAAYYLNDLDRIAQPNY IPTQQDVLRTRVKTTGIVETHFTFKDLHFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLV 233
Gai2-human  -IDFADPSRADDARQLFALSCTAEE--------QGVLPDDLSGVIRRLWADHGVQACFGRSREYQLNDSAAYYLNDLDRIAQSDYIPTQQDVLRTRVKTTGIVETHFTFKDLYFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLV 234
Gai3-human  -IDFGEAARADDARQLFVLAGSAE--------EGVMTPELAGVIKRLWRDGGVQACFSRSREYQLNDSASYYLNDLDRISQSNYIPTQQDVLRTRVKTTGIVETHFTFKDLYFKMFDVGGQRSERKKWIHCFEGVTAIIFCVALSDYDLV 233
Gat-bovine  -IQYGDSARQDDARKLMHMADTIE--------EGTMPKEMSDIIQRLWKDSGIQACFDRASEYQLNDSAQYYLSDLERLVTPGYVPTEQDVLRSVKTTGIIETQFSFKDLNFRMFDVGGQRSERKKWIHCFEGVTCIIFIAALSAYDMV 229
Gas-human   PVELANPENQFRVDYILSV--MNVP-------DFDFPPEFYEHAKALWEDEGVRACYERSNEYQLIDCAQYFLDKIDVIKQADYVPSDQDLLRCVLTSGIFETKFQVDKVNFHMFDVGGQRDERRKWIQCFNDVTAIIFVVASSSYNMV 256
Gao-human   -IEYGDKERKADAKMVCDVVSRMED--------TEPFSAELLSAMMRLWGDSGIQECFNRSREYQLNDSAKYYLDSLDRIGAADYQPTEQDILRTRVKTTGIVETHFTFKNLHFRLFDVGGQRSERKKWIQCFEDVTAIIFCVALSGYDQV 234
Golf-human  PVPLANPENQFRSDYIKSI--APIT-------DFEYSQEFFDHVKKLWDDEGVKACFERSNEYQLIDCAQYFLERIDSVSLVDYTPTDQDLLRCRVLTSGIFETRFQVDKVNFHMFDVGGQRDERKWIQCFNDVTAIIYVAACSSYNMV 243
Gaq-human   -IPYKYEHNKAHAQLVREV--DVEK-------VSAFENPYVDAIKSLWNDPGIQECYDRRREYQLSDSTKYYLNDLDRVADPAYLPTQQDVLRVRVPTTGIIEYPFDLQSVIFRMVDVGGQRSERRKWIHCFENVTSIMFLVALSEYDQV 238
Gaz-human   -IDFHNPDRAYDAVQLFALTGPAES--------KGEITPELLGVMRRLWADPGAQACFSRSSEYHLEDNAAYYLNDLERIAAADYIPTVEDILRSRDMTTGIVENKFTFKELTFKMVDVGGQRSERKKWIHCFEGVTAIIFCVELSGYDLK 234
Ga11-human  -ILYKYEQNKANALLIREV--DVEK-------VTTFEHQYVSAIKTLWEDPGIQECYDRRREYQLSDSAKYYLTDVDRIATLGYLPTQQDVLRVRVPTTGIIEYPFDLENIIFRMVDVGGQRSERRKWIHCFENVTSIMFLVALSEYDQV 238
Ga12-human  -IPWQYSENEKHGMFLMAF--ENKAGL----PVEPATFQLYVPALSALWRDSGIREAFSRSSEFQLGESVKYFLDNLDRIGQLNYFPSKQDILLARKATKGIVEHDFVIKKIPFKMVDVGGQRSQRQKWFQCFDGITSILFMVSSSEYDQV 260
Ga13-human  -IPWGDNSNQQHGDKMMSF--DTRAPMAAQGMVETRVFLQYLPAIRALWADSGIQNAYDRRREFQLGESVKYFLDNLDKLGEPDYIPSQQDILLARRPTKGIHEYDFEIKNVPFKMVDVGGQRSERKRWFECFDSVTSILFLVSSSEFDQV 255
Ga14-human  -IQYVCEQNKENAQIIREV--EVDK-------VSMLSREQVEAIKQLWQDPGIQECYDRRREYQLSDSAKYYLTDIDRIATPSFVPTQQDVLRVRVPTTGIIEYPFDLENIIFRMVDVGGQRSERKKWIHCFESVTSIIFLVALSEYDQV 234
Ga15-human  -IPFSRPESKHHASLVMSQ--DPYK-------VTTFEKRYAAAMQWLWRDAGIRAYYERRREFHLLDSAVYYLSHLERITEEGYVPTAQDVLRSRMPTIGINEYCFSVQKTNLRIVDVGGQKSERKKWIHCFENVIALIYLASLSEYDQC 241
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α3 β5 αG α4 β6 α5

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Gai1-human  LAEDEEMNRMHESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKIK--KSPLTICYPEYAGSNTYEE-------------AAAYIQCQFEDLN----------K--RKDTKEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKDCGLF   354
Gai2-human  LAEDEEMNRMHESMKLFDSICNNKWFTDTSIILFLNKKDLFEEKIT--HSPLTICFPEYTGANKYDE-------------AASYIQSKFEDLN----------K--RKDTKEIYTHFTCATDTKNVQFVFDAVTDVIIKNNLKDCGLF   355
Gai3-human  LAEDEEMNRMHESMKLFDSICNNKWFTETSIILFLNKKDLFEEKIK--RSPLTICYPEYTGSNTYEE-------------AAAYIQCQFEDLN----------R--RKDTKEIYTHFTCATDTKNVQFVFDAVTDIIIKNNLKECGLY   354
Gat-bovine  LVEDDEVNRMHESLHLFNSICNHRYFATTSIVLFLNKKDVFSEKIK--KAHLSICFPDYNGPNTYED-------------AGNYIKVQFLELN----------M--RRDVKEIYSHMTCATDTQNVKFVFDAVTDIIIKENLKDCGLF   350
Gas-human   IREDNQTNRLQEALNLFKSIWNNRWLRTISVILFLNKQDLLAEKVLAGKSKIEDYFPEFARYTTPEDATPEPGEDPRVTRAKYFIRDEFLRIS----------TASGDGRHYCYPHFTCAVDTENIRRVFNDCRDIIQRMHLRQYELL   394
Gao-human   LHEDETTNRMHESLMLFDSICNNKFFIDTSIILFLNKKDLFGEKIK--KSPLTICFPEYTGPNTYED-------------AAAYIQAQFESKN----------R--S-PNKEIYCHMTCATDTNNIQVVFDAVTDIIIANNLRGCGLY   381
Golf-human  IREDNNTNRLRESLDLFESIWNNRWLRTISVILFLNKQDMLAEKVLAGKSKIEDYFPEYANYTVPEDATPDAGEDPKVTRAKFFIRDLFLRIS----------TATGDGKHYCYPHFTCAVDTENIRRVFNDCRDIIQRMHLKQYELL   381
Gaq-human   LVESDNENRMEESKALFRTIITYPWFQNSSVILFLNKKDLLEEKIM--YSHLVDYFPEYDGPQRDAQA-----------AREFILKMFVDLN---------P--D-SDKIIYSHFTCATDTENIRFVFAAVKDTILQLNLKEYNLV   359
Gaz-human   LYEDNQTSRMAESLRLFDSICNNNWFINTSLILFLNKKDLLAEKIR--RIPLTICFPEYKGQNTYEE-------------AAVYIQRQFEDLN----------R--NKETKEIYSHMTCATDTSNIQFVFDAVTDVIIQNNLKYIGLC   355
Ga11-human  LVESDNENRMEESKALFRTIITYPWFQNSSVILFLNKKDLLEDKIL--YSHLVDYFPEFDGPQRDAQA-----------AREFILKMFVDLN---------P--D-SDKIIYSHFTCATDTENIRFVFAAVKDTILQLNLKEYNLV   359
Ga12-human  LMEDRRTNRLVESMNIFETIVNNKLFFNVSIILFLNKMDLLVEKVK--TVSIKKHFPDFRGDPHRLED-----------VQRYLVQCFDRKR----------R--N-RSKPLFHHFTTAIDTENVRFVFHAVKDTILQENLKDIMLQ   381
Ga13-human  LMEDRLTNRLTESLNIFETIVNNRVFSNVSIILFLNKTDLLVEKVQ--IVSIKDYFLEFEGDPHCLRD-----------VQKFLVECFRNKR----------R--DQQQKPLYHHFTTAINTENIRLVFRDVKDTILHDNLKQLMLQ   377
Ga14-human  LAECDNENRMEESKALFKTIITYPWFLNSSVILFLNKKDLLEEKIM--YSHLISYFPEYTGPKQDVRA-----------ARDFILKLYQDQN----------P--D-KEKVIYSHFTCATDTDNIRFVFAAVKDTILQLNLREFNLV   355
Ga15-human  LEENNQENRMKESLALFGTIILELPWFKSTSVILFLNKTDILEEKIP--TSHLATYFPSFQGPKQDAEA----------AKRFILDMYTRMYTGCVDGPEGSKKG-A-RSRRLFSHYTCATDTQNIRKVFKDVRDSVLARYLDEINLL   374
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F1. Multiple Sequence alignment of Gα subunit. Sequence alignment was performed with Jalview software (Waterhouse, A. M., et al. (2009). "Jalview Version 2--a multiple sequence alignment editor and analysis workbench." Bioinformatics **25**(9): 1189-1191, www.jalview.org) based on Clustal algorithm. The conservation of residues is highlighted by blue: the darker the color, the more conserved the residues. The residues which are involved in activation cluster I and stabilisation cluster II of GTPase domain are indicated as light coral and yellow triangle, respectively. The residues which are involved in stabilisation cluster III of HD domain and inter-domain interface are indicated as cyan triangle and green triangle.