Supplementary Information

Tyrosine phosphorylation activates 6-phosphogluconate dehydrogenase and promotes tumor growth and radiation resistance

Liu et al.

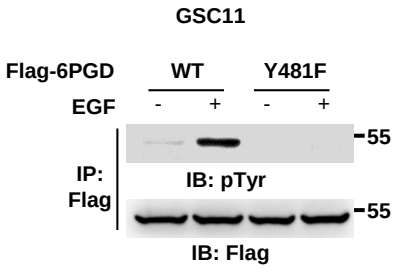
Supplementary Fig. 1

a

	b^{3+}	b^{4+}	Seq.
33	1183.22704	887.67210	S
34	1264.23692	948.42951	Y-Phospho

Charge: +4,
Monoisotopic m/z: 999.20270 Da (+0.54 mmu/+0.54 ppm),
RT: 73.1367 min

b



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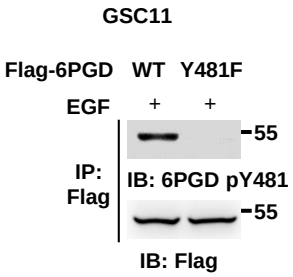
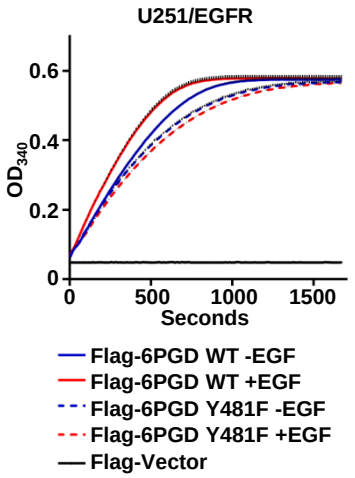


d **Shown in next page.**

e



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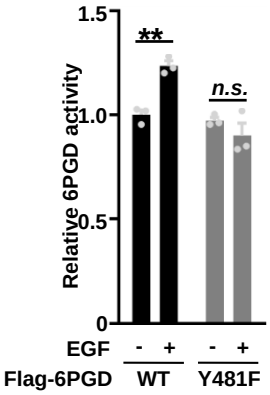

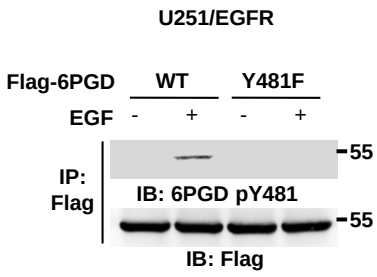

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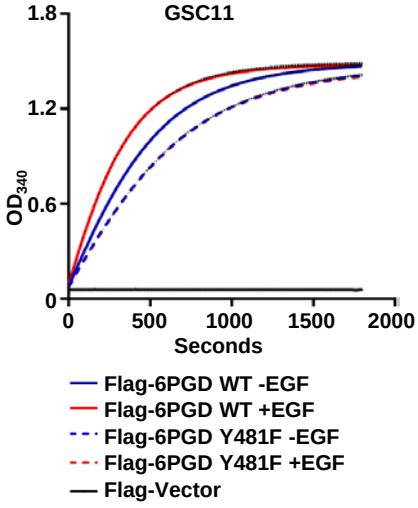

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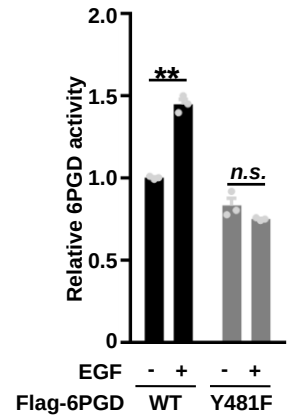

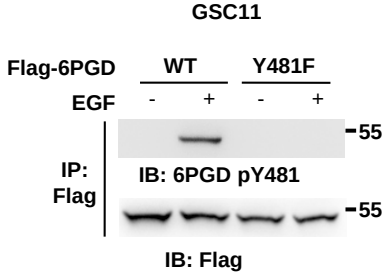

Supplementary Fig.1 (continued)

d

```
CLUSTAL O(1.2.4) multiple sequence alignment

Human                          --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVVGA     55
Rat                            --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---KEAKGTKVIGA     55
Mouse                          --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVVGA     55
Sheep                          --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVLGA     55
Bovine                         --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVLGA     55
Dog                            --MAEADVALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVVGA     55
Pig                            --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTRVVGA     55
Giant_panda                    ---SRADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVVGA     54
Horse                          -----RADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVDDFLA---NEAKGTKVVGA     53
Atlantic_salmon                --MAEADIALIGLAVMGQNIILNMNDHGFVVCAYNRTVSKVHDFLA---NEAKGTKIIGA     55
Osmerus_mordax                 --MAQADIALIGLAVMGQNIILNMNDNGFVVCAYNRTVSKVHDFLK---NEAKGTKVIGA     55
Black_porgy                    --MAEADIALIGLAVMGQNLIMNMNDHGFVVCAYNRTVSKVHDFLK---NEAKGSKVVGA     55
Anthurium_amnicola             MSKPVGDFGLIGLAVMGQNLILNINDHGYTVVAYNRTVSKVDHFLA---NEAKGTNIVGA     57
Chlamydomonas_reinhardtii      --MAVAEIGLVGLAVMGQNLALNIAEKGFPISVYNRSYDKTEAAVKRAQKEGLGEKLHGY     58
Zebrafish                      --MAQADIALIGLAVMGQNLILNMNDHGFVVCAFNRTVSKVHDFLN---NEAKGTKVIGA     55
Caenorhabditis_elegans         --MAEADIAVIGLAVMGQNLILNMNDHGFTVCAFNRTVKLVDDFLA---NEAKGTKIIGA     55
Drosophila_melanogaster        -MSGQADIALIGLAVMGQNLILNMDEKGFVVCAYNRTVAKVKEFLA---NEAKDTKVIGA     56
Yeast                          MSKAVGDLGLVGLAVMGQNLILNAADHGFTVVAYNRTQSKVDRFLA---NEAKGKSIIGA     57
                                    .:..::********: :*  ::*: : .:**:   ..  :    :*. .  : *

Human                          QSLKEMVSKLKKPRRIILLVKAGQAVDDFIEKLVPLLDTGDIIIDGGNSEYRDTTRRCRD     115
Rat                            KSLKDMVSKLKKPRRVILLVKAGQAVDDFIEKLVPLLDTGDIIIDGGNSEYRDTTRRCQD     115
Mouse                          QSLKDMVSKLKKPRRVILLVKAGQAVDDFIEKLVPLLDTGDIIIDGGNSEYRDTTRRCRD     115
Sheep                          HSLEEMVSKLKKPRRIILLVKAGQAVDNFIEKLVPLLDIGDIIIDGGNSEYRDTMRRCRD     115
Bovine                         HSLEEMASKLKKPRRIILLVKAGQAVDDFIEKLVPLLDIGDIIIDGGNSEYRDTMRRCRD     115
Dog                            HSLEEMVSKLKKPRRIILLVKAGQAVDDFIGKLVPLLNTGDIIIDGGNSEYRDTTRRCRD     115
Pig                            RSLEEMVSMLKKPRRIILLVKAGQAVDDFIEKLVPLLDTGDIIIDGGNSEYRDTTRRCRD     115
Giant_panda                    HSLEEMVSKLKTPRRIILLVKAGQAVDDFIDRLVPLLDTGDIIIDGGNSEYRDTTRRCRS     114
Horse                          HSLEEMVSKLKKPRRIILLVKAGQAVDDFIEKLVPLLDTGDIIIDGGNSEYRDTTRRCRD     113
Atlantic_salmon                ESLEDMVAKLKKPRRIVMLVKAGQAVDDFIDKLVPLLEAGDIIIDGGNSEYRDTTRRCKS     115
Osmerus_mordax                 ESLEDMVSKLKKPRRIILLVKAGQAVDDFIDKLVPLLEAGDIIIDGGNSEYRDTTRRCQS     115
Black_porgy                    ESLEDMVSKLKKPRRIILLVKAGQAVDDFIDKLVPLLEAGDIIIDGGNSEYRDTTRRCQS     115
Anthurium_amnicola             HSIEDLAKKLKTPRKIMLLVKAGSAVDDFIEQIIPHLEKGDIIIDGGNSHFPDTIRRCKY     117
Chlamydomonas_reinhardtii      EQVKDFVQSLQRPRRVIILVKAGAPVDQTIDQLCEFMEPGDIIIDGGNEWYENTEKRMAK     118
Zebrafish                      ESLEDMVSKLKKPRRIILLVKAGQAVDDFIDKLVPLLEPGDIIIDGGNSEYRDTTRRCKS     115
Caenorhabditis_elegans         HSIEEMCKKLKRPRRVMMLIKAGTPVDMMIDAIVPHLEEGDIIIDGGNSEYTDSNRRSEQ     115
Drosophila_melanogaster        DSLEDMVSKLKSPRKVMLLVKAGSAVDDFIQQLVPLLSAGDVIIDGGNSEYQDTSRRCDE     116
Yeast                          TSIEDLVAKLKKPRKIMLLIKAGAPVDTLIKELVPHLDKGDIIIDGGNSHFPDTNRRYEE     117
                                .::::   *: **:::*:***  **  *  :   :. **:******. : :: :*

Human                          LKAKGILFVGSGVSGGEEGARYGPSLMPGGNKEAWPHIKTIFQGIAAKVGTGEPCCDWV-     174
Rat                            LKAKGILFVGSGVSGGEEGARYGPSLMPGGNKEAWPHIKTIFQAIAAKVGTGEPCCDWV-     174
Mouse                          LKAKGILFVGSGVSGGEEGARYGPSLMPGGNKEAWPHIKAIFQAIAAKVGTGEPCCDWV-     174
Sheep                          LKDKGILFVGSGVSGGEDGARYGPSLMPGGNKEAWPHIKAIFQGIAAKVGTGEPCCDWV-     174
Bovine                         LKEKGILFVGSGVSGGEDGARYGPSLMPGGNKEAWPHIKAIFQGIAAKVGTGEPCCDWV-     174
Dog                            LKAKGILFVGSGVSGGEEGARYGPSLMPGGDKEAWPHIKTIFQGIAAKVGSGEPCCDWV-     174
Pig                            LKAKGILFVGSGVSGGEEGARYGPSLMPGGNREAWPHLKEIFQSIAAKVGTGEPCCDWV-     174
Giant_panda                    LKAKGILFVGSGVSGGEEGARYGPSLMPGGDKEAWPHIKTIFQGIAAKVGTGEPCCDWV-     173
Horse                          LKAKGILFVGSGVSGGEEGARHGPSLMPGGNKEAWPHIKTIFQGIAAKVGTGEPCCDWAK     173
Atlantic_salmon                LKEKNLLFVGSGVSGGEEGARYGPSLMPGGHKEAWPHIKEIFQSIAAKVGTGEPCCDWV-     174
Osmerus_mordax                 MKDKKLLFVGSGVSGGEEGARYGPSLMPGGHKEAWPHIKDIFQSIAAKVGTGEACCDWV-     174
Black_porgy                    LKAKGLLFVGSGVSGGEEGARYGPSLMPGGHIEAWPHIKDIFQSIAAKVGTGEPCCDWV-     174
Anthurium_amnicola             LEEKGFLFIGCGVSGGEDGARYGPSLMPGGSKAAWEHVKPIFQSISAK-VKDEPCCEWV-     175
Chlamydomonas_reinhardtii      VAAKGILYMGMGVSGGEEGARRGPSMMPGGSPEAYSHIKSVVEKVAAQ-VDDGPCVMYI-     176
Zebrafish                      LKEKNLLFVGSGVSGGEDGARYGPSLMPGGHKDAWPHLKDIFQSIAAKVGTGEPCCDWV-     174
Caenorhabditis_elegans         LAAKGIMFVGCGVSGGEEGARFGPSLMPGGNPKAWPHLKDIFQKIAAK-SNGEPCCDWV-     173
Drosophila_melanogaster        LAKLGLLFVGSGVSGGEEGARHGPSLMPGGHEAAWPLIQPIFQAICAK-ADGEPCCEWV-     174
Yeast                          LTKQGILFVGSGVSGGEDGARFGPSLMPGGSAEAWPHIKNIFQSIAAK-SNGEPCCEWV-     175
                               :    ::::* ******:*** ***:****   *:  :: :.: :.*:   .  *  :
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Supplementary Fig.1 (continued)

d (continued)

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Human                          -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMAQDEMAQAFEDWNKTELDSFLI   233
Rat                            -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMRHEEMAQAFEDWNKTELDSFLI   233
Mouse                          -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMRHEEMAQAFEEWNKTELDSFLI   233
Sheep                          -GDDGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGLGHKEMAKAFEEWNKTELDSFLI   233
Bovine                         -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMRDVLCMGHAEMAKAFEEWNKTELDSFLI   233
Dog                            -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMRDVLGMEHNGMAEAFEEWNKTELDSFLI   233
Pig                            -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMEQHEMAKAFEEWNKTELDSFLI   233
Giant_panda                    -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMRDVLGMGHDEMAKVFEEWNKTELDSFLI   232
Horse                          VGSEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMEHNEMAKAFEEWNKTELDSFLI   233
Atlantic_salmon                -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMDHDEMAQAFEDWNKTELDSFLI   233
Osmerus_mordax                 -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMDHDEMAKAFNEWNKTELDSFLI   233
Black_porgy                    -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLGMDHDEMAQAFDKWNKTELDSFLI   233
Anthurium_amnicola             -GETGAGHYVKMVHNGIEYGDMQLICEAYHLMKEGLDLTHDEIGDVFESWNKEELDSFLI   234
Chlamydomonas_reinhardtii      -GGGGAGNFVKMVHNGIEYGDMQLISEAYDVLKTLGGLNNEELAAVFKEWNDAELKSFLV   235
Zebrafish                      -GDEGAGHFVKMVHNGIEYGDMQLICEAYHLMKDVLCMNHDEMAQVFEQWNKTELDSFLI   233
Caenorhabditis_elegans         -GNAGSGHFVKMVHNGIEYGDMQLIAEAYHLLSKAVELNHDQMAEVLDDWNKGELESFLI   232
Drosophila_melanogaster        -GDGGAGHFVKMVHNGIEYGDMQLICEAYHIMKS-LGLSADQMADEFGKWNSAELDSFLI   232
Yeast                          -GPAGSGHYVKMVHNGIEYGDMQLICEAYDIMKRIGRFTDKEISEVFDKWNTGVLDSFLI   234
                                *  *:*::*****************.***.::     :    :.  : .**   *.***:

Human                          EITANILKFQDT-DGKHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Rat                            EITANILKFQDT-DGKELLPKIRDSAGQKGTGKWTAISALEYGMPVTLIGEAVFARCLSS   292
Mouse                          EITANILKYRDT-DGKELLPKIRDSAGQKGTGKWTAISALEYGMPVTLIGEAVFARCLSS   292
Sheep                          EITASILKFQDA-DGKHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Bovine                         EITANILKFQDA-DGKHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Dog                            EITANILKFRDS-DGQHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Pig                            EITANILKFQDA-DGKHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Giant_panda                    EITANILKFQDS-DGKHLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   291
Horse                          EITANILKFQDT-DGKYLLPKIRDSAGQKGTGKWTAISALEYGVPVTLIGEAVFARCLSS   292
Atlantic_salmon                EITAGILKFRDT-DGTHLLPKIRDAAGQKGTGKWTAISALEYGTPVTLIGEAVFARCLSA   292
Osmerus_mordax                 EITANILKFRDA-DGTHLLPKIRDSAGQKGTGKWTAISALEYGTPVTLIGEAVFARCLSS   292
Black_porgy                    EITANIFKYRDS-DGTHLLPKIRDSAGQKGTGKWTAISALEYGTPVTLIGEAVFARCLSS   292
Anthurium_amnicola             EITKDIMRFKDE-DGKPLVEKIKDTAGQKGTGKWTAISSLDLGVPVTLIGEAVYSRTLSS   293
Chlamydomonas_reinhardtii      EITAIIVNKKDDQAPGYLVDQIVDQTGSKGTGKWTVQQAAELAVAAPTMASALDARYMSA   295
Zebrafish                      EITANILKFKDA-DGTNLLPKIRDSAGQKGTGKWTAISALEYGTPVTLIGEAVFARCLSS   292
Caenorhabditis_elegans         EITANILKYRDE-QGEPIVPKIRDSAGQKGTGKWTCFAALEYGLPVTLIGEAVFARCLSA   291
Drosophila_melanogaster        EITRDILKYKDG-KG-YLLERIRDTAGQKGTGKWTAIAALQYGVPVTLIGEAVFSRCLSA   290
Yeast                          EITRDILKFDDV-DGKPLVEKIMDTAGQKGTGKWTAINALDLGMPVTLIGEAVFARCLSA   293
                               ***  *.  *      :: :* * :*.*******   : : .  .  :..*: :* :*:

Human                          LKDERIQASKKLKGPQKF--QFDGDKKSFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Rat                            LKEERVQASRKLKGPKMV--QLEGSKQAFLEDVRKALYASKIISYAQGFMLLRQAATEFG   350
Mouse                          LKEERVQASQKLKGPKVV--QLEGSKKSFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Sheep                          LKDERIQASKKLKGPQNI--PFEGDKKSFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Bovine                         LKDERIQASKKLKGPQNV--PFEGDKKSFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Dog                            LKDERIQASKKLKGPQKM--QFEGDKKAFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Pig                            LKDERVQASKKLKGPQKI--QFSGDKKSFLEDIRKALYASKIISYTQGFMLLRQAAAEFG   350
Giant_panda                    LKDERIQASKKLKGPQKI--QFEGDKKAFLEDIRKALYASKIVSYAQGFMLLRQAATELG   349
Horse                          LKDERIQASGKLKGPRKI--QFEGDKKSFLEDIRKALYASKIISYAQGFMLLRQAATEFG   350
Atlantic_salmon                LKDERVEASRSLAGPQGA--KFNGDKASFLEDIRKALYASKIISYAQGFMLLRQAAKEFG   350
Osmerus_mordax                 LKEERVEASKSLSGPEGT--KFSGNKTSFLEDIRKALYASKIISYAQGFMLLRQAAKEFG   350
Black_porgy                    LKDERVEASRSLSGPQGV--KFSGDKEAFLEDIRKALYASKIISYAQGFMLLRQAAKEFG   350
Anthurium_amnicola             IKDERVRASKILPGPKNK-K-YSGDKKLFVKQLGQALYASKLISYAQGFMLMREAAKDNN   351
Chlamydomonas_reinhardtii      LKSERVAASKSFTSCVTPGPVAGVDKAQLINDVRAALYASKICSYAQGMNIIKAKSVEMK   355
Zebrafish                      LKDERVQASKSLSGPQGV--KFTGNKEQFLEDIRKALYASKIISYAQGFMLLRQAALEFG   350
Caenorhabditis_elegans         LKDERVRASKQLPRPQVSPDTVVQDKRVFIKQISKALYASKIVSYAQGFMLLAEASKQFN   351
Drosophila_melanogaster        LKDERVQASSVLKGPSTK--AQVANLTKFLDDIKHALYCAKIVSYAQGFMLMREAARENK   348
Yeast                          IKDERKRASKLLAGPTVP-KDAIHDREQFVYDLEQALYASKIISYAQGFMLIREAARSYG   352
                               :*.**  **  :            .   :: ::  ***.:*: **:**: ::   : .
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Supplementary Fig.1 (continued)

d (continued)

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Human                          WTLNYGGIALMWRGGCIIRSVFLGKIKDAFDRNPELQNLLLDDFFKSAVENCQDSWRRAV     410
Rat                            WTLNYGGIALMWRGGCIIRSVFLGKIKDAFERNPELQNLLLDDFFKSAVDDCQDSWRRVI     410
Mouse                          WTLNYGGIALMWRGGCIIRSVFLGKIKDAFERNPELQNLLLDDFFKSAVDNCQDSWRRVI     410
Sheep                          WTLNYGGIALMWRGGCIIRSVFLGKIKDAFDRNPGLQNLLLDDFFKSAVENCQDSWRRAI     410
Bovine                         WTLNYGGIALMWRGGCIIRSVFLGKIKDAFDRNPGLQNLLLDDFFKSAVENCQDSWRRAI     410
Dog                            WTLNYGAIALMWRGGCIIRSVFLGKIKDAFDRNPQLQNLLLDDFFKSAVENCQDSWRRAV     410
Pig                            WSLNYGGIALM--------CVFLGKIKDAFDRNPGLQNLLLDDFFKSAVEDCQDSWRRAV     402
Giant_panda                    WTLNYGGVALMWRGGCIIRSVFLGKIKDAFDRNPQLQNLLLDDFFKSAVEDCQGSWRRAV     409
Horse                          WTLNYGGIALMWRGGCIIRSVFLGKIKDAFDRNPELENLLLDDFFRSAVESCQDSWRRAV     410
Atlantic_salmon                WSLNYGAIALMWRGGCIIRSVFLGKIKEAFDRDAELQNLLLDTFFSNAVQDCQDSWRRTV     410
Osmerus_mordax                 WSLNYGAIALMWRGGCIIRSVFLGKIKEAFDRDFELQSLLLDNFFSNAVQDCQDSWRRTI     410
Black_porgy                    WSLNYGAIALMWRGGCIIRSVFLGKIKEAFDRDAELQNLLLDTFFSNAVQDCQESWRRAV     410
Anthurium_amnicola             WDLNNAGIALMWRGGCIIRSAFLGDIKNAYTNNPNLENLLFDPFFKKAIDDAQDSWRRVV     411
Chlamydomonas_reinhardtii      WNVDLGGLARIWKGGCIIRAQFLDRIRVAYERNPELPSLLVDPDFAKELTAAEASWRRVA     415
Zebrafish                      WSLNYGAIALMWRGGCIIRSVFLGKIKEAFDRNPELQSLLLDSFFSKAVQDCQDSWRRVV     410
Caenorhabditis_elegans         WNLNFGAIALMWRGGCIIRSRFLGDIEHAFQKNKQLSNLLLDDFFTKAITEAQDSWRVVV     411
Drosophila_melanogaster        WRLNYGGIALMWRGGCIIRSVFLGNIKDAYTSQPELSNLLLDDFFKKAIERGQDSWREVV     408
Yeast                          WKLNNPAIALMWRGGCIIRSVFLAEITKAYRDDPDLENLLFNEFFASAVTKAQSGWRRTI     412
                               * ::  .:* :        . **  *  *:  :  * .**.:  * . :   : .** .

Human                          STGVQAGIPMPCFTTALSFYDGYRHEMLPASLIQAQRDYFGAHTYELLAKP-------GQ     463
Rat                            STGVQAGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLSKP-------GE     463
Mouse                          STGVQAGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLTKP-------GE     463
Sheep                          STGVQAGIPMPCFTTALSFYDGYRHAMLPANLIQAQRDYFGAHTYELLAKP-------GQ     463
Bovine                         STGVQAGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLAKP-------GQ     463
Dog                            STGVQAGVPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLAKP-------GQ     463
Pig                            STGVQTGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLAKP-------GH     455
Giant_panda                    STGVQAGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLAKP-------GQ     462
Horse                          STGVQMGIPMPCFTTALSFYDGYRHEMLPANLIQAQRDYFGAHTYELLAKP-------GQ     463
Atlantic_salmon                SIGVQQGIPMPCFTTALSFYDGYRHDMLPANLLQAQRDYFGAHTYELLSNP-------GK     463
Osmerus_mordax                 STGVQQGIPMPCFTTALSFYDGYRHGMLPANLLQAQRDYFGAHTYELLSNP-------GT     463
Black_porgy                    STGVQHGIPMPCFTTALSFYDGYRHEKLPANLLQAQRDYFGAHTYELLSNP-------GH     463
Anthurium_amnicola             AESAILGIPTPALSTALSFYDGYRHERLPANLLQAQRDYFGAHTFRYLDEYTDEKHPKDT     471
Chlamydomonas_reinhardtii      ALSITHGVPIPSMTSSLGYFDTYRRERLPANLVQAQRDFFGSHTYQRFDKE--------G     467
Zebrafish                      STGVQQGIPMPSFTTALSFYDGYRHEMLPANLLQAQRDYFGAHTYELLSNP-------GT     463
Caenorhabditis_elegans         CAAVRLGIPVPAFSSALAFYDGYTSEVVPANLLQAQRDYFGAHTYELLAKP-------GT     464
Drosophila_melanogaster        ANAFRWGIPVPALSTALSFYDGYRTAKLPANLLQAQRDYFGAHTYELLGQE-------GQ     461
Yeast                          ALAATYGIPTPAFSTALAFYDGYRSERLPANLLQAQRDYFGAHTFRILPECASAHLPVDK     472
                               . .   *:* *.::::*.::* *    :**.*:*****:**:**:. : :

Human                          FIHTNWTGHGGTVSSS---SYNA  483
Rat                            FIHTNWTGHGGSVSSS---SYNA  483
Mouse                          FIHTNWTGHGGSVSSS---SYNA  483
Sheep                          FIHTNWTGHGGSVSSS---SYNA  483
Bovine                         FIHTNWTGHGGSVSSS---SYNA  483
Dog                            FIHTNWTGHGGSVSSS---SYNA  483
Pig                            FVHTNWTGHGGSVSSS---SYNA  475
Giant_panda                    FIHTNWTGHGGSVSSS---SYNA  482
Horse                          FIHTNWTGHGGSVSSS---SYNA  483
Atlantic_salmon                YIHTNWTGHGGNVSSS---SYNA  483
Osmerus_mordax                 HIHTNWTGHGGNVSSS---SYNA  483
Black_porgy                    FIHTNWTGHGGNVSSS---SYNA  483
Anthurium_amnicola             DVHINWTGHGGNVSSS---AYLA  491
Chlamydomonas_reinhardtii      WYHTVWDETFGSADSITTSGYVV  490
Zebrafish                      FIHTNWTGHGGKVSSS---SYNA  483
Caenorhabditis_elegans         WVHTNWTGTGGRVTSN---AYNA  484
Drosophila_melanogaster        FHHTNWTGTGGNVSAS---TYQA  481
Yeast                          DIHINWTGHGGNISSS---TYQA  492
                                 *  *    *   :     *.
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Supplementary Fig. 1, related to Fig. 1

a, The peptides cover 92.55% of 6PGD sequences, and 6PGD pY481 was the only phosphorylation site detected in 6PGD (top panel). The presence of the b_{33}^{3+} at 1183.22704 and the b_{34}^{3+} at 1264.23692 indicates that the Y481 residue is phosphorylation modified (bottom panel).

b, GSC11 cells stably expressing Flag-6PGD WT or Y481F were treated with or without EGF (100 ng·ml^{-1}) for 30 min.

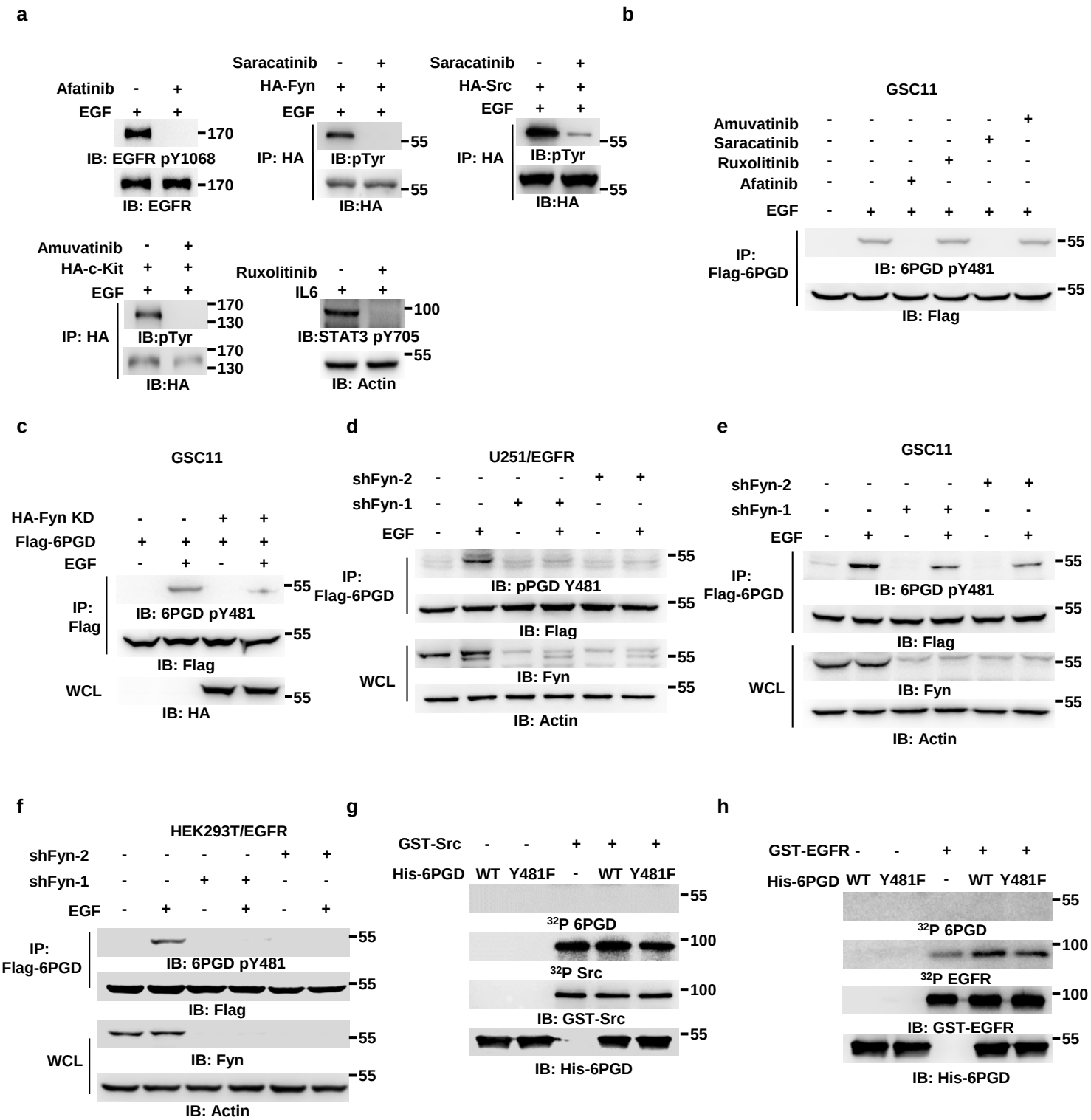
c, GSC11 cells stably expressing Flag-6PGD WT or Y481F were treated with EGF (100 ng·ml^{-1}) for 30 min.

d, Sequence alignment of full length 6PGD among indicated species.

e-h, Flag-6PGD WT or Y481F were immunoprecipitated from U251/EGFR cells or GSC11 cells with or without EGF (100 ng·ml^{-1}) treatment for 30 min. The enzymatic activities of immunoprecipitated Flag-6PGD proteins were examined **(e, g)**. Statistical analyses of 6PGD activities **(f, h)**. The activity of 6PGD was normalized against protein amounts. 6PGD WT activity without EGF treatment was normalized to 1.0. Data represent the mean ± SD of normalized 6PGD activities. Student's t test (unpaired, two-tailed), **p<0.01; n.s.: not significant

Immunoprecipitation and immunoblotting analyses were performed with the indicated antibodies. Data are representative of at least three independent experiments. **(b, c, f, h)** Source data are provided as a Source Data file.

Supplementary Fig. 2



Supplementary Fig. 2, related to Fig. 2

a, HEK293T/EGFR cells were transfected with HA-Src, HA-Fyn or HA-c-Kit and then pretreated with EGFR inhibitor Afatinib (1 μM), Src family kinases inhibitor Saracatinib (1 μM) or c-Kit kinase inhibitor Amuvatinib (10 μM) for 3 hrs, followed by EGF treatment (100 ng·ml^{-1}) for 30 min. U87 cells were pretreated with or without Ruxolitinib (1 μM) for 3 hrs, followed by the treatment of IL6 for 1 hr.

b, GSC11 cells stably expressing Flag-6PGD were pretreated with Afatinib (1 μM), Ruxolitinib (1 μM), Saracatinib (1 μM) or Amuvatinib (10 μM) for 3 hrs and then treated with EGF (100 ng·ml^{-1}) for 30 min.

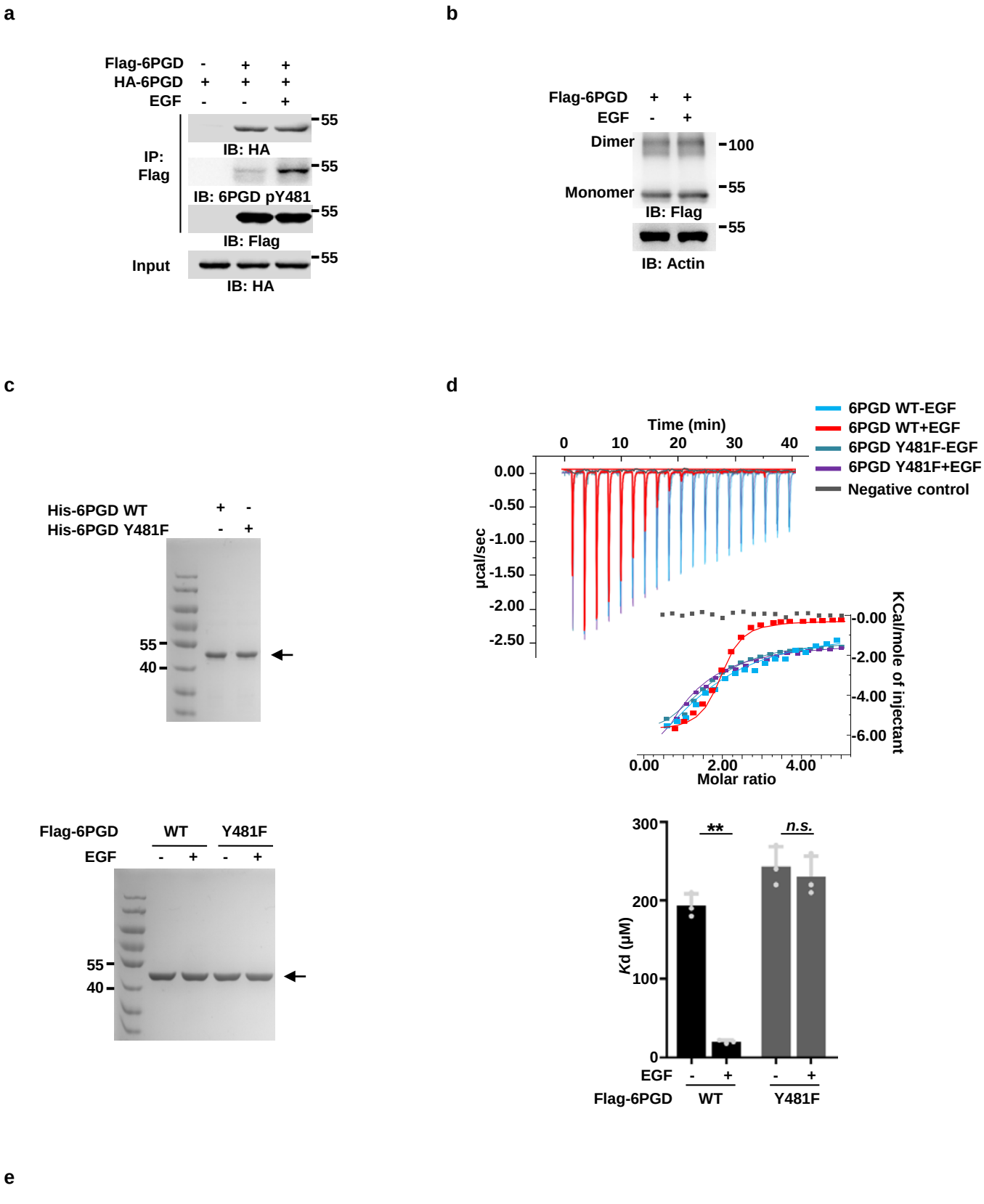
c, GSC11 cells stably expressing Flag-6PGD were infected with or without the lentivirus expressing a kinase-dead HA-Fyn (KD). These cells were then treated with or without EGF (100 ng·ml^{-1}) for 30 min.

d-f, U251/EGFR cells **(d),** GSC11 cells **(e)** or HEK293T/EGFR cells **(f)** were infected with or without the lentivirus expressing shNT or two shRNA sequences against Fyn (shFyn-1 and shFyn-2). These cells were then treated with or without EGF (100 ng·ml^{-1}) for 30 min as indicated.

g,h, *In vitro* kinase assays were carried out with purified recombinant His-6PGD WT or Y481F and commercial purchased recombinant GST-EGFR **(g)** or GST-Src **(h).**

Immunoprecipitation and immunoblotting analyses were performed with the indicated antibodies. Data are representative of at least three independent experiments. Source data are provided as a Source Data file.

Supplementary Fig. 3



Supplementary Fig. 3, related to Fig. 3

a, U87/EGFR cells were transiently transfected with Flag-6PGD and HA-6PGD. The cells were treated with or without EGF (100 ng·ml^{-1}) for 30 min.

b, U87/EGFR cells stably expressing Flag-6PGD were treated with or without EGF (100 ng·ml^{-1}) for 30 min. Cell lysates were mixed with glutaraldehyde to the final concentration of 0.025% for 15 min.

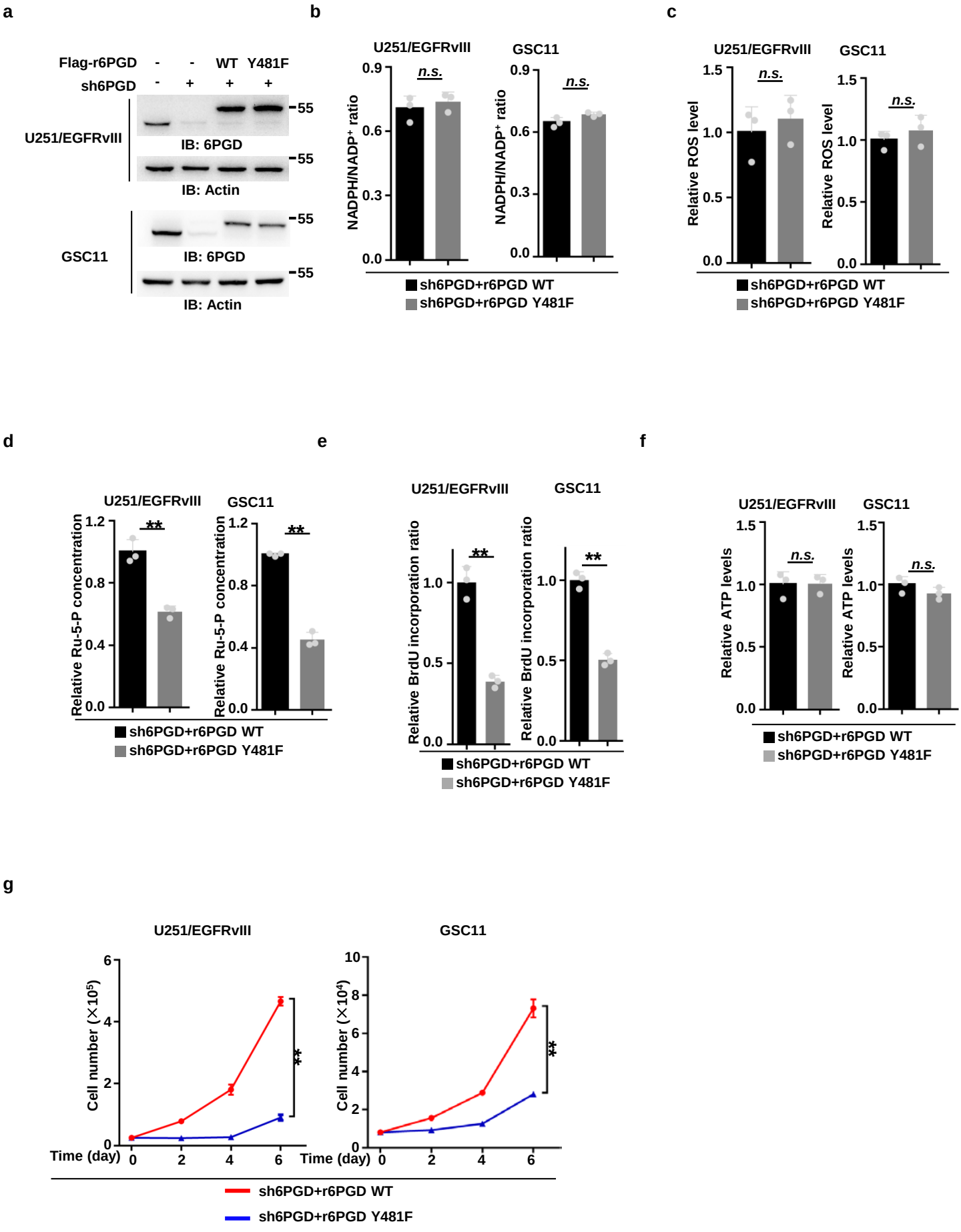
c, The purities of bacterial purified recombinant His-6PGD WT and Y481F were verified by Coomassie blue staining (top panel). HEK293T/EGFR cells transfected with 6PGD WT and Y481F were treated with or without EGF (100 ng·ml^{-1}) for 30 min. The purities of immunoprecipitated 6PGD variants were verified by Coomassie blue staining (bottom panel).

d, HEK293T/EGFR cells transfected with 6PGD WT or Y481F were treated with or without EGF (100 ng·ml^{-1}) for 30 min. ITC assays were performed with immunoprecipitated 6PGD variants (0.05 mM) and $NADP^+$ (1 mM) (top panel). Flag peptides were used as negative control. Statistical analyses of *K*d values of 6PGD variants for $NADP^+$ were presented (bottom panel). Data represent the mean ± SD of three independent experiments. Student's t test (unpaired, two-tailed), **p<0.01; n.s.: not significant

e, *In vitro* kinase assays were performed by incubating bacterial purified recombinant His-6PGD WT or Y481F with or without active recombinant Fyn.

Immunoprecipitation and immunoblotting analyses were performed with the indicated antibodies. Data are representative of at least three independent experiments. Source data are provided as a Source Data file.

Supplementary Fig. 4



Supplementary Fig. 4, related to Fig. 4

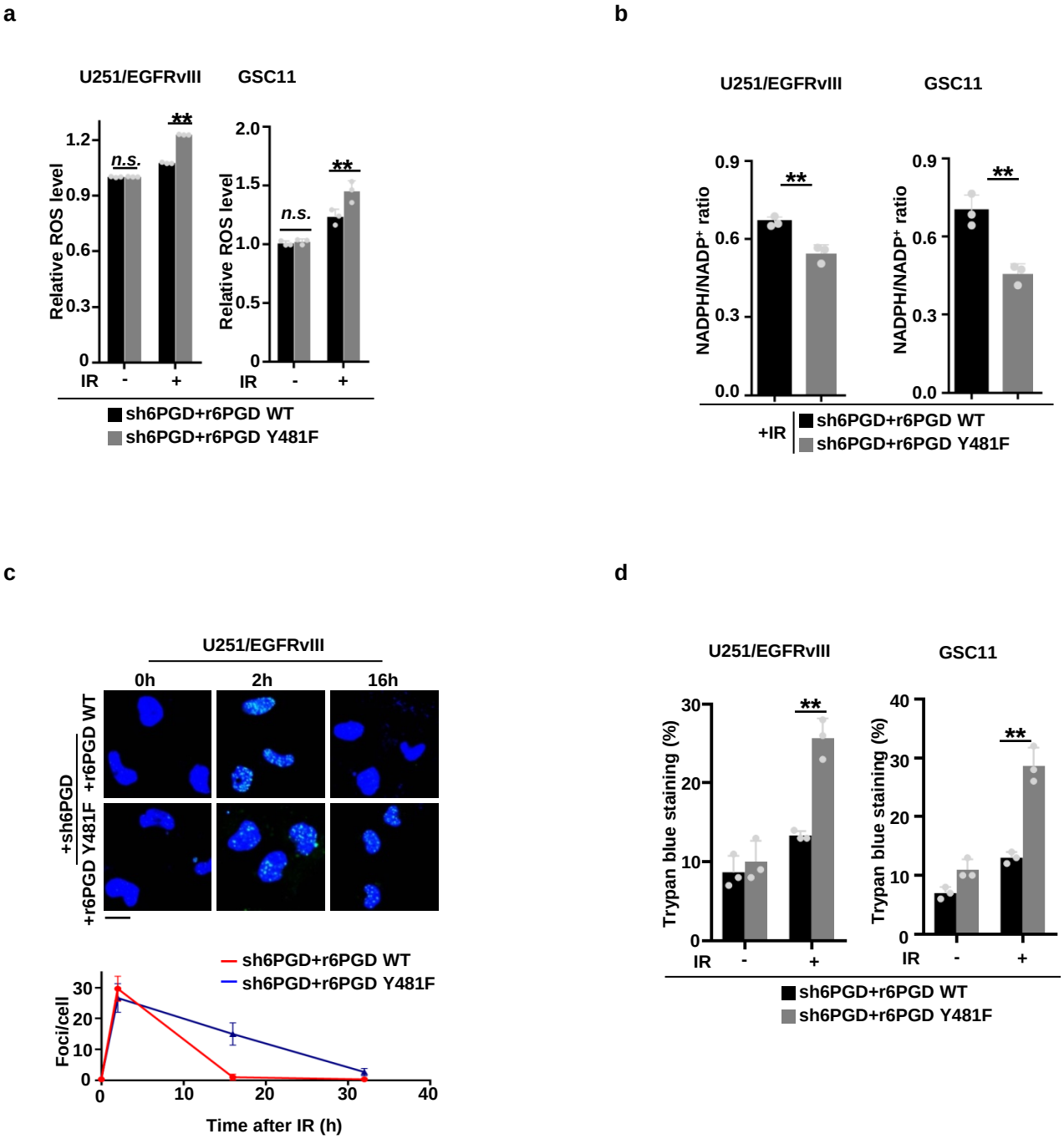
a, U251/EGFRvIII cells or GSC11 cells stably expressing luciferase were depleted of endogenous 6PGD and reconstituted with the expression of r6PGD WT or Y481F. The expression of 6PGD was examined using immunoblotting assays. Data are representative of at least three independent experiments.

b-f, $NADP^+$/NADPH ratio **(b)**, ROS levels **(c)**, cellular Ru-5-P level **(d),** BrdU incorporation ratio **(e)** and cellular ATP level **(f)** were measured in these cells generated in **(a)**.

g, Cell proliferation was determined in these cells generated in **(a)**.

(b-g) Data represent the mean ± SD of three independent experiments. Student's t test (unpaired, two-tailed), **p<0.01; n.s.: not significant. Source data are provided as a Source Data file.

Supplementary Fig. 5



Supplementary Fig. 5, related to Fig. 5

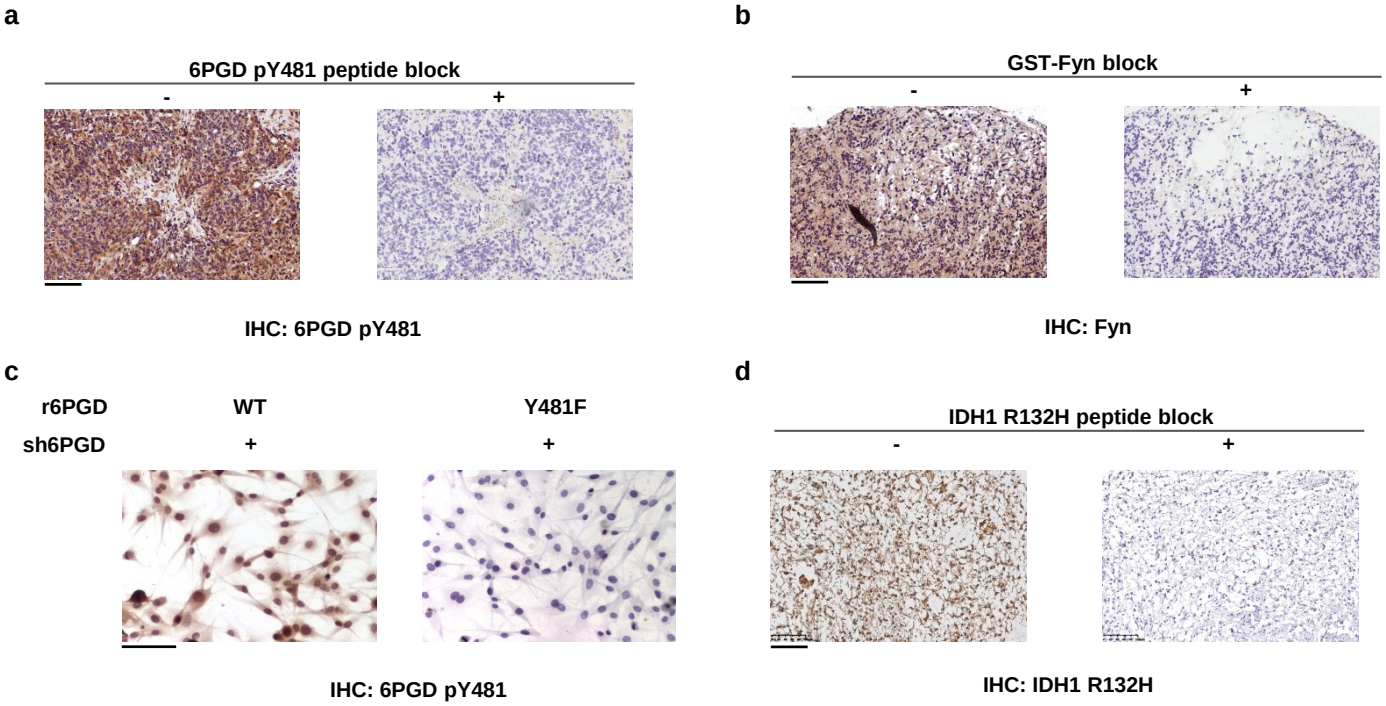
a,b, U251/EGFRvIII cells or GSC11 cells stably expressing luciferase were depleted of endogenous 6PGD and reconstituted with the expression of r6PGD WT or Y481F. These cells were treated with or without X-ray radiation (10 Gy) and cultured for 8 hrs. ROS levels were measured using ROS assay kit **(a)**. $NADPH/NADP^+$ ratio were determined using $NADP^+$/NADPH quantitation kit **(b)**.

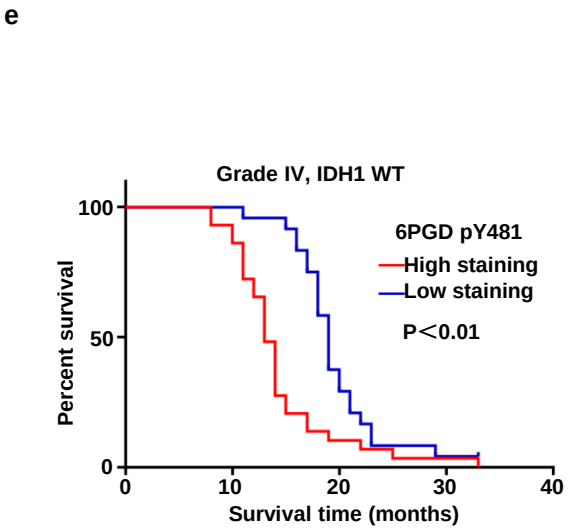
c, These genetically-modified U251/EGFRvIII cells generated in **(a)** were subjected to X-ray radiation (2 Gy) and cultured for indicated times. Immunofluorescence staining was performed using anti-γH2AX antibody. Scale bar, 20 μm

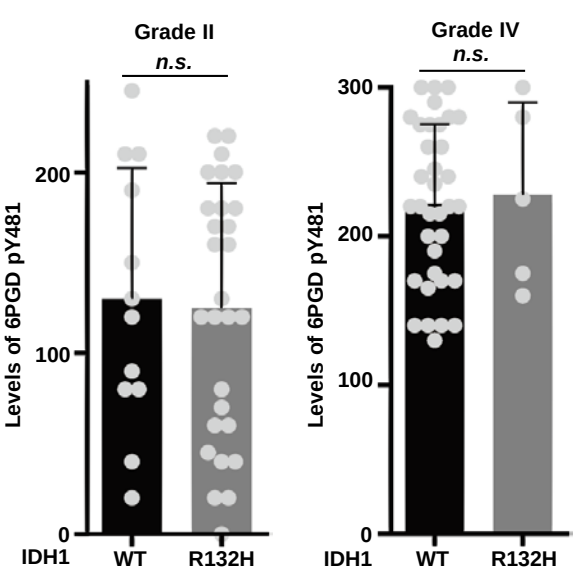
d, These cells generated in **(a)** were subjected to X-ray radiation (10 Gy) and cultured for 48 hrs. Cell death was determined using trypan blue staining.

Data represent the mean ± SD of three independent experiments. Student's t test (unpaired, two-tailed), **p<0.01; n.s.: not significant. Source data are provided as a Source Data file.

Supplementary Fig. 6







Supplementary Fig. 6, related to Fig. 6

a,b, Validation of the specificities of anti-6PGD pY481 or anti-Fyn antibody. IHC analyses of 6PGD pY481 or Fyn were performed in human GBM tissues with the indicated antibodies in the presence or absence of specific blocking peptides or proteins. Scale bar, 100 μm

c, Validation of the specificity of anti-6PGD pY481 antibody. IHC analyses of 6PGD pY481 were performed in endogenous 6PGD-depleted U87/EGFRvIII cells with rescued expression of r6PGD WT or Y481F. Scale bar, 100 μm

d, Validation of the specificity of anti-IDH1 R132H antibody. IHC analyses of IDH1 R132H were performed in human GBM tissues with this antibody in the presence or absence of specific blocking peptides. Scale bar, 100 μm

e, Survival durations of 53 GBM (IDH WT) patients with low (0-170 staining scores, blue curve) versus high (175-300 staining scores, red curve) 6PGD pY481 levels (low, 23 patients; high, 30 patients) were compared. Landmark represents censored (alive at last clinical follow-up) patients. Log-rank test, $p<0.01$.

f, IHC analyses of 6PGD pY481 or IDH1 R132H was performed in 40 diffuse astrocytoma (WHO grade II) specimens and 40 GBM (WHO grade IV) specimens using anti-6PGD pY481 and anti-IDH1 R132H antibody. IHC scores of 6PGD pY481 were compared between the low grade glioma patients with IDH1 WT (n=12) and the low grade glioma patients with IDH1 R132H (n=28) (left panel) or between the high grade GBM patients with IDH1 WT (n=35) and the high grade GBM patients with IDH1 R132H (n=5). Student's t-test (unpaired, two tailed), n.s.: not significant.

(e, f) Source data are provided as a Source Data file.

Supplementary Table 1. Parameters for LC/MS/MS analysis

Compounds	Transition (m/z)	DP (V)	CE (eV)	Retention Time (min)
G-6-P/F-6-P-m0, …, m6	259>97, …, 265>97	-50	-22	9.83
R-5-P-m0, …, m5	229>97, …, 234>97	-80	-19	9.73
Ru-5-P-m0, …, m5	229>97, …, 234>97	-80	-19	9.74
S-7-P-m0, …, m7	289>97, …, 296>97	-80	-20	10.22
glucose-m0, …, m6	239>179, …, 245>185	-50	-11	6.75