

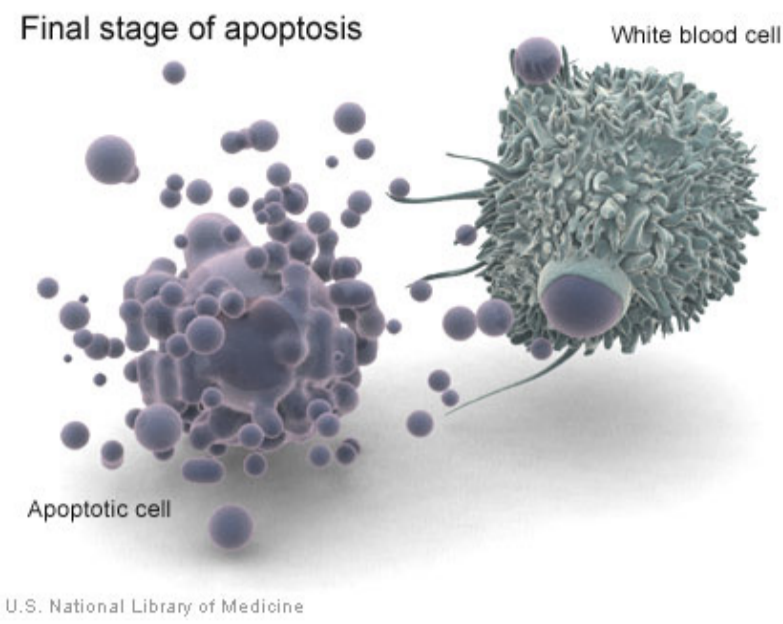


Starvation as a new way to increase the efficiency of anti-cancer therapy



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Introduction: Development of effective anticancer therapy is one of the important tasks of modern medicine. The tumor formation results from dysfunction of programmed cell death – apoptosis. Apoptosis plays a crucial role in the developmental processes and in the elimination of the damaged cells, including cancer cells. One of oncotherapeutic strategies is to use special chemical agents which are able to induce damage of DNA and trigger apoptotic death of cancer cells, for example cisplatin (Cis). However, these drugs have toxic effects on normal cells.

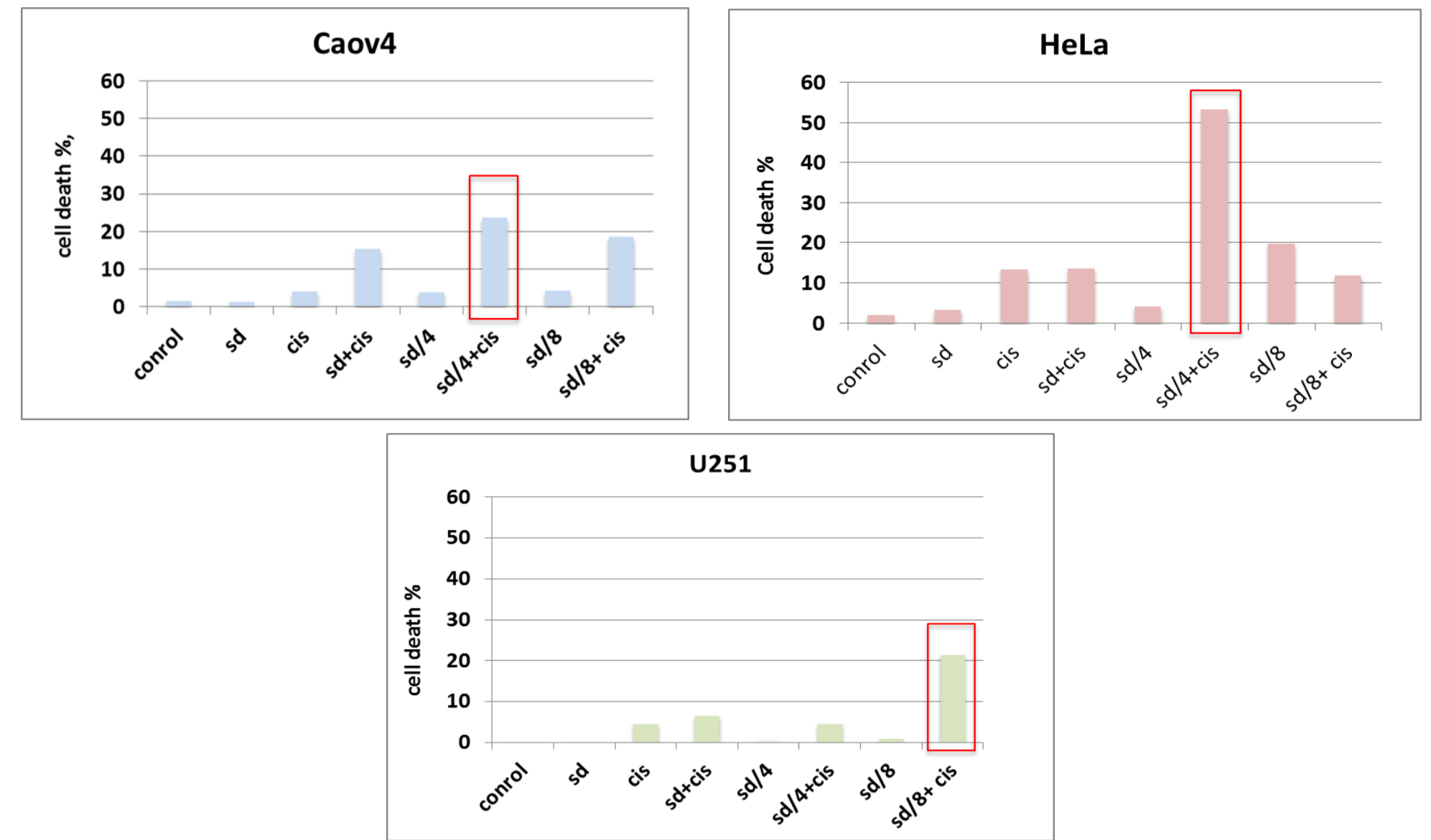


We are looking for a new approach to promote therapeutic effect of cancer drugs. The combination of starvation and DNA damage caused by cisplatin might enhance apoptotic death of cancer cells. In this case dosage used in anti-cancer therapy can be decreased making the treatment less harmful for the organism.

We have tested whether or not starvation affects cisplatin caused apoptosis in three different cancer cell lines: Caov4, HeLa and U251.

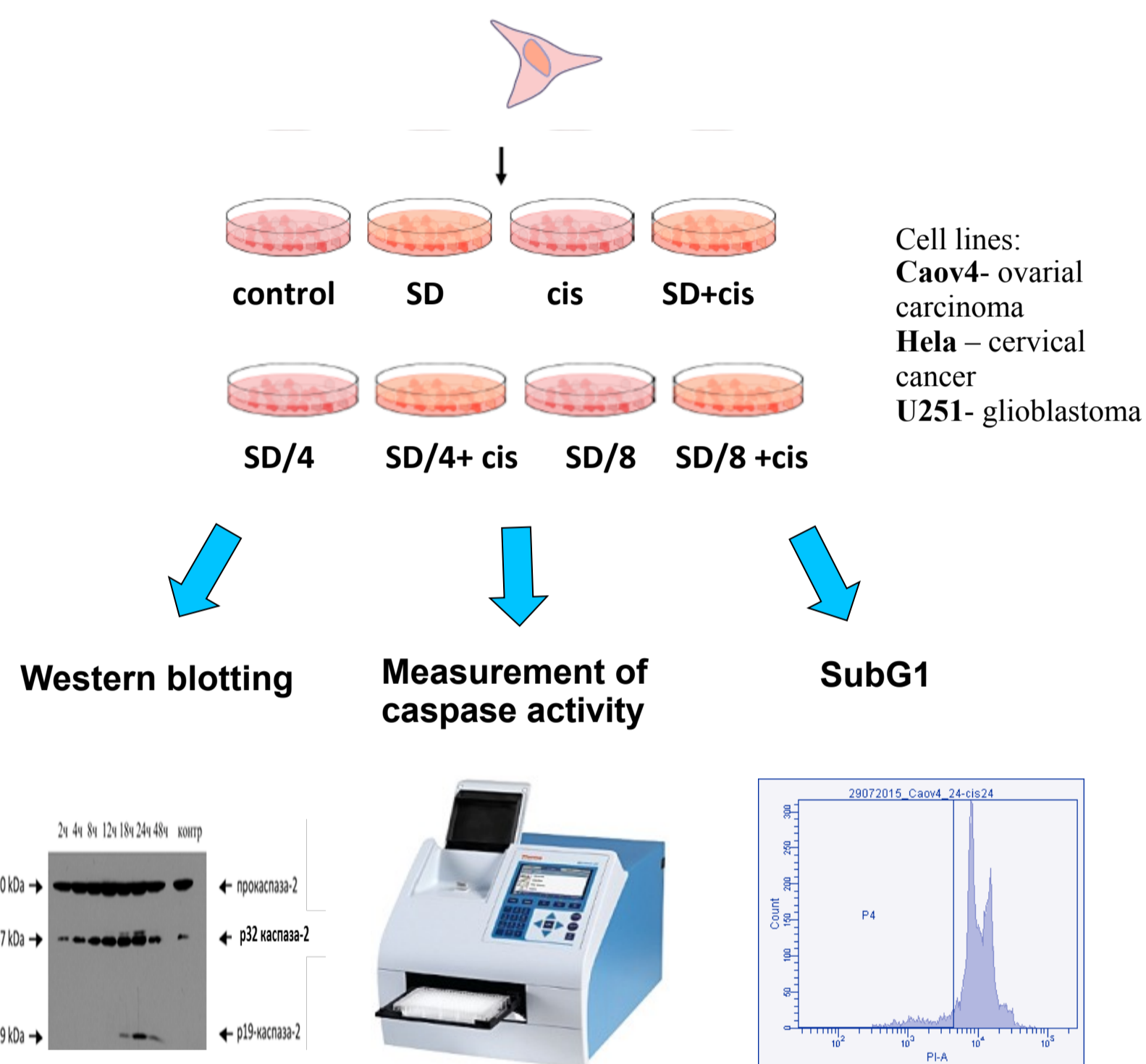
Aim: To investigate the effect of combination of starvation and cisplatin treatment on cancer cell lines.

SubG1 analysis



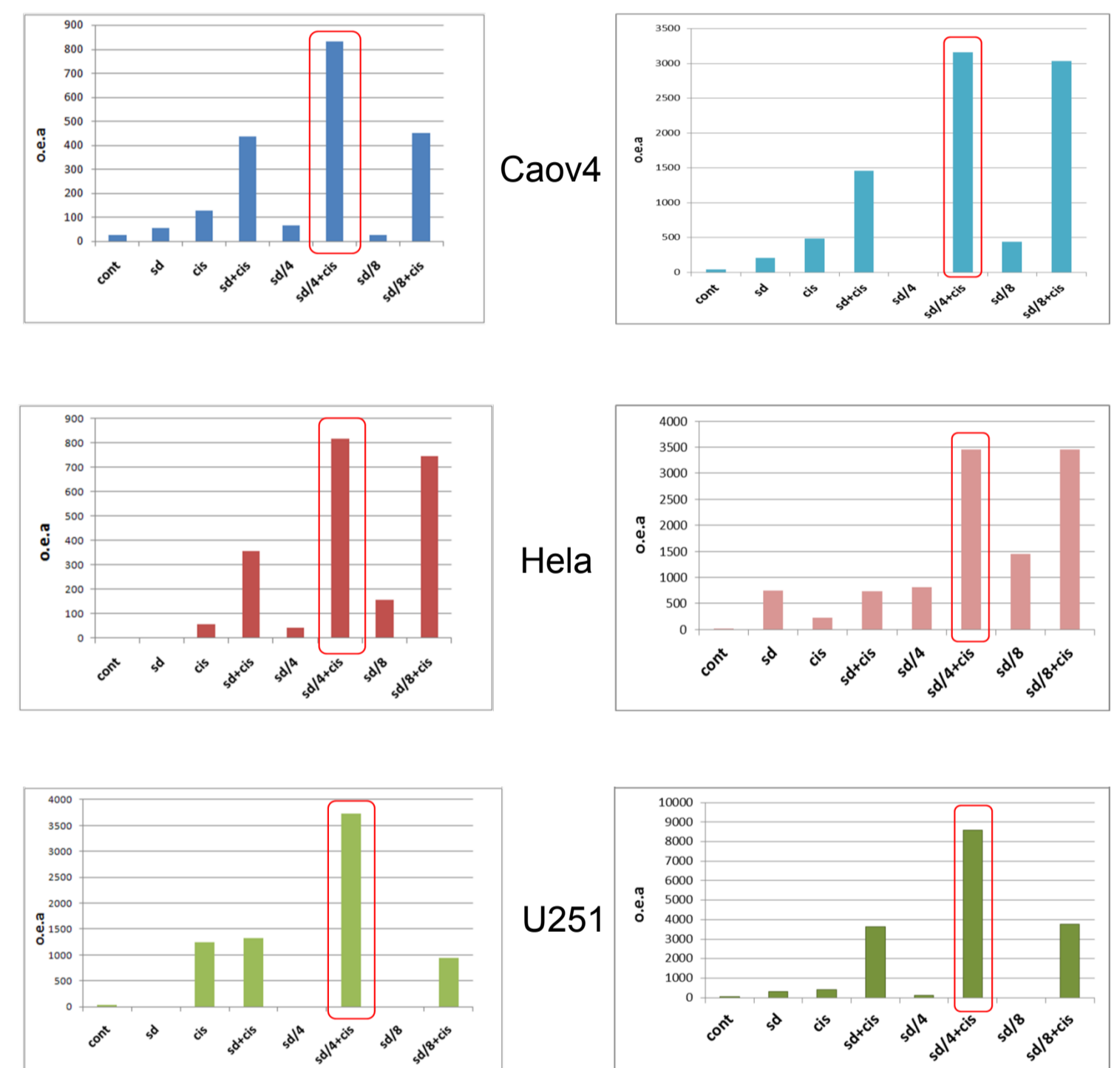
Starvation increases the caspases activation upon DNA damage

Experimental design



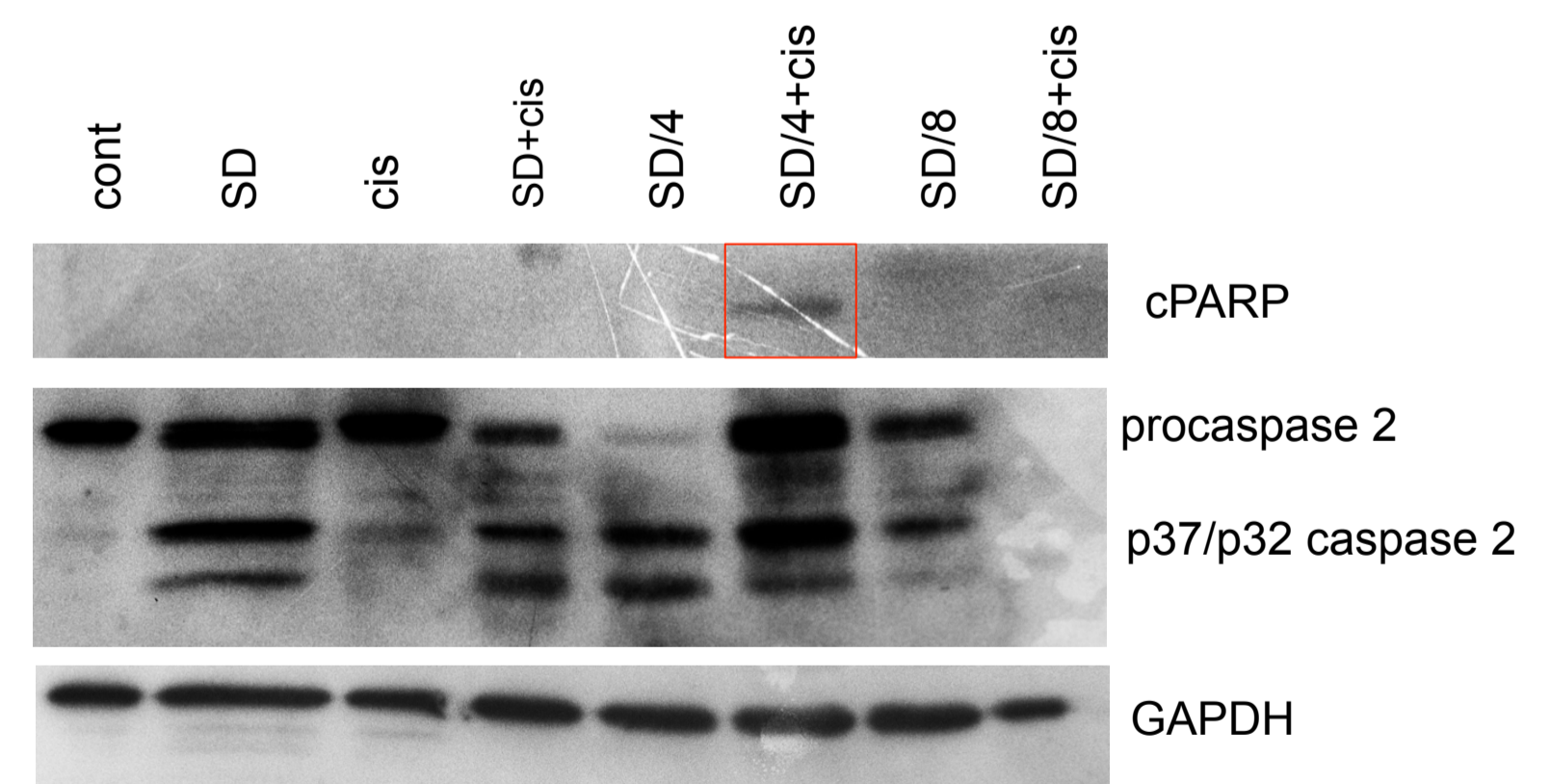
The activity of caspase-2

The activity of caspase-3



o.e.a. – relative activity units

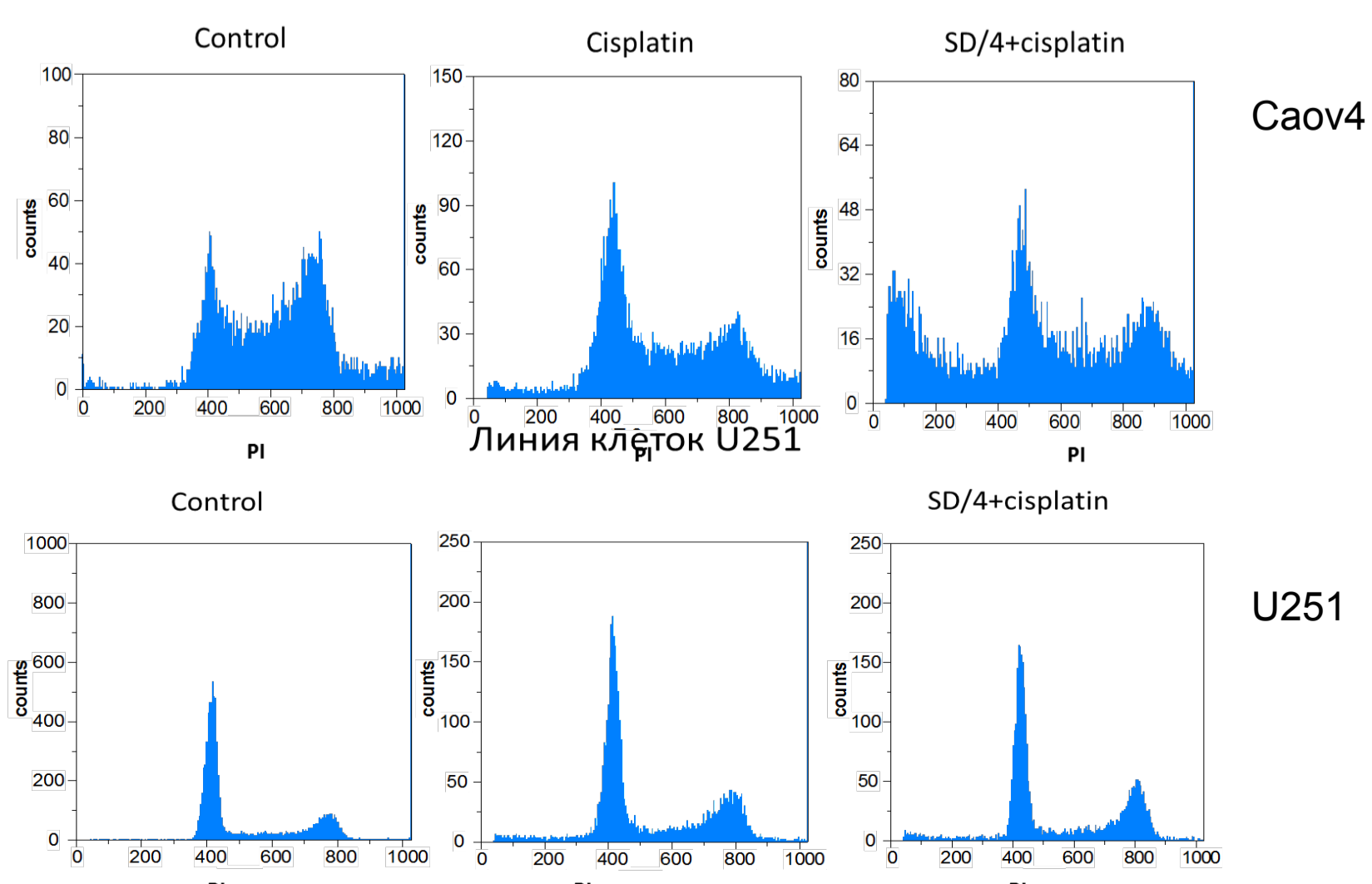
Western blot analysis



cPARP – PARP cleaved by caspase-3
 p37/p32 caspase 2 – active fragments of caspase-2
 GAPDH – protein loading control

Results:

Starvation increases the rate of apoptotic cell death upon DNA damage



Conclusions:

1. Chemotherapeutic drug cisplatin induces programmed death of cancer cells lines Caov4, HeLa, U251
2. Starvation enhances cytotoxic effect of cisplatin:
 - the fraction of apoptotic population is increased (SubG1)
 - the activity of initiator and effector caspases is enhanced
 - apoptotic markers appear
3. The biggest effect was observed when starvation (SD/4) was combined with cisplatin treatment
4. Instead of supper walk a mile ☺