| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---------------------|--------|------------|
| Actin               | Abcam  | ab179467   |
| Alpha-Tubulin       | Thermo Fisher Scientific | A11126 |
| p38                 | Santa Cruz | sc-7972  |
| P-p38 (T180/Y182)   | Cell Signaling  | 9215S  |
| ikBa                | Santa Cruz | sc-203  |
| P-ikBa (S32/36)     | Cell Signaling  | 9246  |
| p65                 | Cell Signaling  | 8242S  |
| P- p65 (S536)       | Cell Signaling  | 3033S  |
| ERK 1/2             | Cell Signaling  | 4695S  |
| P-ERK 1/2 (T202/Y204) | Cell Signaling  | 4370S  |
| JNK2                | Cell Signaling  | 9258S  |
| P-JNK (T183/T185)   | BioConcept  | 98F2   |
| UBASH3B             | Santa Cruz | sc-514612 |
| UBASH3B             | Eurogentec, in-house designed | / |
| WHIP                | Santa Cruz | sc-377402 |
| WHIP                | Eurogentec, in-house designed | / |
| RIPK1               | BD Biosciences | 610459 |
| Mouse (Secondary)   | Jackson Immuno Research Labs | 115035003 |
| Rabbit (Secondary)  | Cell Signaling  | 7074S  |
| GADPH               | EMD Millipore | MAB374 |

**Chemicals, Peptides, and Recombinant Proteins**

| REAGENT or RESOURCE | SOURCE | IDENTIFIER |
|---------------------|--------|------------|
| Trypsin-EDTA        | Life Technologies Europe BV | 25300-054 |
| X-tremeGENE 9 DNA Transfection Reagent | Sigma Aldrich Chemie | 6365787001 |
| Blasticidin S – Hydrochlorid | HUBERLAB.AG | A3784.0025 |
| B-PER™ Bacterial Protein Extraction Reagent | Thermo Fisher Scientific | 78243 |
| cOmplete™, EDTA-free Protease Inhibitor Cocktail | Roche | 11873580001 |
| DNase I             | Roche  | 10104159001 |
| PreScission Protease | GE Healthcare | 27-0843-01 |
| USP21 Catalytic Domain, GST tag | Boston Biochem | E-622 |
| PMSF                | Sigma-Aldrich | P7626-5G |
| Avidin              | IBA Life Sciences | 2-0204-015 |
| TCEP                | Sigma-Aldrich | C4706-2G |
| IAA                 | Sigma-Aldrich | 16125-5G |
| Sequencing grade modified trypsin (100μg) | Promega | V5113 |
| Lysyl Endopeptidase | Wako | WA3 125-05061 |
| NuPAGE™ MOPS SDS Running Buffer (20X) | Thermo Fisher Scientific | NP0001 |
| NuPAGE™ MES SDS Running Buffer (20X) | Thermo Fisher Scientific | NP0002 |
| Fireflycectamine RNAiMAX | Thermo Fisher Scientific | 13778.150 |
| Chemical Name                  | Supplier                        | Catalog Number |
|-------------------------------|---------------------------------|----------------|
| Methanol                      | Fisher Chemicals                | M/4058/17-4    |
| Acetonitrile                  | Fisher Chemicals                | A995-212-4     |
| Formic Acid, LC-MS grade      | Pierce                          |               |
| 3X Flag Peptide               | Sigma-Aldrich Chemie GmbH      | F4799          |
| Glycerol                      | Chemie Brunschwig AG            | 15892-0010     |
| Ethanol                       | Honeywell                       | 2860           |
| Hydrochloric Acid             | VWR International GmbH          | 1.00317.1000   |
| Acetic Acid                   | VWR International GmbH          | 1.00063.1000   |
| Hapes                         | Sigma Aldrich Chemie GmbH      | H4034          |
| DTT                           | Sigma Aldrich Chemie GmbH      | D0632          |
| Sodium chloride               | Merck                           | 1.06404.5000   |
| EDTA                          | Biosolve                        | 5142391        |
| Penicillin-Streptomycin       | Sigma Aldrich Chemie GmbH      | P0781-100ML    |
| Foetal Calf serum (FCS)       | BioConcept AG                   | 2-01F10-I      |
| Hygromycin B liquid (50 mg/ml)| Invitrogen                      | 10687010       |

### Critical Commercial Assays

- **QIAPrep Spin Miniprep Kit**: Qiagen, 27104
- **ECL™ Prime Western Blotting System**: GE Healthcare, RPN2232
- **Pierce™ Quantitative Colorimetric Peptide Assay**: Thermo Fisher Scientific, 23275
- **Pierce™ BCA Protein Assay Kit**: Thermo Fisher Scientific, 23225

### Deposited Data

- **SEC-MS data**: Heusel et al., 2020, [https://sec-explorer.shinyapps.io/hela_cellcycle/](https://sec-explorer.shinyapps.io/hela_cellcycle/)
- **Bioplex v.3**: Gygi laboratory, Harvard University, [https://bioplex.hms.harvard.edu/](https://bioplex.hms.harvard.edu/)
- **Biogrid**: Oughtred et al., 2019, [https://thebiogrid.org/](https://thebiogrid.org/)
- **CORUM**: Giurgiu et al., 2019, [http://mips.helmholtz-muenchen.de/corum/](http://mips.helmholtz-muenchen.de/corum/)
- **Raw Mass Spectrometry data**: This study, ProteomeXChange (final identifiers to be updated)
- **Skyline/Quantification/Parameter files**: This study, ProteomeXChange (final identifiers to be updated)
- **Proteome Profiling of 29 human tissues**: Eraslan et al., 2019, [https://www.proteomicsdb.org/](https://www.proteomicsdb.org/)

### Experimental Models: Cell Lines

- **A549 cells**: ATCC, ATCC® CCL-185™
- **Flp-Ln T-Rex 293 Cell Line**: Thermo Fisher Scientific (Invitrogen), R78007

### Oligonucleotides

- Refer to table 7

### Recombinant DNA

- **pTOSH-GW-FRT-HA-Strep**: Glatter et al., 2009, N/A
- **pOG44 Flp recombinase expression vector**: Invitrogen, V600520
- **hORFeome V5.1**: Horizon Discovery/ Dharmacon, Open Biosystem

### Software and Algorithms

- **MaxQuant**: Cox and Mann, 2008, https://www.maxquant.org/, RRID:SCR_014485
- **Spectronaut**: Biognoys, [https://biognoys.com/](https://biognoys.com/)
- **Skyline**: Maclean et al., 2010, [https://skyline.ms/project/home/begin.view?](https://skyline.ms/project/home/begin.view?), RRID:SCR_014080
- **DAVID Bioinformatics Resources 6.8**: DAVID, NCI, [https://david-d.ncifcrf.gov/](https://david-d.ncifcrf.gov/), RRID:SCR_001881
- **ImageJ/Fiji**: Schindelin et al., 2012, [https://imagej.net/Welcome](https://imagej.net/Welcome)
| TARGET/NAME | MANUFACTURER | CAT # |
|-------------|--------------|-------|
| AllStars Neg. siRNA AF 488 (5 nmol) | QIAGEN | 1027284 |
| UBAH3B | QIAGEN | HS_STS-1_1 FlexiTube siRNA (S100144837) |
| UBAH3B | QIAGEN | HS_STS-1_5 FlexiTube siRNA (S102647022) |
| UBAH3B | QIAGEN | HS_STS-1_7 FlexiTube siRNA (S102647036) |
| UBAH3B | QIAGEN | HS_STS-1_8 FlexiTube siRNA (S103091816) |
| WHIP | QIAGEN | HS_WRNIP1_5 FlexiTube siRNA (S103019492) |
| WHIP | QIAGEN | HS_WRNIP1_7 FlexiTube siRNA (S104158602) |
| WHIP | QIAGEN | HS_WRNIP1_8 FlexiTube siRNA (S104175430) |
| WHIP | QIAGEN | HS_WRNIP1_9 FlexiTube siRNA (S104181779) |
| WHIP | QIAGEN | HS_WRNIP1_10 FlexiTube siRNA (S104223380) |

### OLIGONUCLEOTIDES

| NAME | SEQUENCE |
|------|----------|
| UBAH3b_gRNA_1_exon3_forward | 5'-CACCGAGGGTAGAGGACTCCCG-3' |
| UBAH3b_gRNA_1_exon3_reverse | 5'-AAACCGGGACTACGTCTCCTACTACCTC-3' |
| UBAH3b_gRNA_2_exon4_forward | 5'-CACCGTGGACGACGTATAGAGCTCC-3' |
| UBAH3b_gRNA_2_exon4_reverse | 5'-AAACCGGGACTACGTCTCCTACTACCTC-3' |
| WRNIP1_gRNA_1_exon1_forward | 5'-CACCGTGGACGACGTATAGAGCTCC-3' |
| WRNIP1_gRNA_1_exon1_reverse | 5'-AAACCGGGACTACGTCTCCTACTACCTC-3' |
| WRNIP1_gRNA_2_exon1_forward | 5'-CACCGTGGACGACGTATAGAGCTCC-3' |
| WRNIP1_gRNA_2_exon1_reverse | 5'-AAACCGGGACTACGTCTCCTACTACCTC-3' |

### gRNA TARGET SEQUENCES

| NAME | SEQUENCE |
|------|----------|
| gRNA_1_UBAH3b_exon3 | AGGAGGAGGCTACTCCTACCCG |
| gRNA_2_UBAH3b_exon4 | TGGAGGAGGCTACTCCTACCCG |
| gRNA_1_WRNIP1_exon1 | TGGAGGAGGCTACTCCTACCCG |
| gRNA_2_WRNIP1_exon1 | TGGAGGAGGCTACTCCTACCCG |