a

```
Human_KIT       LFTPLLIGFVIVAGMMCIIVMILTYKYLQKPMYEVQWKVVEEINGNNYVYIDPTQLPYDH
Danio_KITA      LFTPLLIGFVAAAVILVLILIVLTYKYMQKPKYQIQWKVIEGIHGNNYVYIDPTQLPYDH
Danio_KITB      LFTPLLSGVVSTSVLLSFILVVLLYKYMQKPKYEIHWKVIDSFDGNNYTYIDPTQLPYDP
                ****** *.* .: :: :*:::* ***:*** *:::***:: :.****.**********.
                          Transmembrane region                Juxtamembrane domain

Human_KIT       KWEFPRNRLSFGKTLGAGAFGKVVEATAYGLIKSDAAMTVAVKMLKPSAHLTEREALMSE
Danio_KITA      QWEFPRDKLRFGKTLGSGAFGKVVEATAYGMSKADTVMTVAVKMLKPSAHATEKEALMSE
Danio_KITB      KWEFPRERLRFGKILGSGAFGKVVAATAYGLCSADTVTTVAVKMLKPSAHSTEKEALMSE
                :*****::* *** **:******* *****: .:*:. ************ **:******
                                P-loop

Human_KIT       LKVLSYLGNHMNIVNLLGACTIGGPTLVITEYCCYGDLLNFLRRKRDSFICSKQEDHAEA
Danio_KITA      LKVLSYLGNHINIVNLLGACTVGGPTLVITEYCCFGDLLNFLRRRRVYFYYTTLG---ED
Danio_KITB      LKVLSYIGNHINIVNLLGACTVGGPTLVITEYCCYGDLLNFLRRKRDAFFSSKTG----D
                ******:***:**********:************:*********:*  *  :.

Human_KIT       ALYKNLLHSKESSCSDSTNEYMDMKPGVSYVVPTKADKRRSVRIG-SYIERDVTPAIMED
Danio_KITA      AYYRNVMMQSEP--NDSRNGYMTMKPSVLGIL--SSENRRSLNKGDSYSDSDAVSEILQE
Danio_KITB      GYYKNLLSQTQPSIEGTDNGYMPMR---------------------SYQKRSNQTEWCDD
                . *:*:: ..:.  ..: * ** *:                     ** . .  .   ::
                          Kinase insertion domain

Human_KIT       -DELALDLEDLLSFSYQVAKGMAFLASKNCIHRDLAARNILLTHGRITKICDFGLARDIK
Danio_KITA      -DGLTLDTEDLLSFSYQVAKGMDFLASKNCIHRDLAARNILLTQGRVAKICDFGLARDIT
Danio_KITB      KDDLSLDTEDLLSFSYQVAKGMDFLTSKNCIHRDLAARNVLLTQGRVAKICDFGLARDIT
                 * *:** ************** **:************:***:**::***********.
                                          Catalytic loop              Activation

Human_KIT       NDSNYVVKGNARLPVKWMAPESIFNCVYTFESDVWSYGIFLWELFSL
Danio_KITA      TDSNYVVKGNARLPVKWMSPESIFECVYTFESDVWSYGILLWEIFSL
Danio_KITB      RDSNYVLRGNARLPVKWMSPESLFACVYTFESDVWSYGILLWEIFSL
                *****::**********:***:* **************:***:***
                    loop
```

b

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Human_FMS       LFTPVVVACMSIMALLLLLLLLLYKYKQKPKYQVRWKIIESYEGNSYTFIDPTQLPYNE
Danio_FMS       IFTSAMCGSTVAMVVLGLLLIFMIYKYKQKPRYEIRWKIIEATNGNNYTFIDPTQLPYNE
                :**.: ..   *.:* ***::::*******:*::******: :**.*************
                          Transmembrane region                Juxtamembrane domain

Human_FMS       KWEFPRNNLQFGKTLGAGAFGKVVEATAFGLGKEDAVLKVAVKMLKSTAHADEKEALMSE
Danio_FMS       KWEFPRDKLKLGKTLGAGAFGKVVEATAYGLGKEDNITRVAVKMLKASAHPDEREALMSE
                ******::*::*****************:****** : :*******::**.**:******
                                P-loop

Human_FMS       LKIMSHLGQHENIVNLLGACTHGGPVLVITEYCCYGDLLNFLRRKAEAMLGPSLSPGQDP
Danio_FMS       LKILSHLGQHKNIVNLLGACTHGGPVLVITEYCCHGDLLNFLRSKAENFLNFVMTIPNFP
                ***:******:***********************:******** *** :*.  ::  : *

Human_FMS       EGGVDYKNIHLEKKYVRRDSGFSSQGVDTYVEMRPV-STSSNDSFSEQDLDKEDGRPLEL
Danio_FMS       EPMTDYKNVSTERMFVRSDSGISSTCSDHYLDMRPVTSRPTNSALDSSSECQEDSWPLDM
                *  .****:  *: :** ***:**   * *::**** * .:*.::....  :**. **::
                                Kinase insertion domain

Human_FMS       RDLLHFSSQVAQGMAFLASKNCIHRDVAARNVLLTNGHVAKIGDFGLARDIMNDSNYIVK
Danio_FMS       DDLLRFSSQVAQGLDFLAAKNCIHRDVAARNVLLTNSRVAKICDFGLARDIMNDSNYVVK
                 ***:********: ***:*****************.:**** ***************:**
                                          Catalytic loop              Activation loop

Human_FMS       GNARLPVKWMAPESIFDCVYTVQSDVWSYGILLWEIFSLGLNPYPGILVNSKFYKLVK
Danio_FMS       GNARLPVKWMAPESIFECVYTVQSDVWSYGIMLWEIFSLGKSPYPNILVDSKFYKMIK
                ****************:**************:******** .***.***:*****::*
```

Figure S2: PLX3397 binding pocket is conserved between human and zebrafish.

Alignment of the protein sequences of Homo sapiens KIT with Danio rerio KITA and KITB (a), and of Homo sapiens FMS with Danio rerio FMS (b) with T-Coffee. Important regions are labeled below the sequences. The residues making direct contact with the FMS/KIT inhibitor are indicated in red. "*"-asterisk denotes the residue at which the position is exactly the same. ":"-colon indicates residues at which positions are very similar, and "."-dot, residues that are more or less similar.