

PC3 – p21

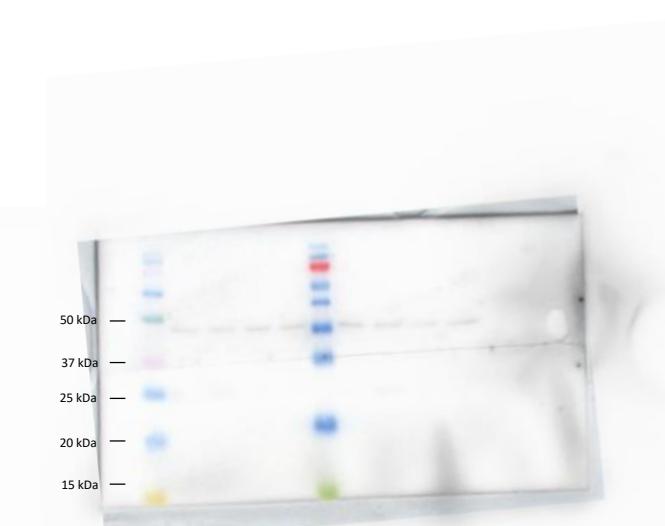
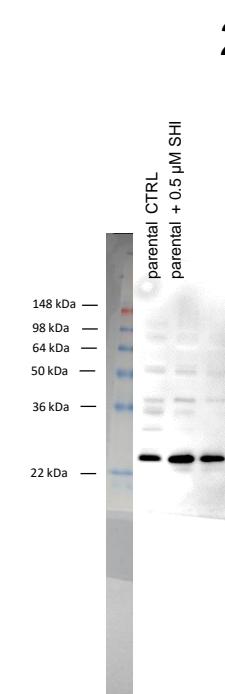
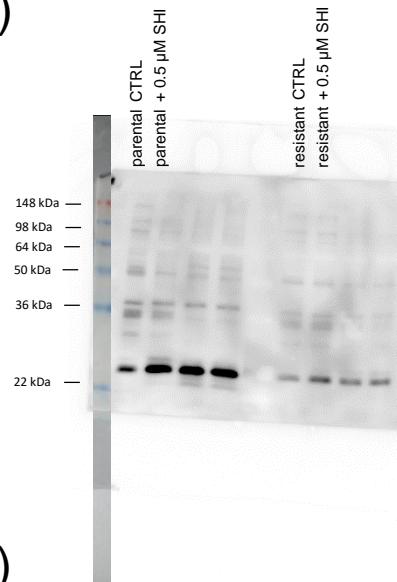
1

3

4

**p21 (21 kDa)**

(1)

**β-actin**

(2)

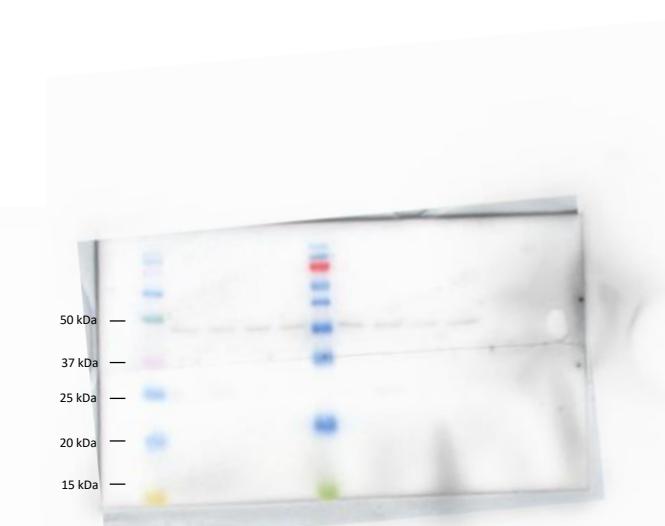
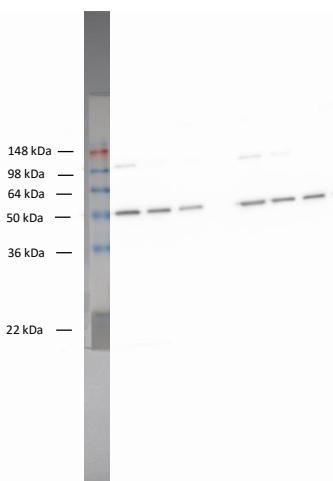
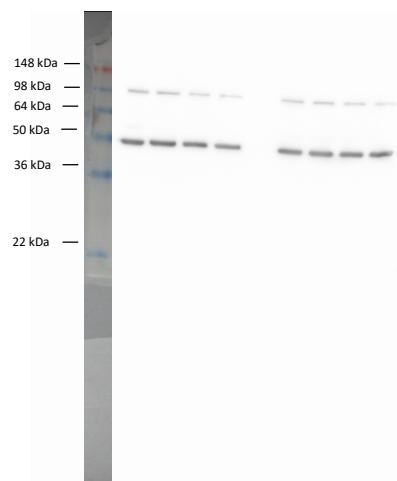
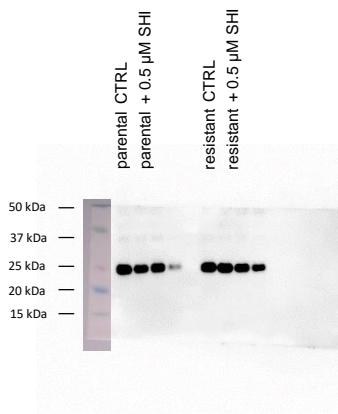


Figure S1a: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of p21 (1), corresponding protein expression of β-actin (2).

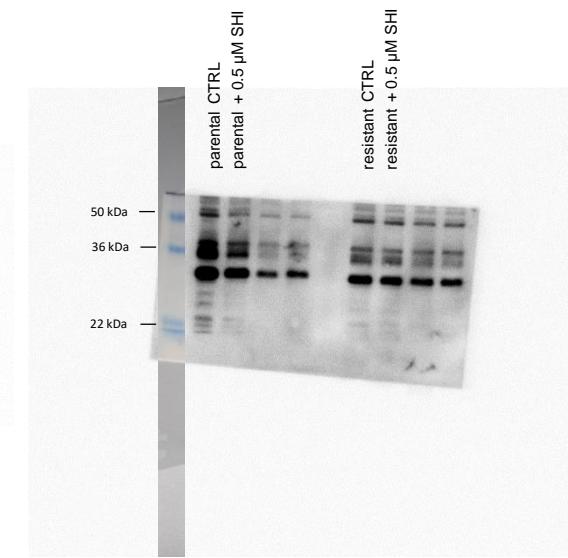
PC3 – p27

1

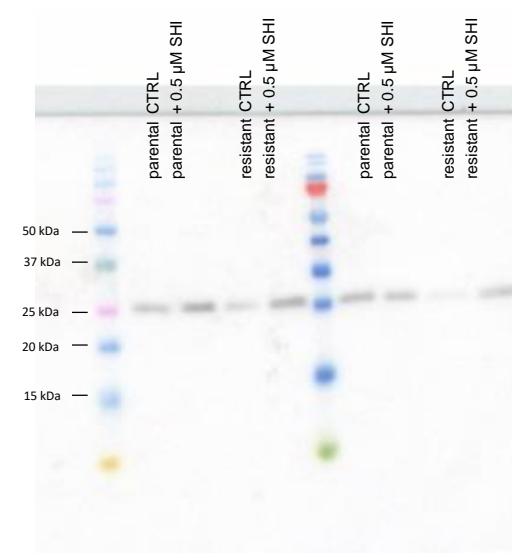
(1)



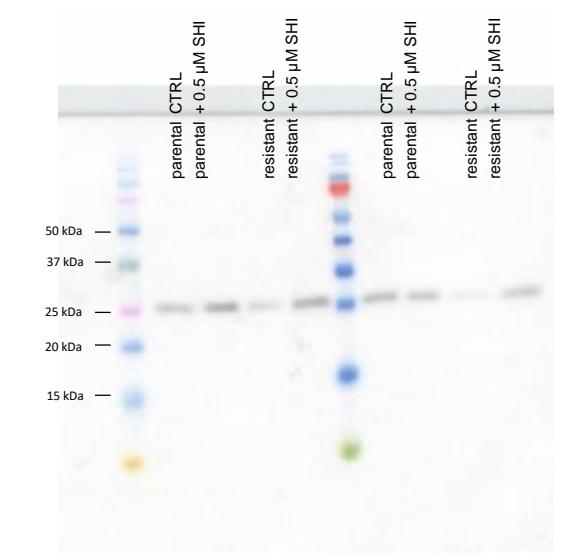
2



3



4



p27 (27 kDa)

β-actin

(2)

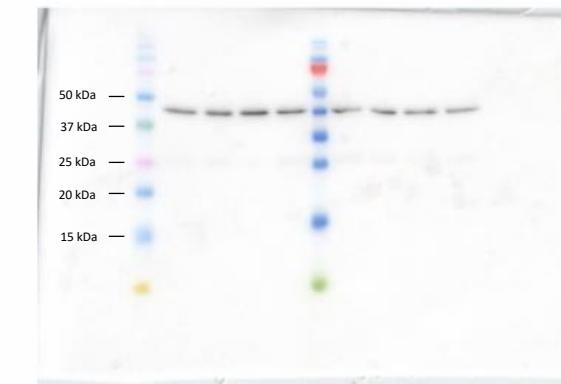
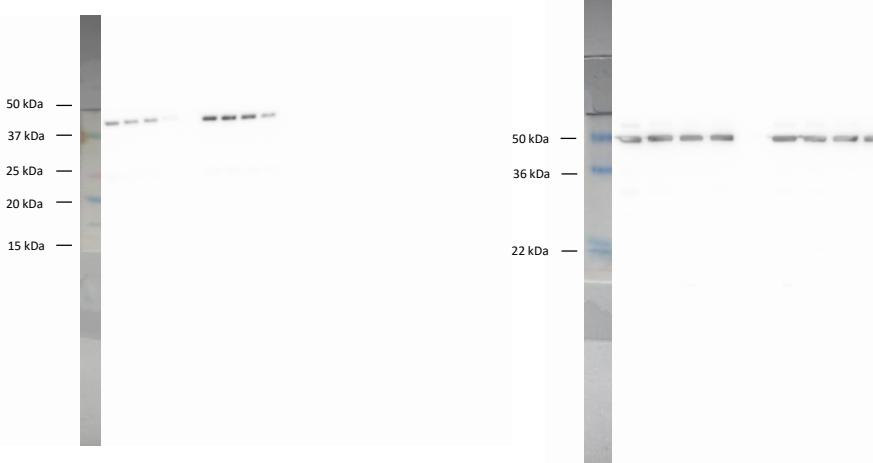
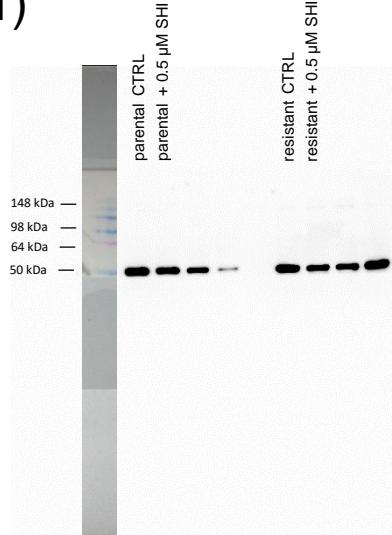


Figure S1b: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of p27 (1), corresponding protein expression of β-actin (2).

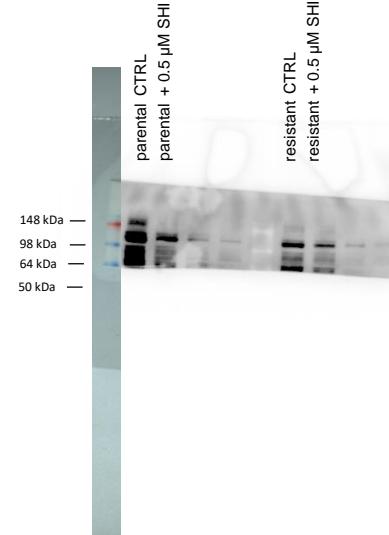
PC3 – Cyclin A

1

(1)

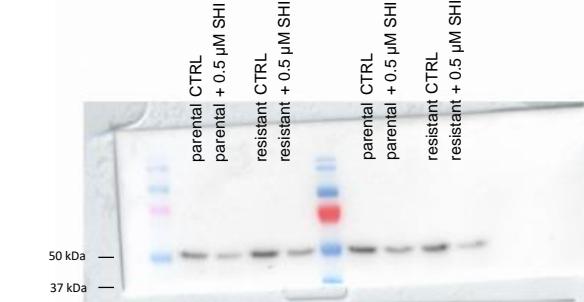


2



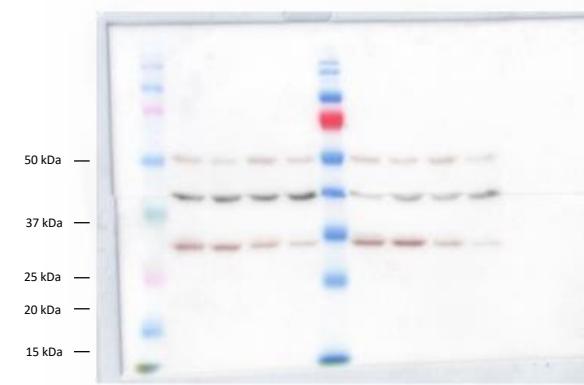
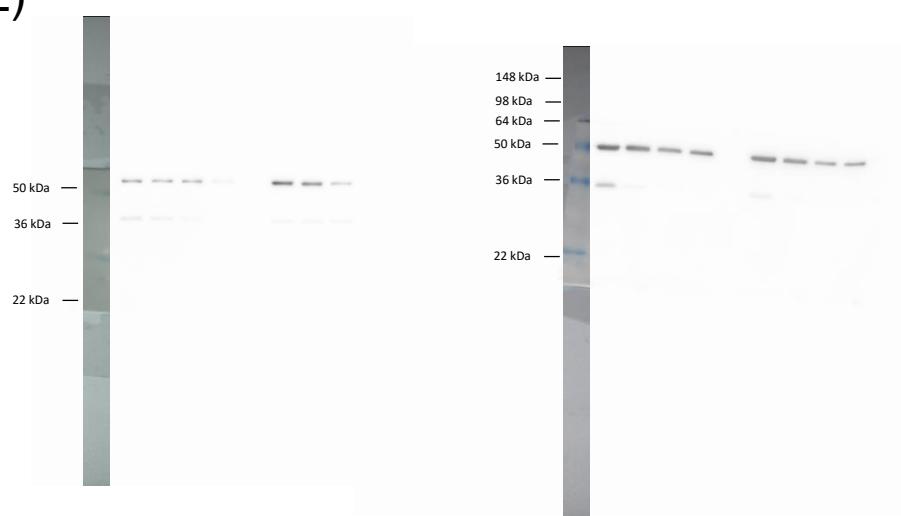
3

4



Cyclin A (55 kDa)

(2)



β-actin

Figure S1c: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of Cyclin A (1), corresponding protein expression of β-actin (2).

1

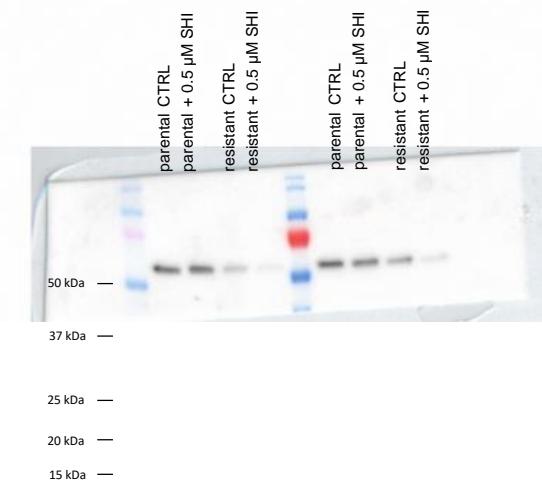
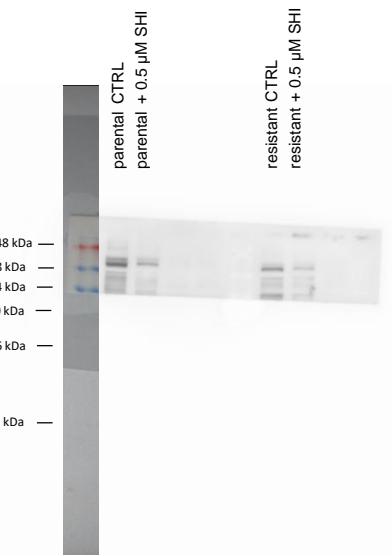
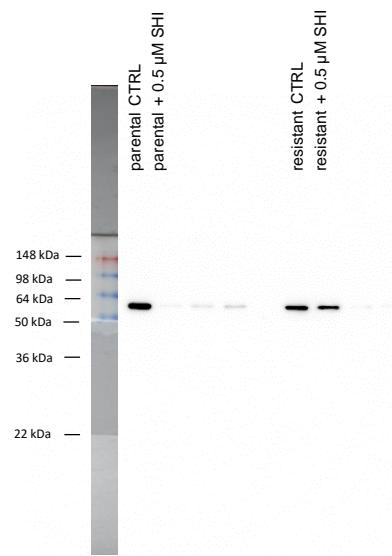
2

3

4

Cyclin B (55 kDa)

(1)



(2)

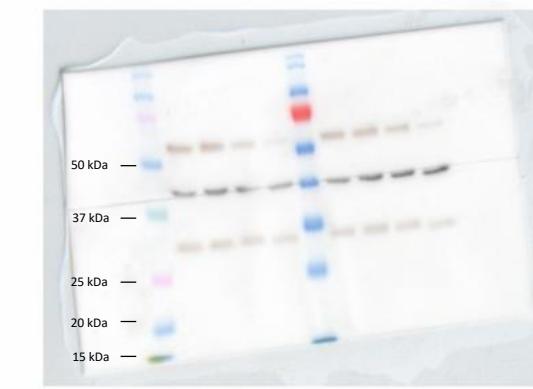
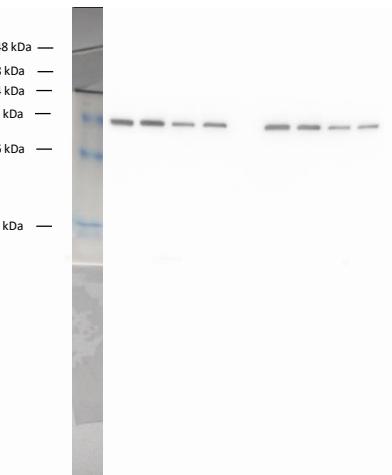
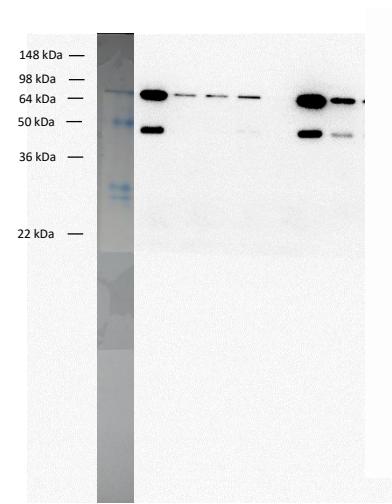
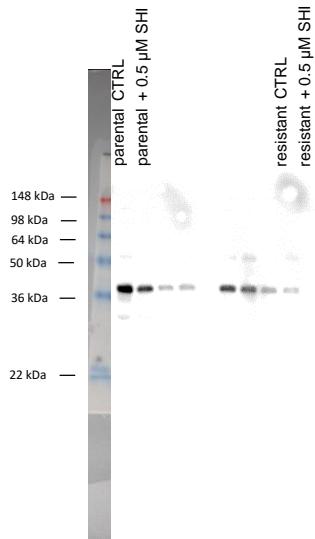


Figure S1d: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of Cyclin B (1), corresponding protein expression of  $\beta$ -actin (2).

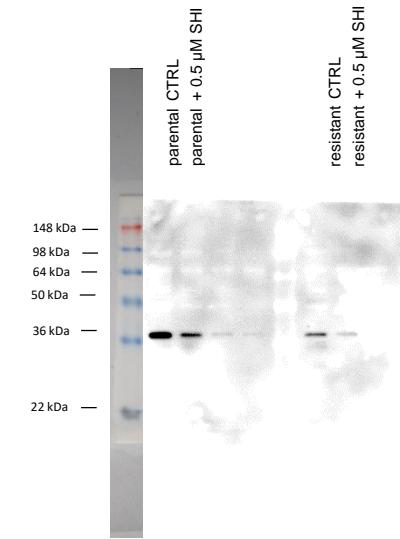
PC3 – Cyclin D1

1

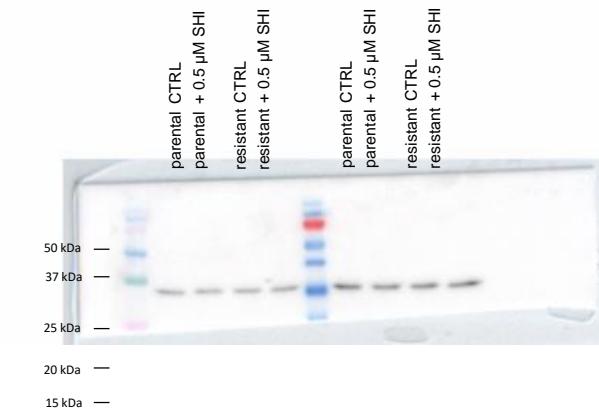
(1)



2



3



4



Cyclin D1 (36 kDa)

β-actin

(2)

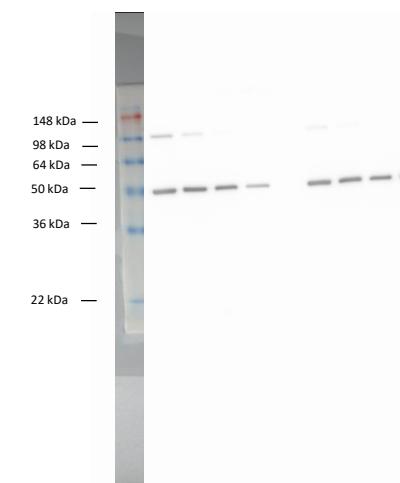
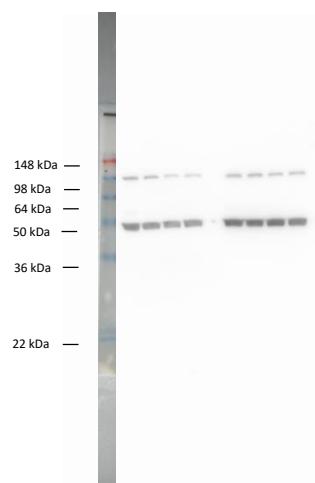


Figure S1e: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of Cyclin D1 (1), corresponding protein expression of β-actin (2).

1

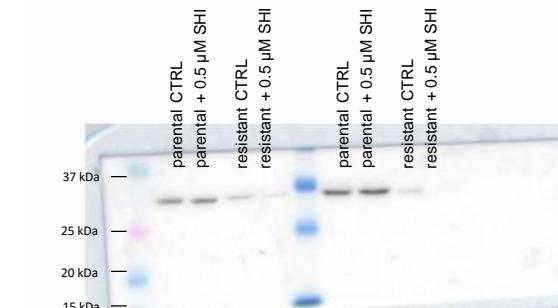
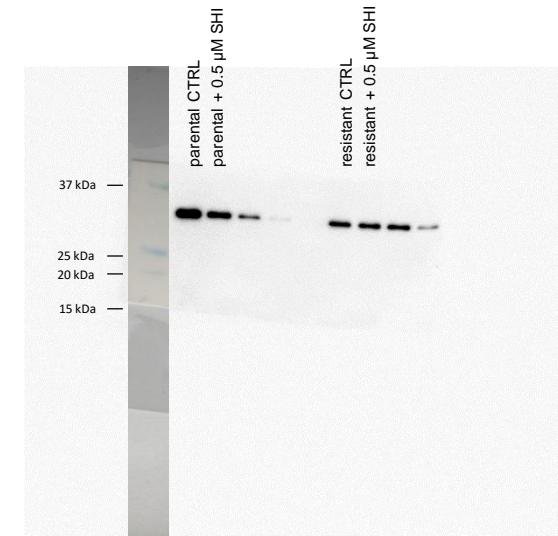
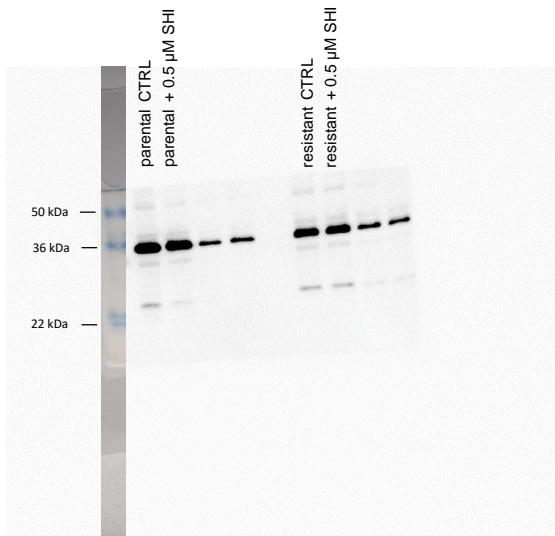
2

3

4

CDK1 (34 kDa)

(1)



(2)

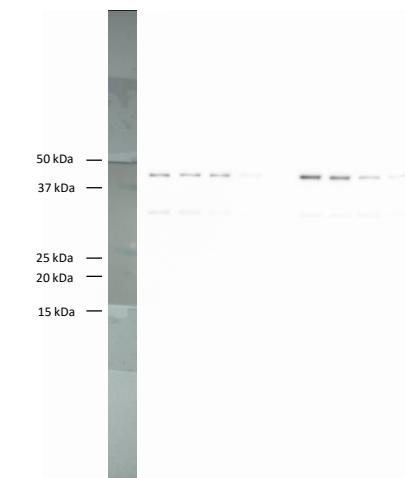
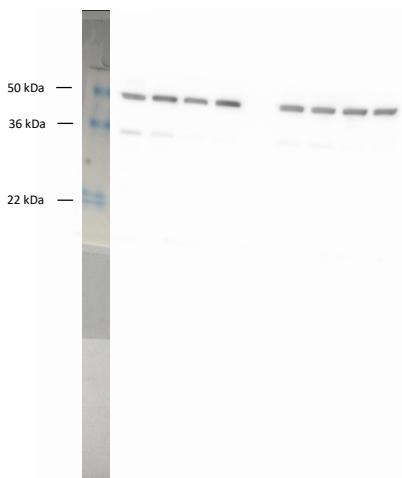


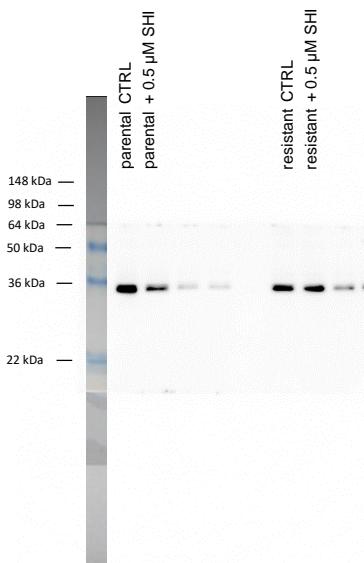
Figure S1f: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of CDK1 (1), corresponding protein expression of β-actin (2).

PC3 – CDK2

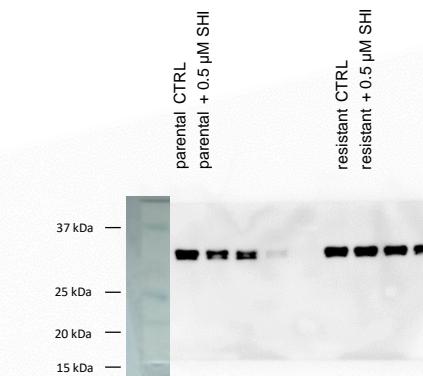
1

(1)

CDK2 (33 kDa)

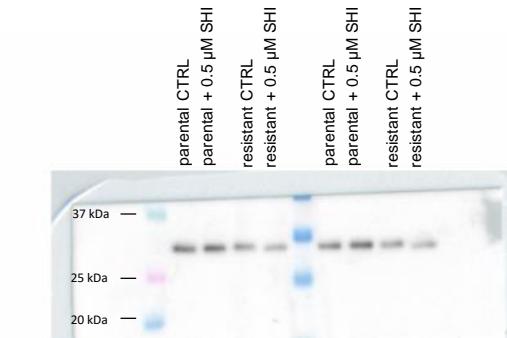


2

resistant CTRL  
parental + 0.5 μM SHI

3

4



β-actin (45 kDa)

(2)

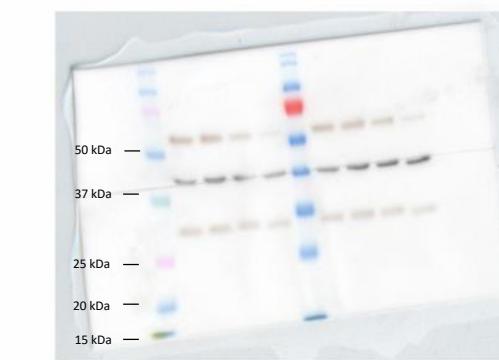
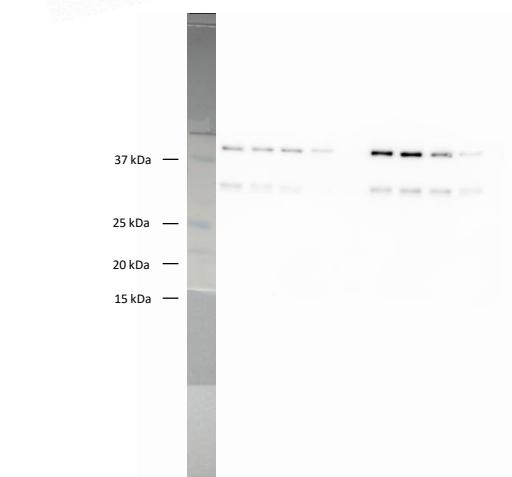
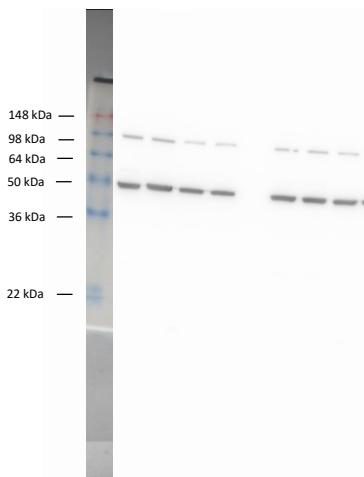
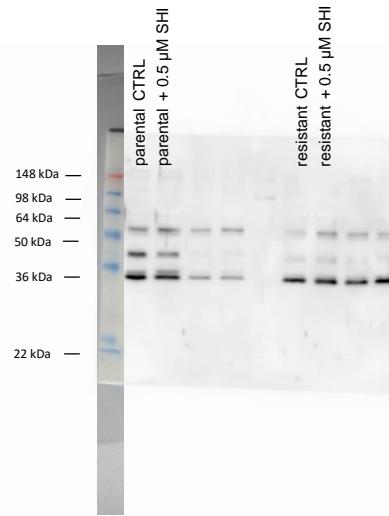


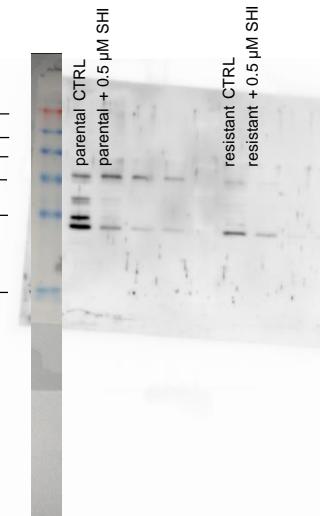
Figure S1g: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of CDK2 (1), corresponding protein expression of β-actin (2).

1

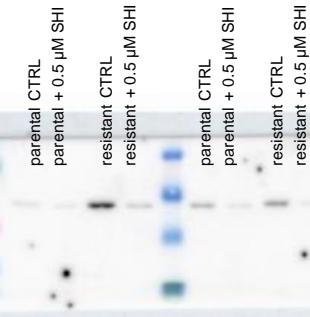
(1)



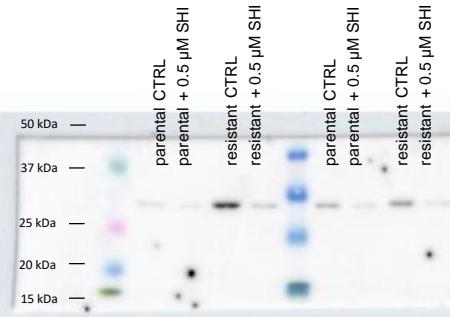
2



3



4



pCDK2 (33 kDa)

(2)

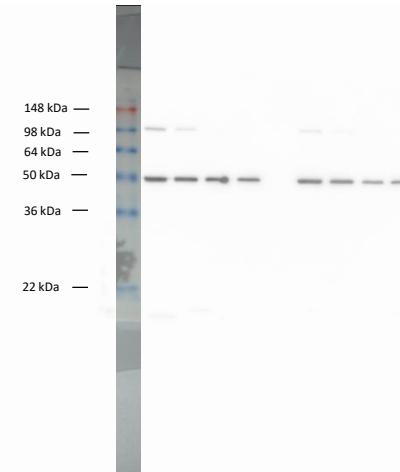


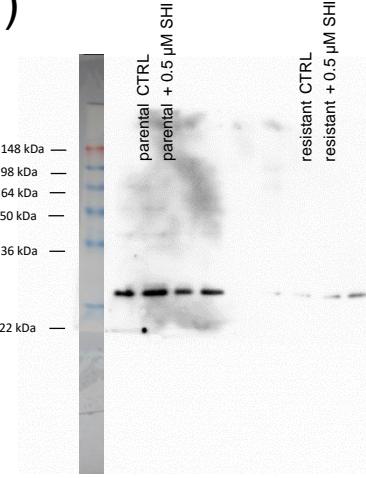
Figure S1h: Detailed information about Figure 5 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant PC3 cells. Protein expression of pCDK2 (1), corresponding protein expression of β-actin (2).

DU145 – p21

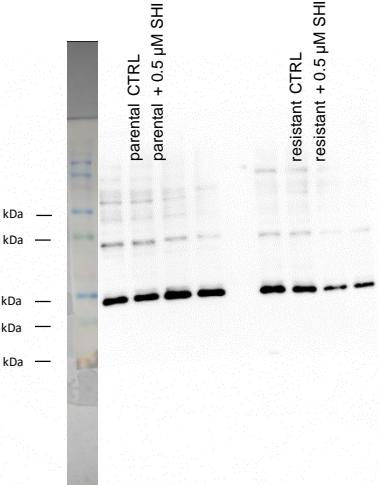
1

p21 (21 kDa)

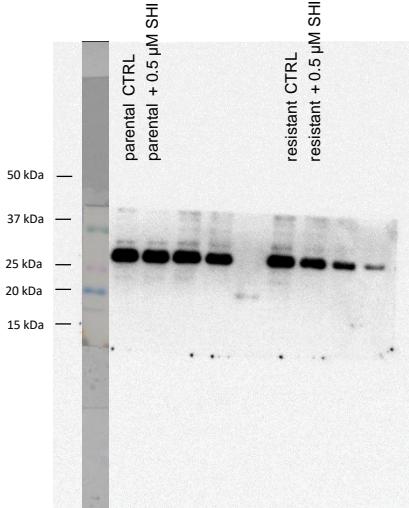
(1)



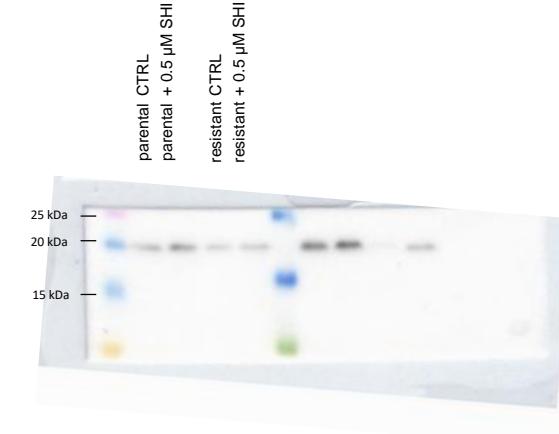
2



3



4

 $\beta$ -actin (45 kDa)

(2)

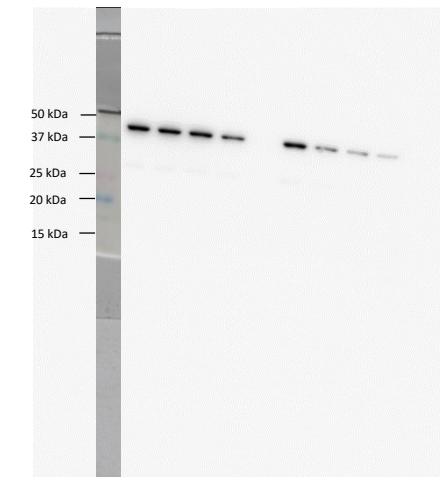
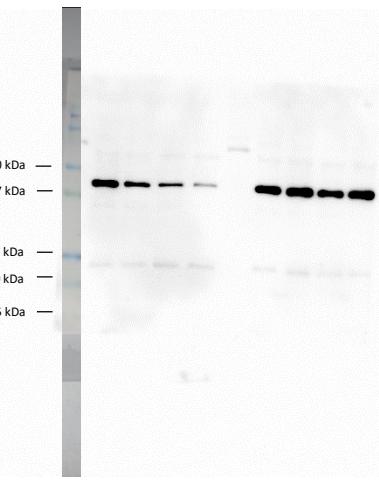
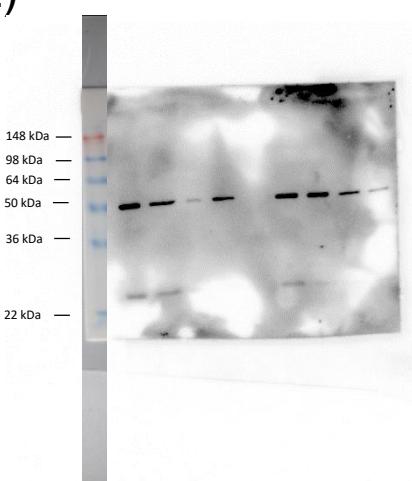
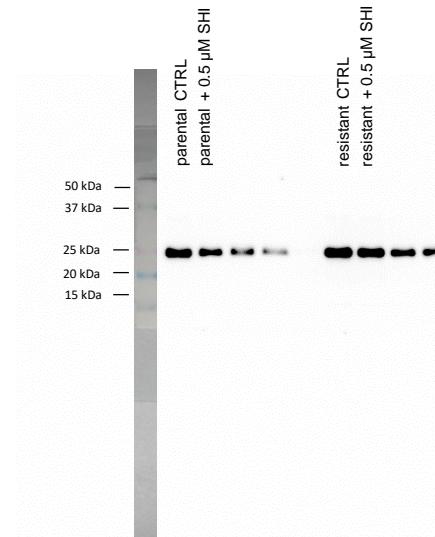


Figure S2a: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of p21 (1), corresponding protein expression of  $\beta$ -actin (2).

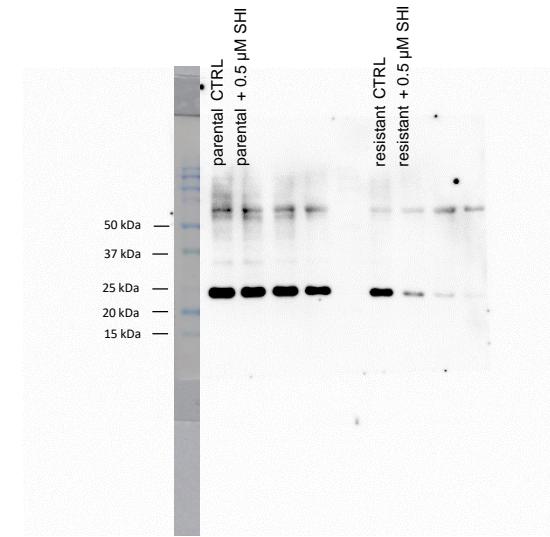
DU145 – p27

1

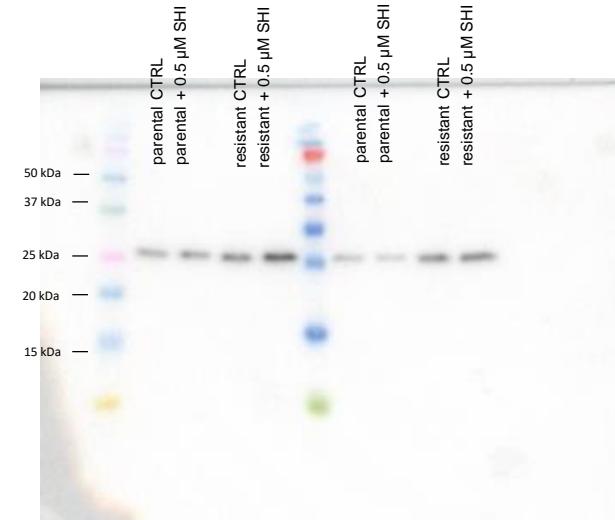
(1)



2



3



4



p27 (27 kDa)

 $\beta$ -actin (45 kDa)

(2)

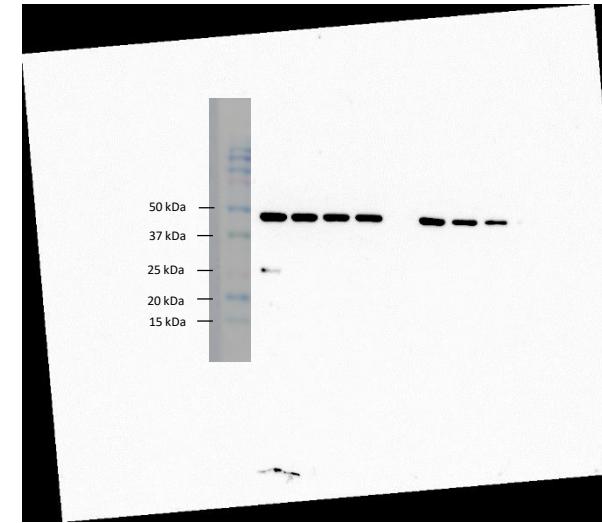
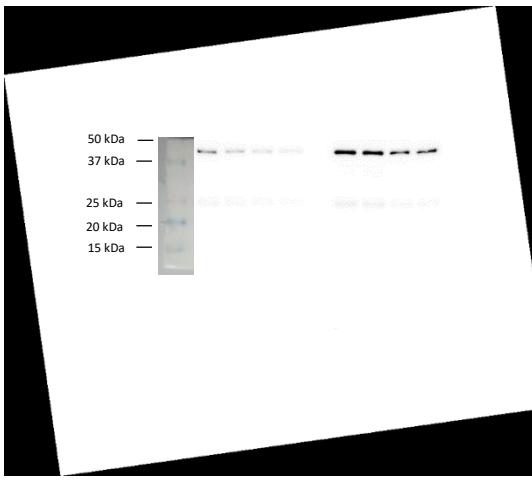
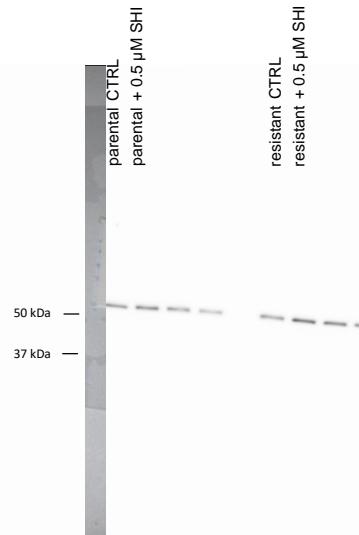


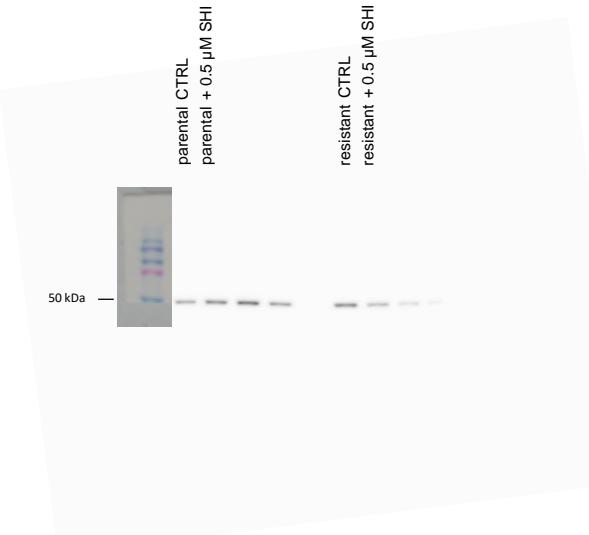
Figure S2b: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of p27 (1), corresponding protein expression of  $\beta$ -actin (2).

1

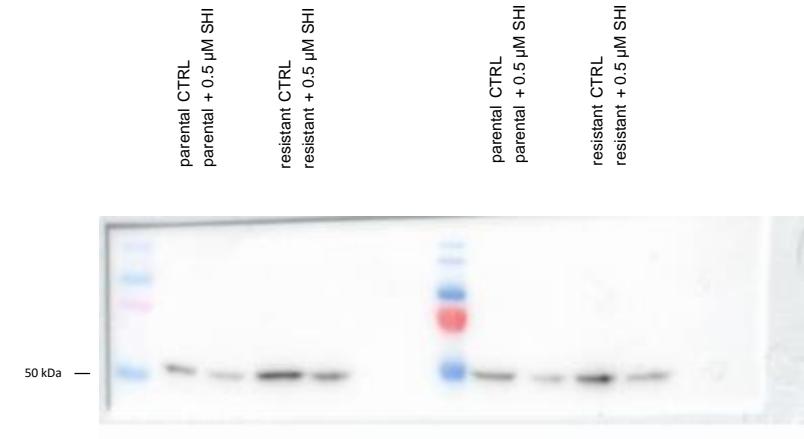
(1)



2



3



4



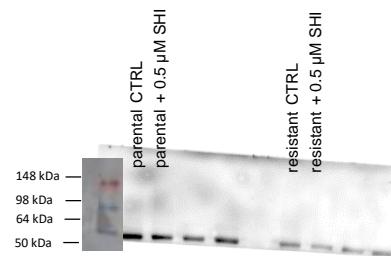
Cyclin A (55 kDa)

β-actin (45 kDa)

Figure S2c: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of Cyclin A (1), corresponding protein expression of β-actin (2).

$\beta$ -actin (45 kDa) Cyclin B (55 kDa)

(1)



1

2

3

4

(2)

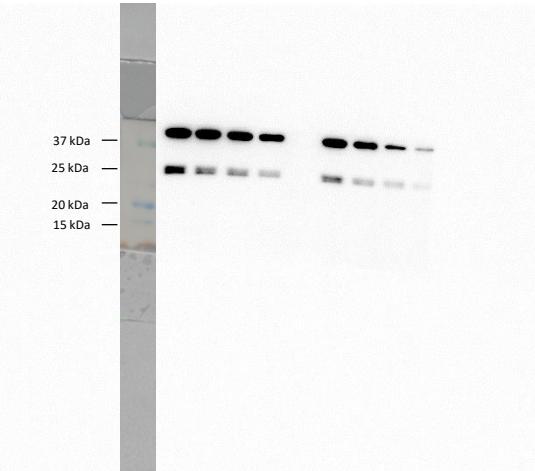
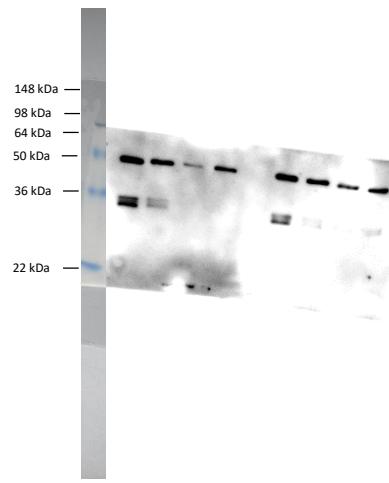


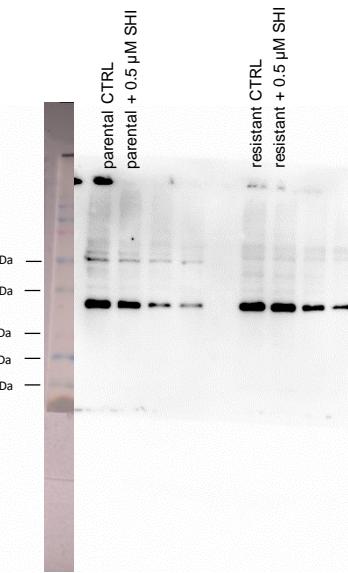
Figure S2d: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of Cyclin B (1), corresponding protein expression of  $\beta$ -actin (2).

DU145 – Cyclin D1

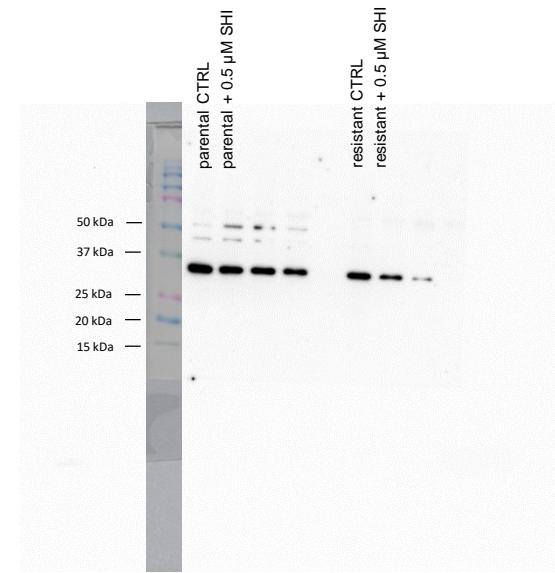
$\beta$ -actin (45 kDa) Cyclin D1 (36 kDa)

1

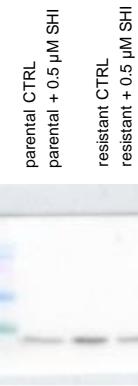
(1)



2



3



4



(2)

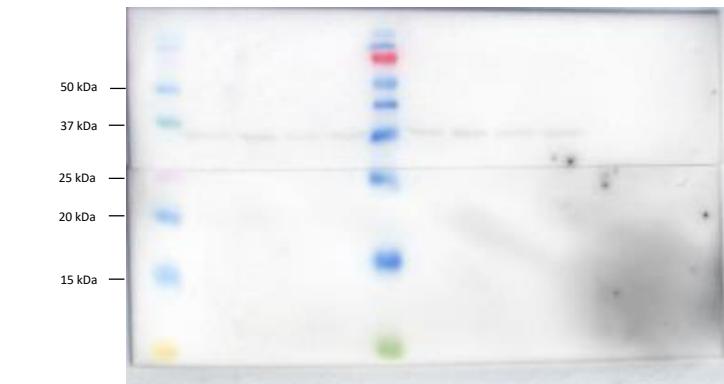
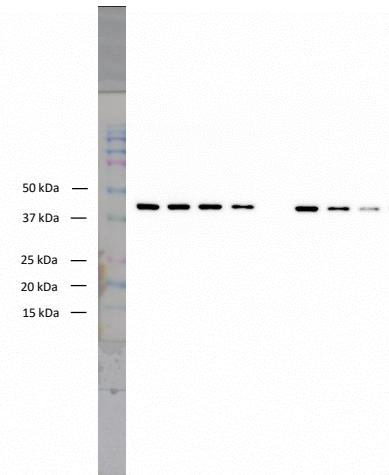
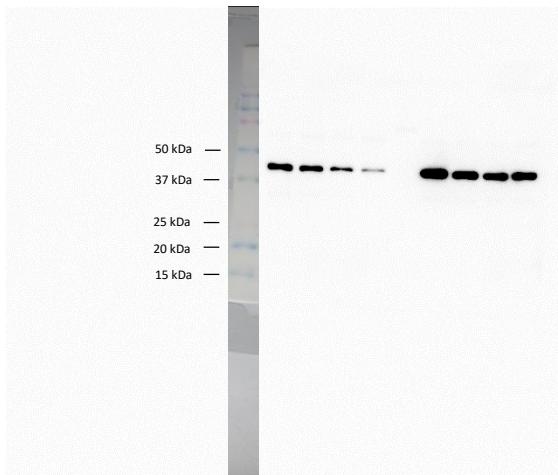


Figure S2e: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of Cyclin D1 (1), corresponding protein expression of  $\beta$ -actin (2).

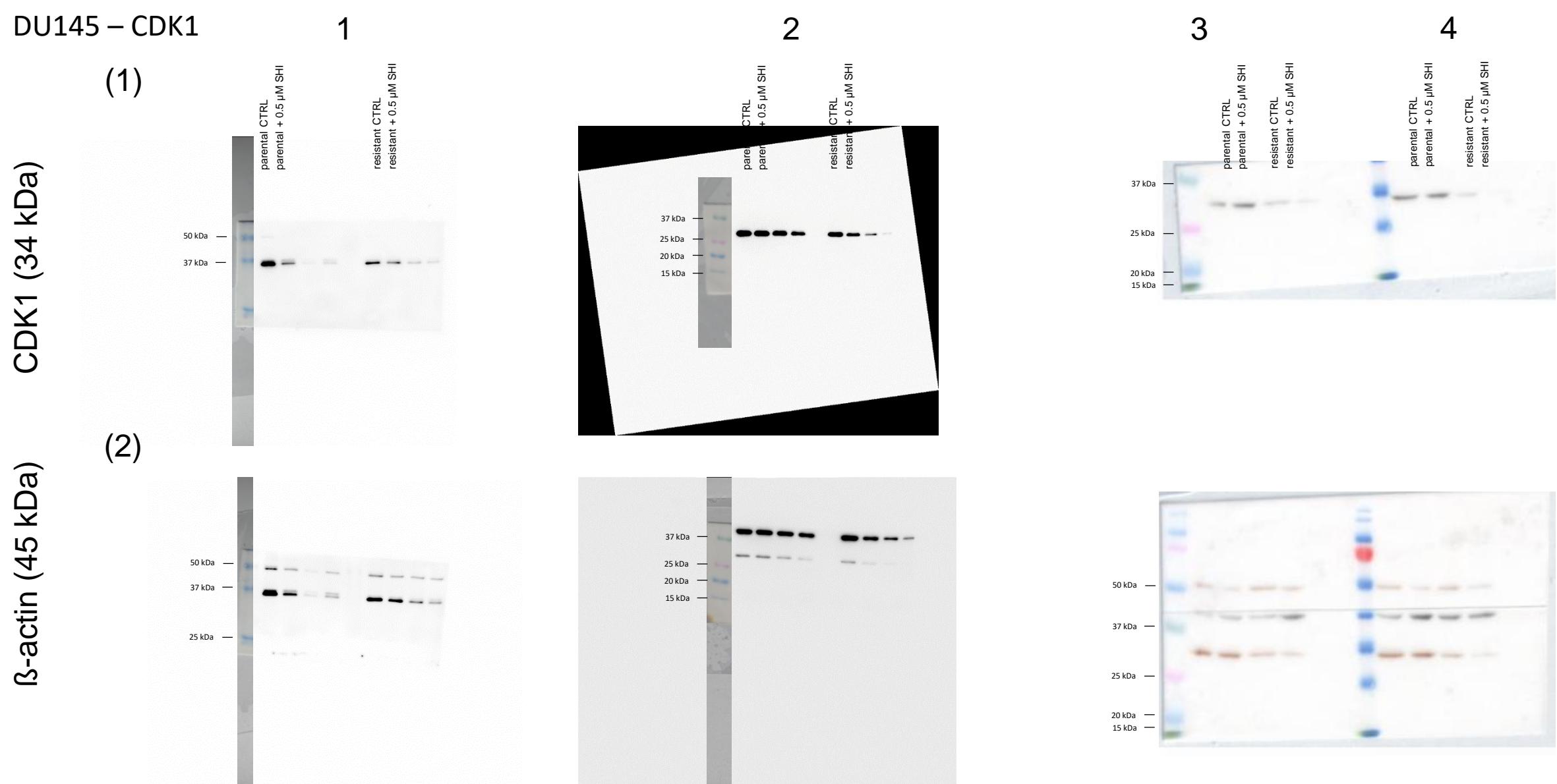
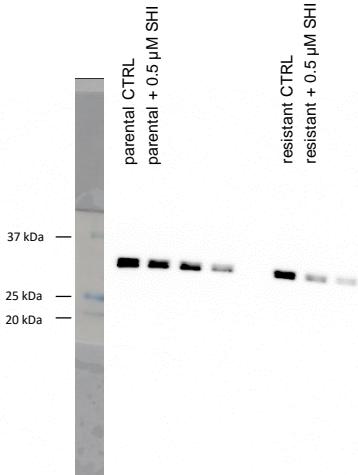


Figure S2f: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of CDK1 (1), corresponding protein expression of  $\beta$ -actin (2).

DU145 – CDK2

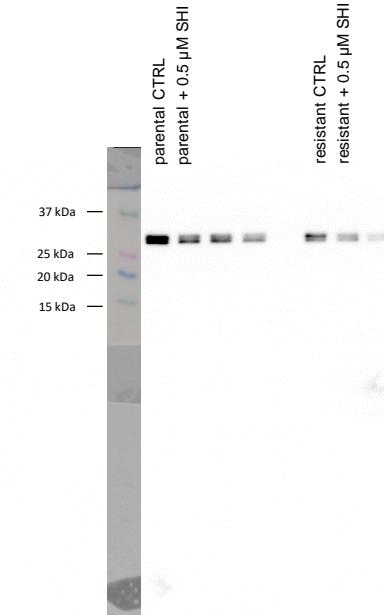


(1)



1

2



2

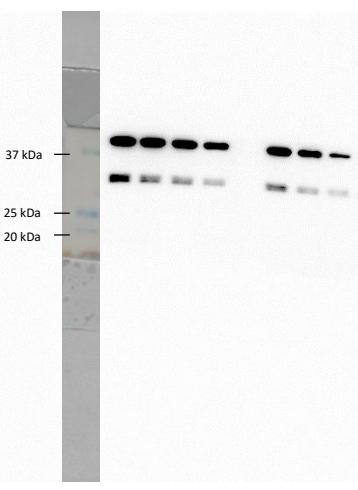
3



4



(2)



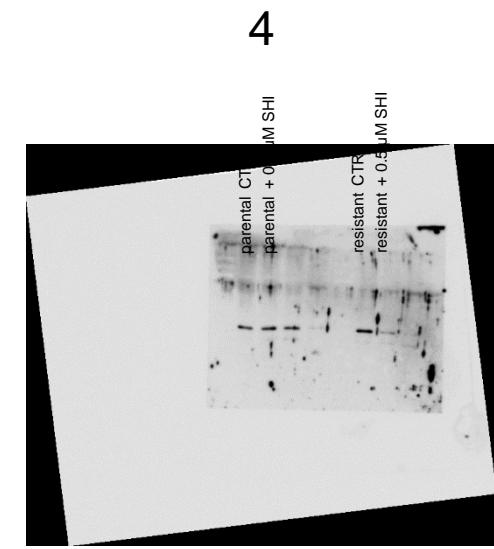
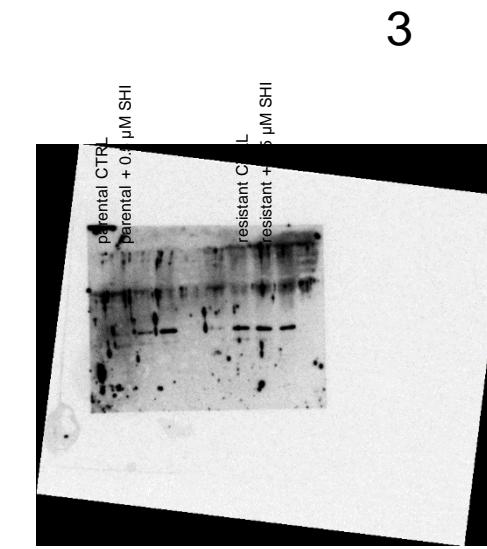
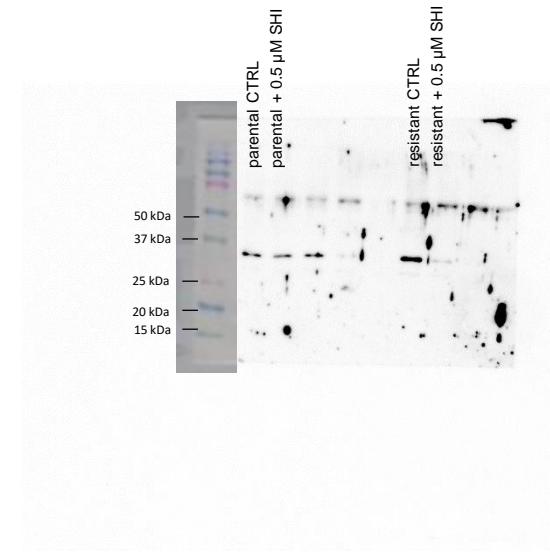
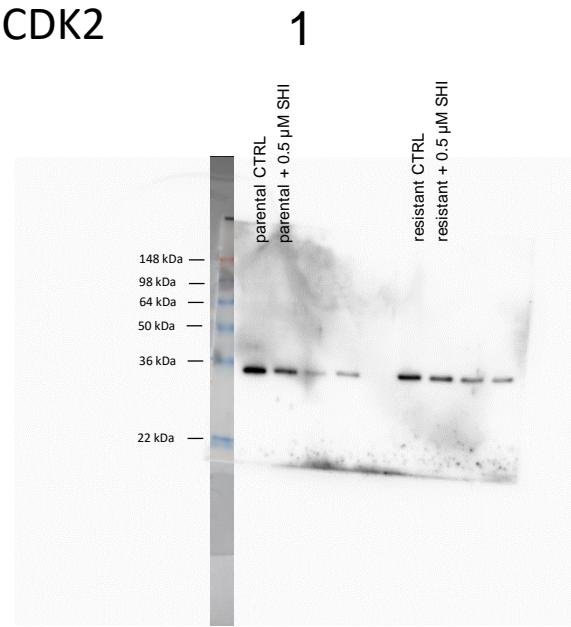
Western blot analysis showing protein expression levels over time (T1, T2, T3, T4) and under different conditions (Control, 100 μM, 200 μM). Molecular weight markers are indicated on the left.

Figure S2g: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of CDK2 (1), corresponding protein expression of  $\beta$ -actin (2).

DU145 – pCDK2

pCDK2 (33 kDa)

(1)



β-actin (45 kDa)

(2)

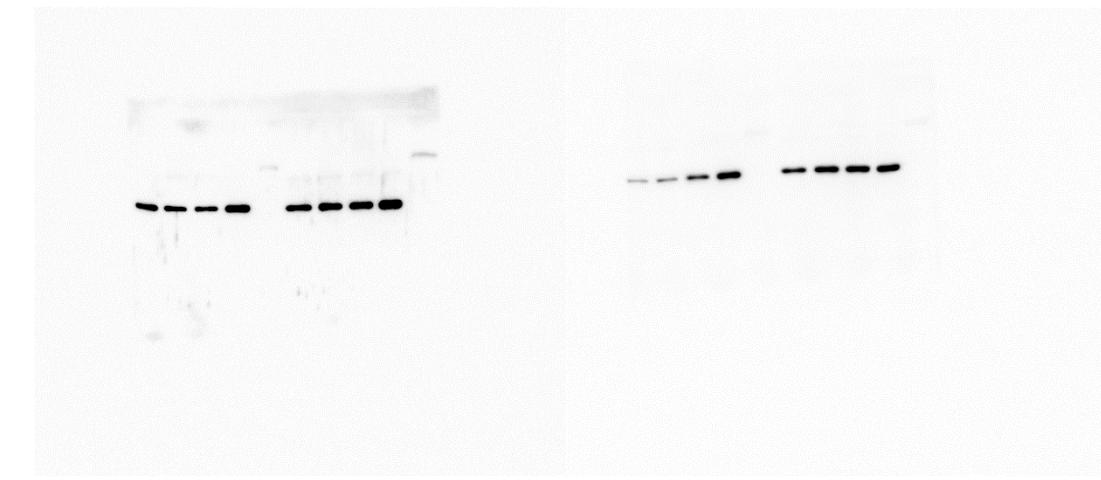
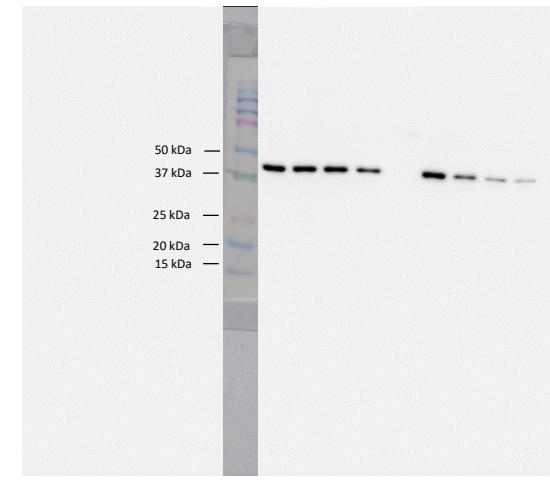
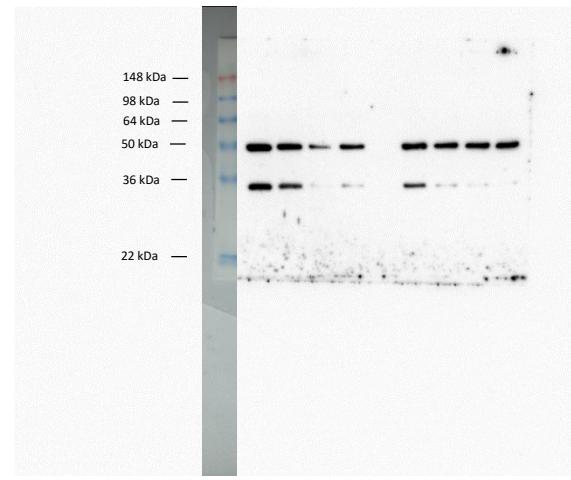


Figure S2h: Detailed information about Figure 6 - Protein expression profile of cell cycle regulating proteins in parental and DX-resistant DU145 cells. Protein expression of pCDK2 (1), corresponding protein expression of β-actin (2).

PARP (116 kDa)

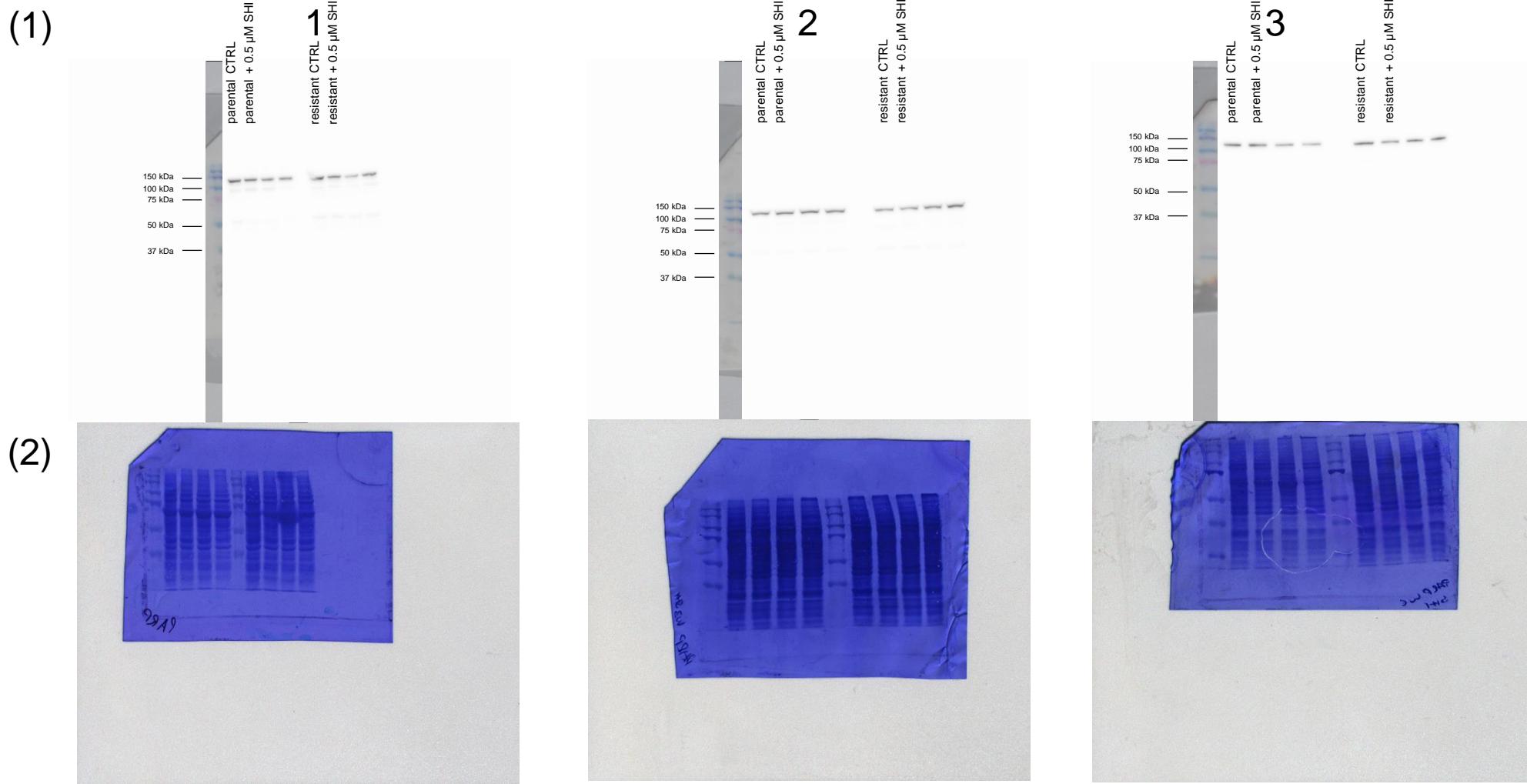


Figure S3: Detailed information about Figure 8h - Protein expression profile of PARP in parental and DX-resistant DU145 cells. Protein expression of PARP (1), corresponding Coomassie blue staining of total protein (2).

# DU145 – Caspase 3

Coomassie staining Caspase 3 (35 kDa)

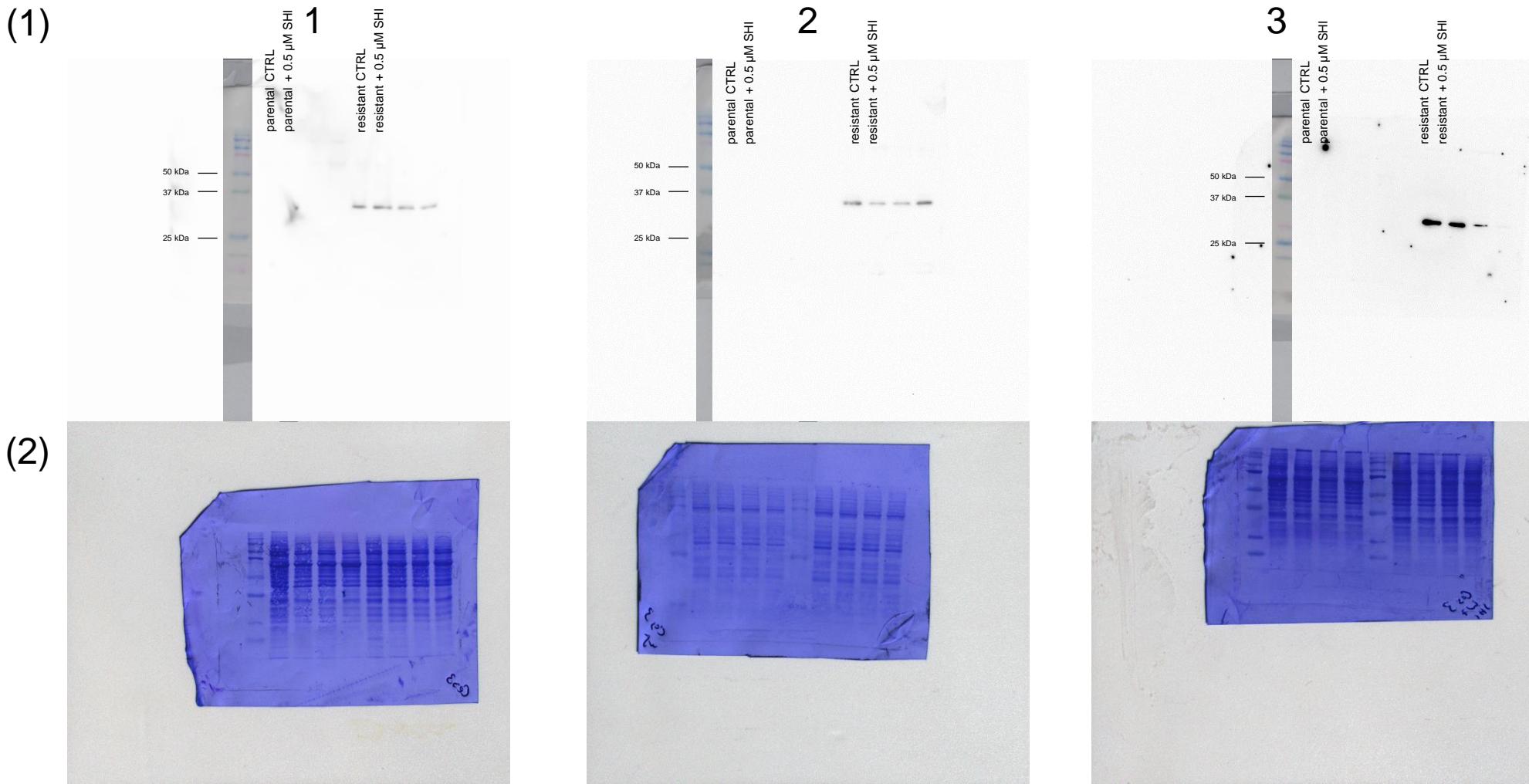


Figure S4: Detailed information about Figure 8i - Protein expression profile of Caspase 3 in parental and DX-resistant DU145 cells. Protein expression of Caspase 3 (1), corresponding Coomassie blue staining of total protein (2).

# DU145 – Caspase 8

Coomassie staining Caspase 8 (57 kDa)

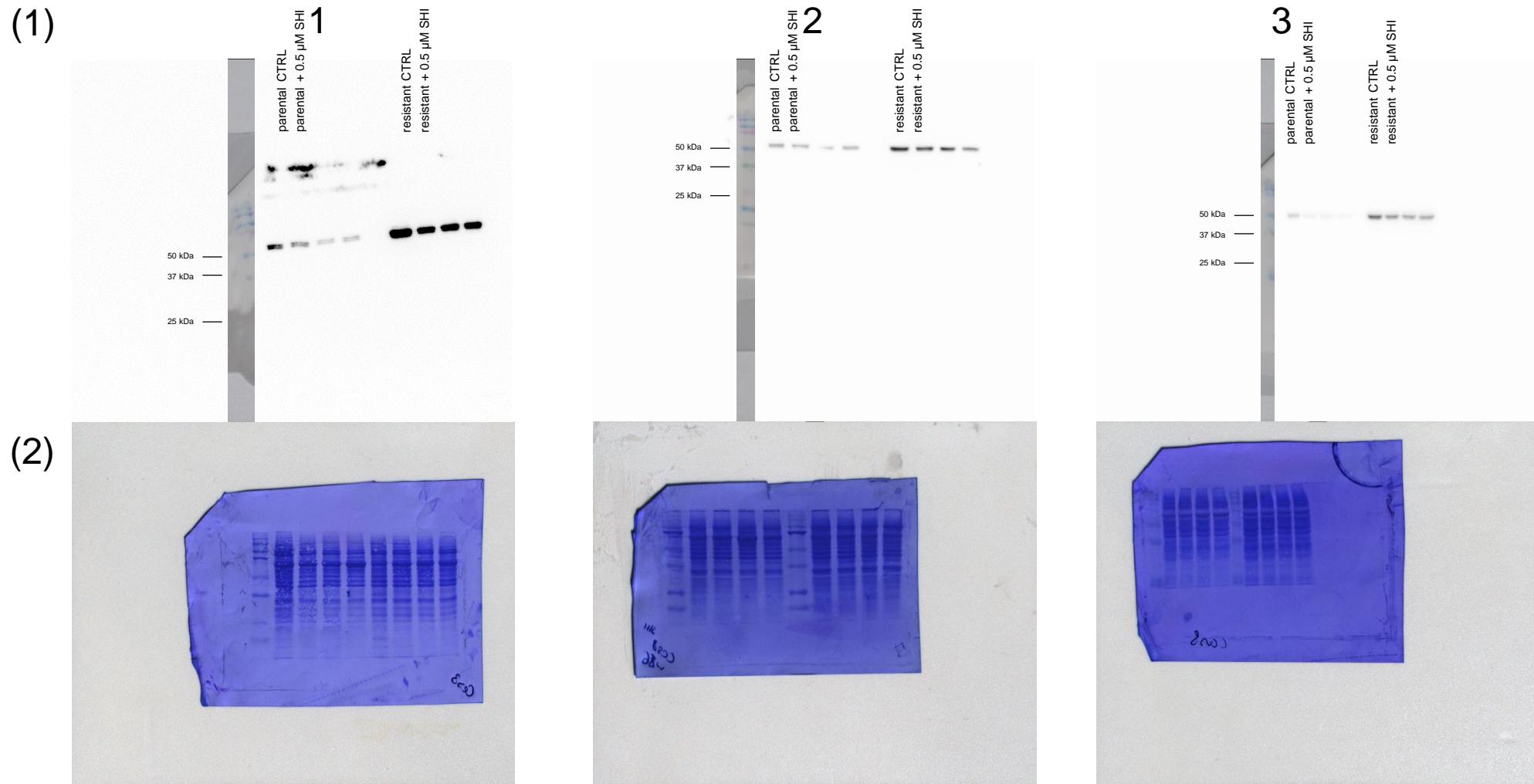
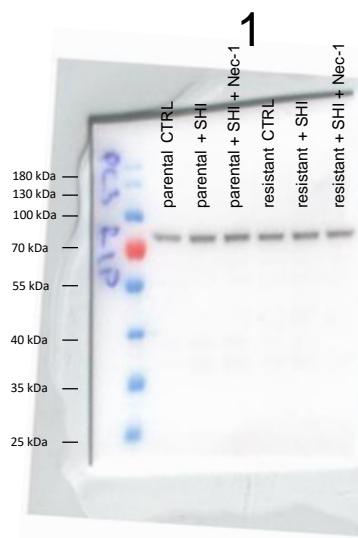


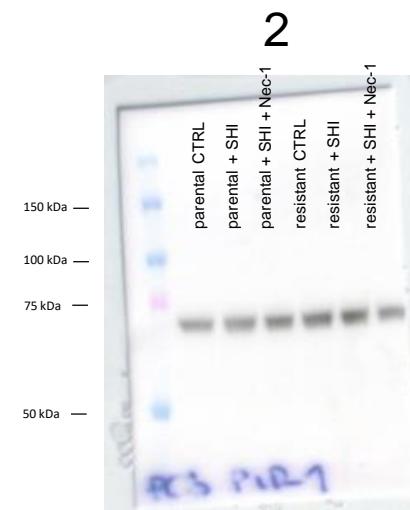
Figure S5: Detailed information about Figure 8j - Protein expression profile of Caspase 8 in parental and DX-resistant DU145 cells. Protein expression of Caspase 8 (1), corresponding Coomassie blue staining of total protein (2).

Coomassie staining RIP1 (78 kDa)

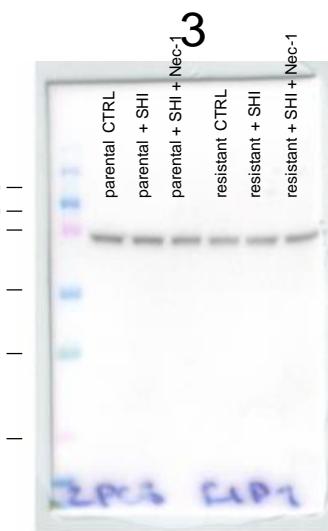
(1)



2



3



(2)

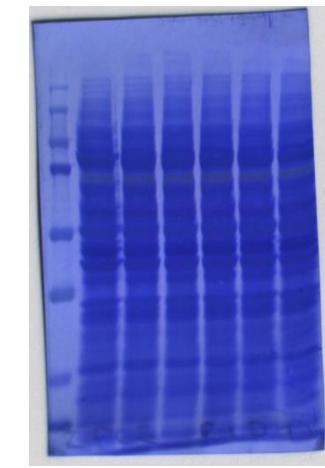
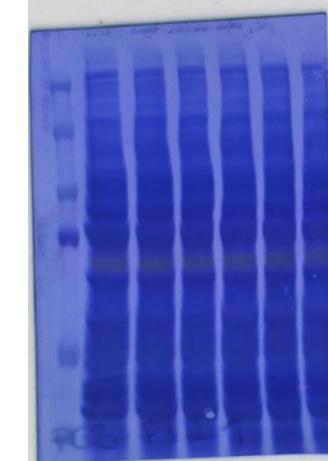
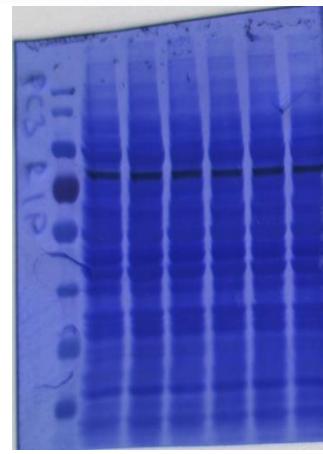
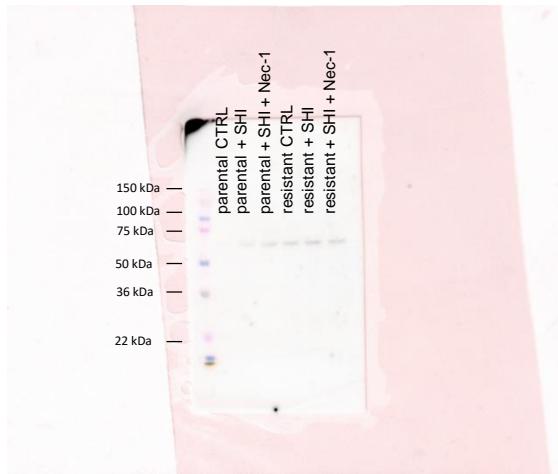


Figure S6: Detailed information about Figure 10a - Protein expression profile of RIP1 in parental and DX-resistant PC3 cells. Protein expression of RIP1 (1), corresponding Coomassie blue staining of total protein (2).

pRIP1 (78 kDa)

(1)



1

2

3

Coomassie staining

(2)

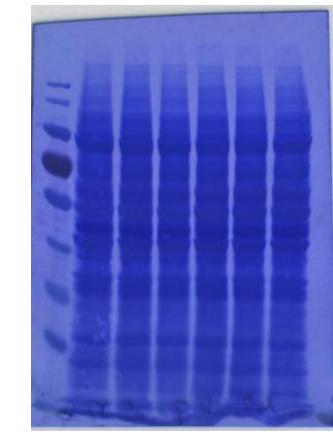
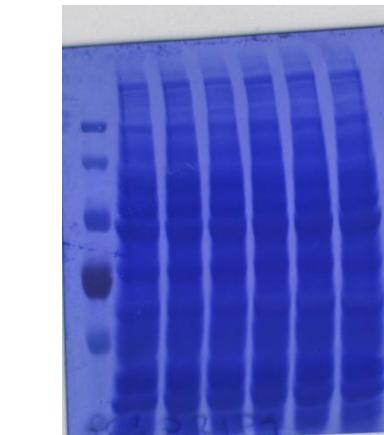
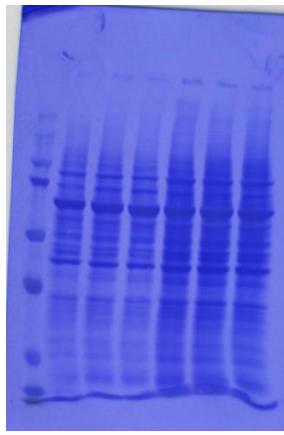
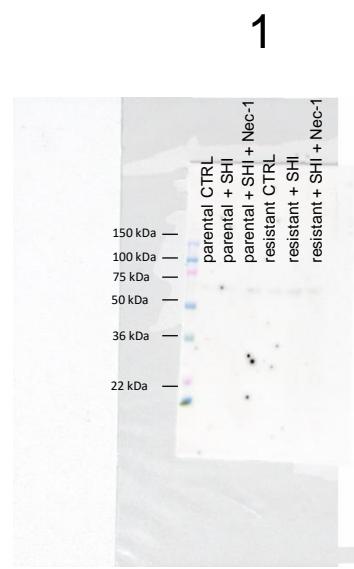


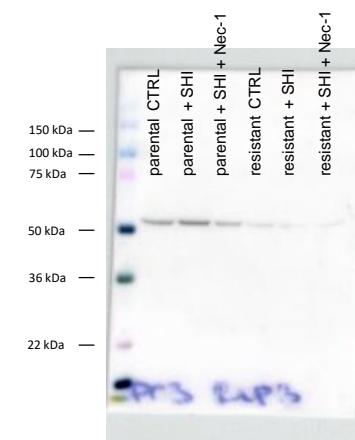
Figure S6: Detailed information about Figure 10b - Protein expression profile of pRIP1 in parental and DX-resistant PC3 cells. Protein expression of pRIP1 (1), corresponding Coomassie blue staining of total protein (2).

RIP3 staining (46-62 kDa)

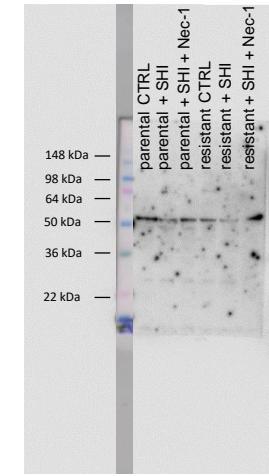
(1)



2



3



(2)

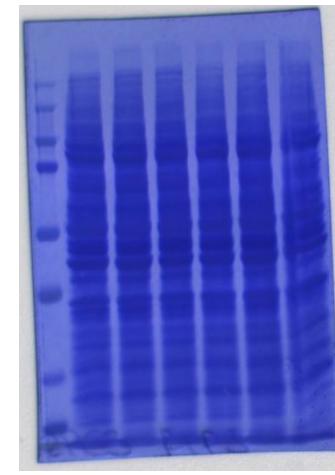
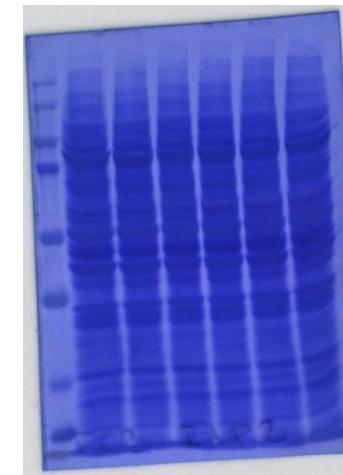
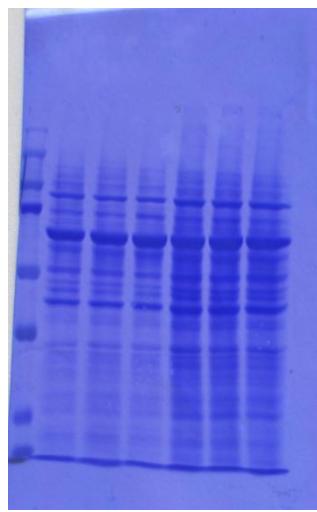
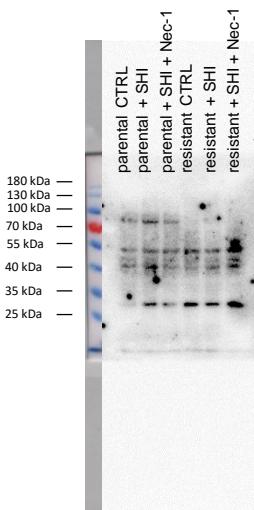


Figure S6: Detailed information about Figure 10c - Protein expression profile of RIP3 in parental and DX-resistant PC3 cells. Protein expression of RIP3 (1), corresponding Coomassie blue staining of total protein (2).

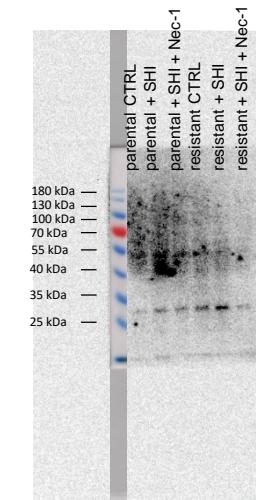
Coomassie staining pRIP3 (46-62 kDa)

(1)

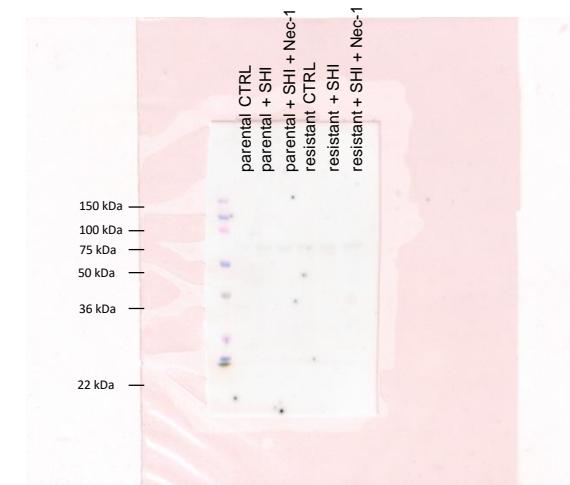
1



2



3



(2)

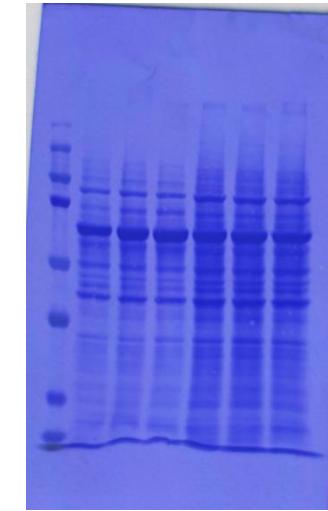
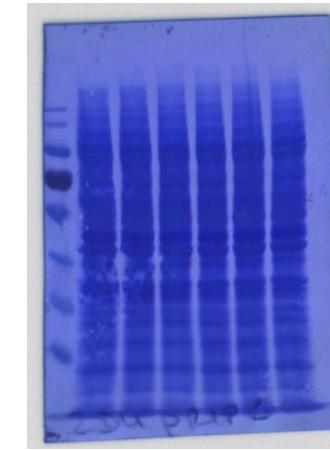
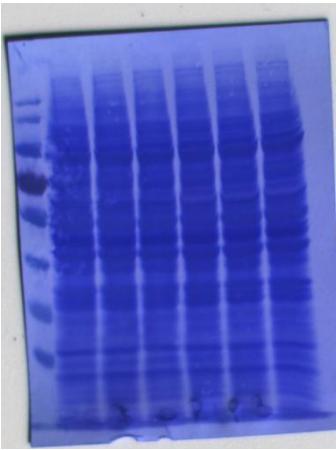
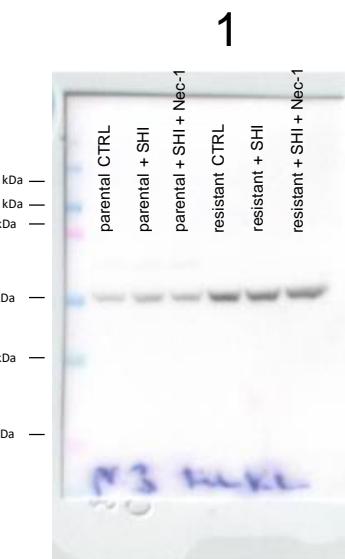


Figure S6: Detailed information about Figure 10d - Protein expression profile of pRIP3 in parental and DX-resistant PC3 cells. Protein expression of pRIP3 (1), corresponding Coomassie blue staining of total protein (2).

Coomassie staining  
MLKL (54 kDa)

(1)



1

2

3

(2)

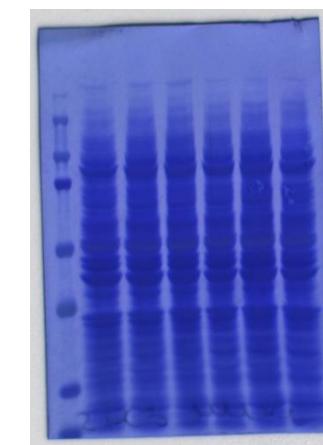
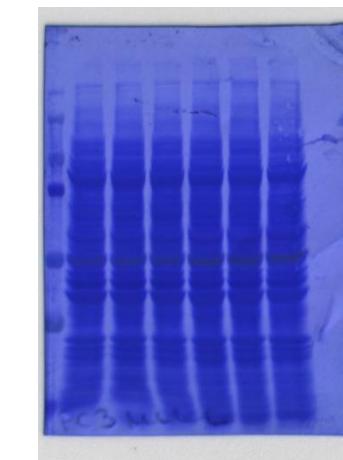
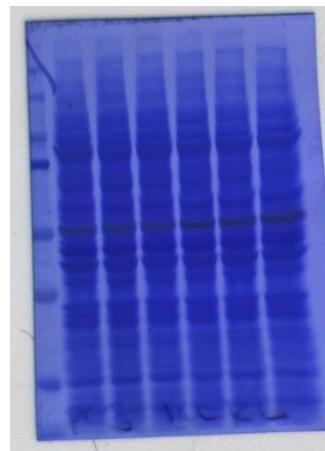
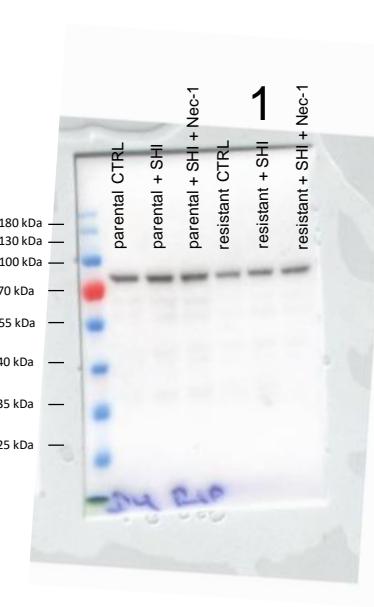


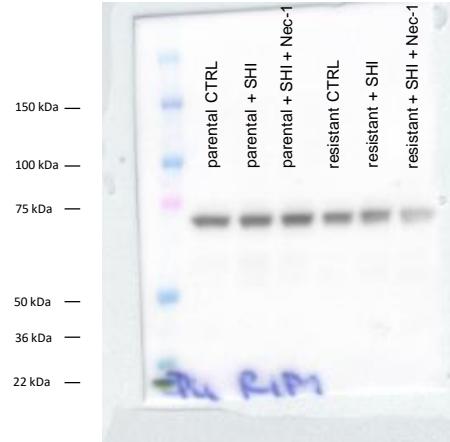
Figure S6: Detailed information about Figure 10e - Protein expression profile of MLKL in parental and DX-resistant PC3 cells. Protein expression of MLKL (1), corresponding Coomassie blue staining of total protein (2).

Coomassie staining  
RIP1 (78 kDa)

(1)



2



3



(2)

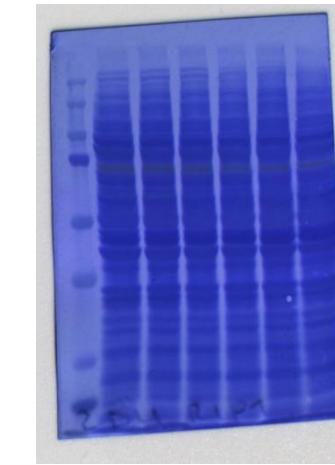
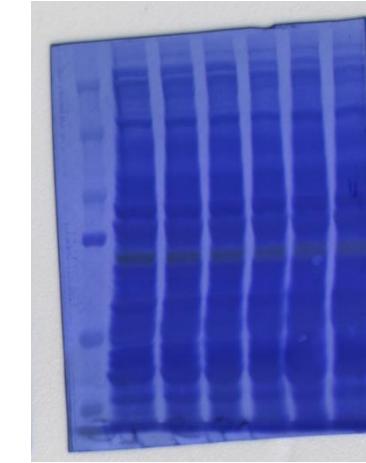
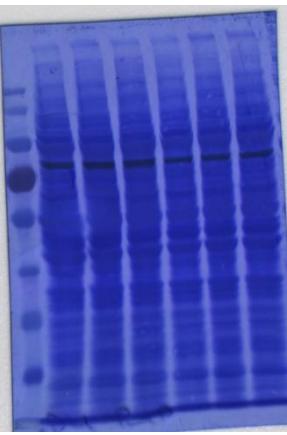
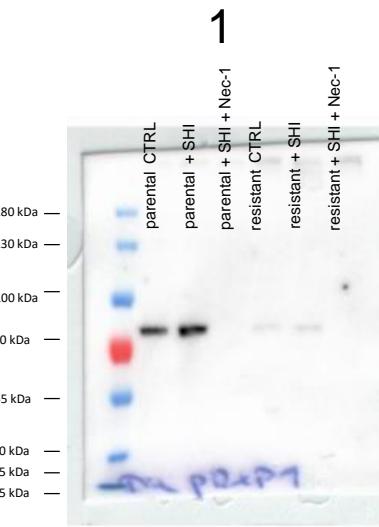


Figure S6: Detailed information about Figure 10f - Protein expression profile of RIP1 in parental and DX-resistant DU145 cells. Protein expression of RIP1 (1), corresponding Coomassie blue staining of total protein (2).

## DU145 – pRIP1

Coomassie staining  
pRIP1 (78 kDa)

(1)



1

2

3

(2)

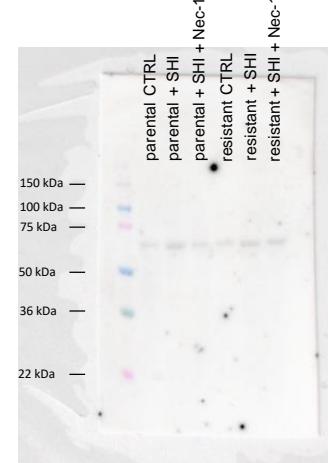
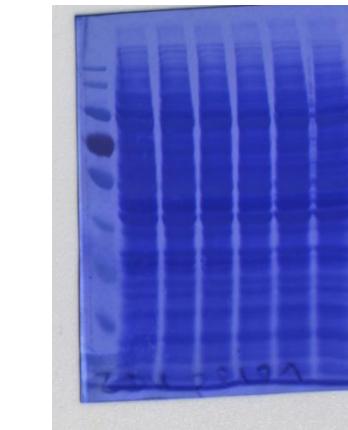
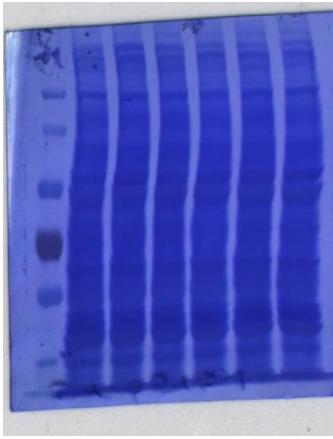
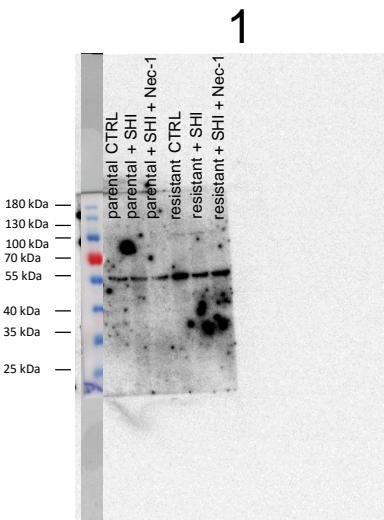


Figure S6: Detailed information about Figure 10g - Protein expression profile of pRIP1 in parental and DX-resistant DU145 cells. Protein expression of pRIP1 (1), corresponding Coomassie blue staining of total protein (2).

RIP3 staining (46-62 kDa)

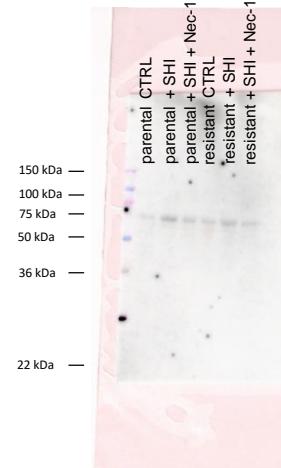
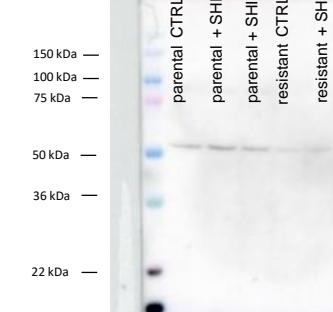
(1)



1

2

3



(2)

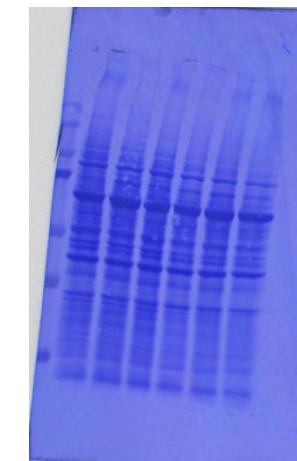
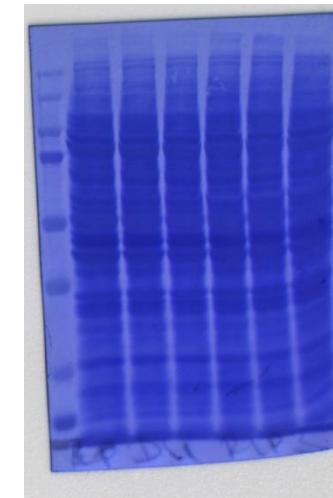
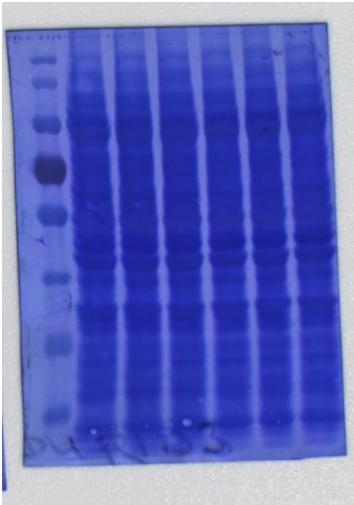
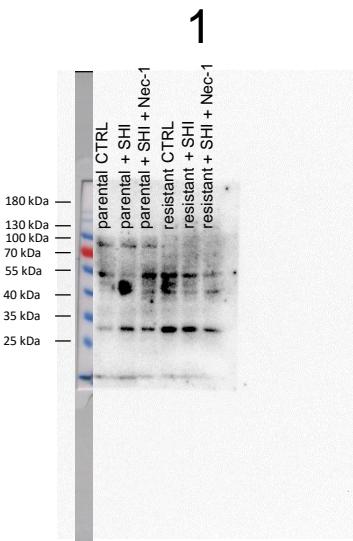


Figure S6: Detailed information about Figure 10h - Protein expression profile of RIP3 in parental and DX-resistant DU145 cells. Protein expression of RIP3 (1), corresponding Coomassie blue staining of total protein (2).

pRIP3 (46-62 kDa)

(1)



1

2

3

(2)

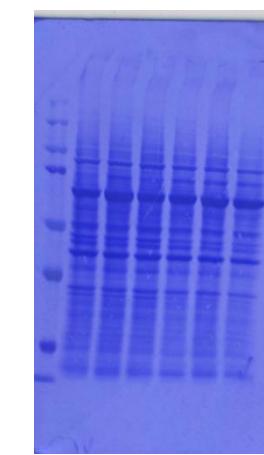
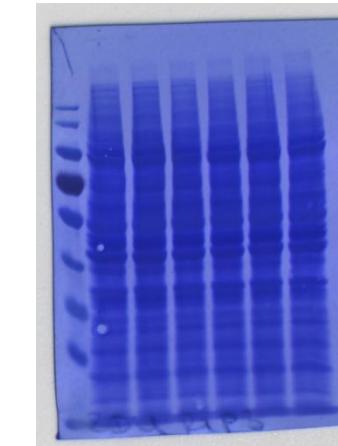
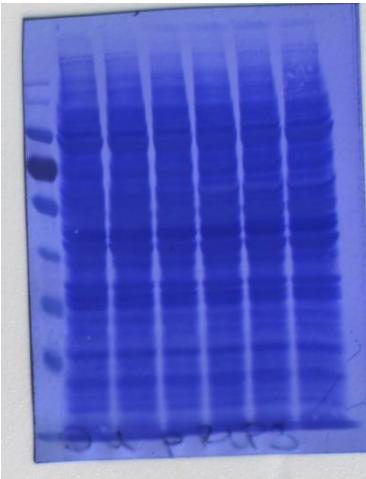


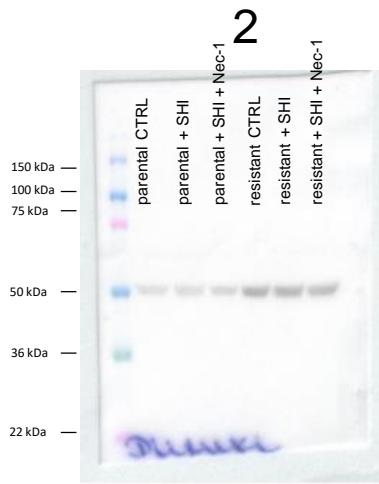
Figure S6: Detailed information about Figure 10i - Protein expression profile of pRIP3 in parental and DX-resistant DU145 cells. Protein expression of pRIP3 (1), corresponding Coomassie blue staining of total protein (2).

MLKL staining

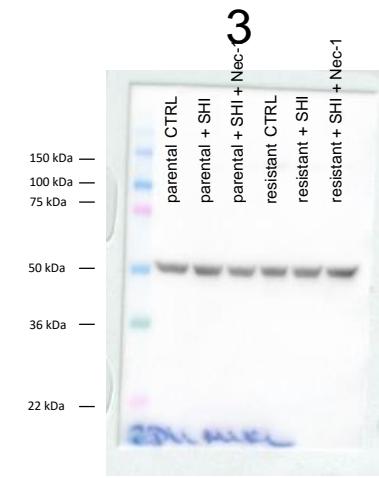
(1)



1



2



3

(2)

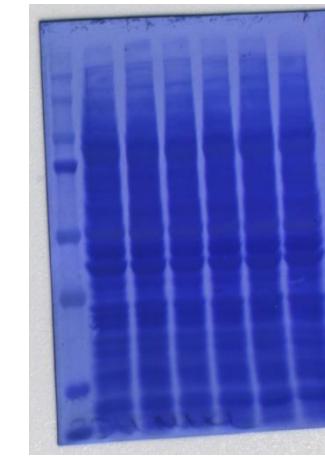
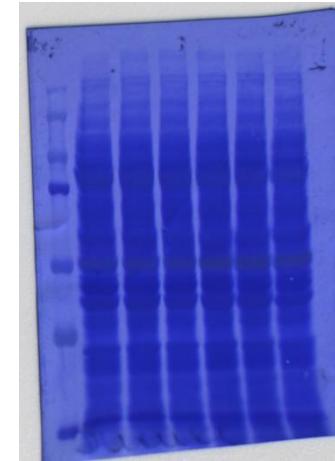
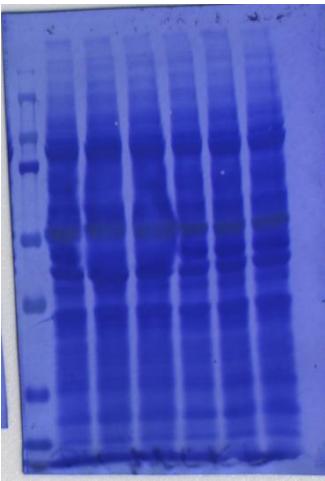
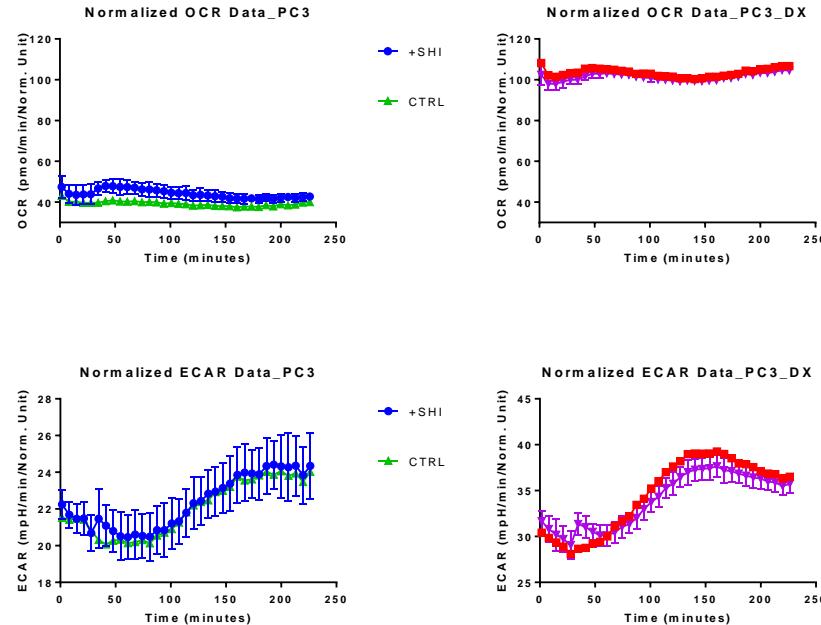


Figure S6: Detailed information about Figure 10j - Protein expression profile of MLKL in parental and DX-resistant DU145 cells. Protein expression of MLKL (1), corresponding Coomassie blue staining of total protein (2).

(a)



(b)

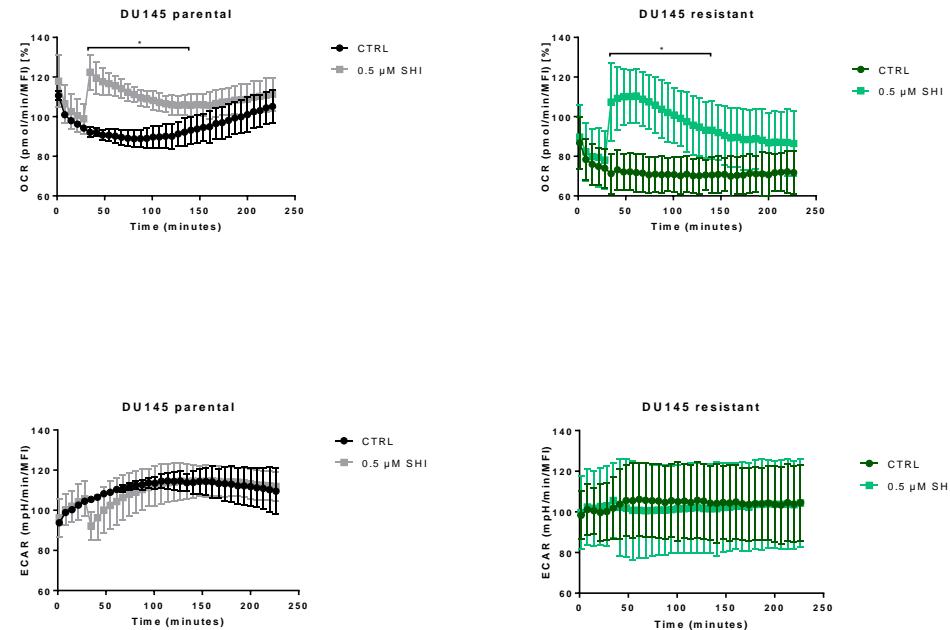


Figure S7: Detailed information about section 2.6 - Shikonin showed no effects on metabolism. Oxygen consumption rate (OCR) (top) and extracellular acidification rate (ECAR) (bottom) of PC3 and PC3\_DX (a) as well as DU145 and DU145\_DX (b) cells. Parental and DX-resistant cells untreated or treated with SHI 0.5  $\mu$ M for 20 h ( $n = 3$ ).