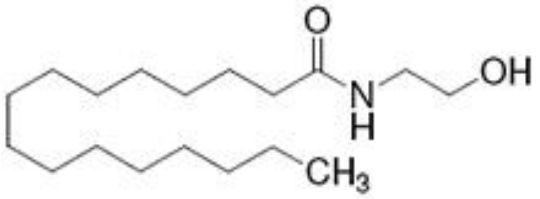
Antiproliferative effects of palmitoylethanolamide on human cervical cancer cells

Laura Bonfili

University of Camerino

ITALY

PEA



- Palmitoylethanolamide (*N* -palmitoylethanolamine or PEA) is an endogenous fatty acid amide belonging to the *N*-acylethanolamine (NAE) class of signalling molecules.

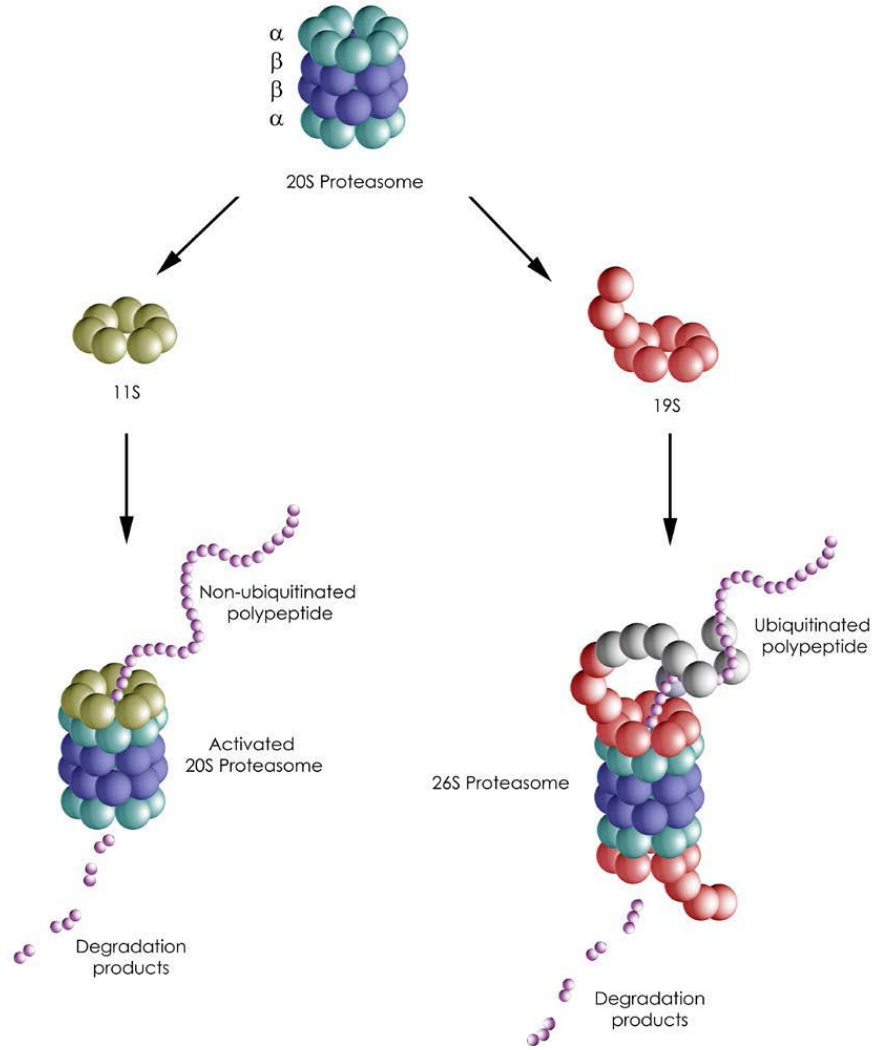
- PEA was identified as a potent and novel analgesic and anti-inflammatory agent, thus representing a promising molecule in the treatment of chronic pain and inflammation

- PEA mechanisms of action have not been completely defined

The proteasome

The ubiquitin-proteasome system is the main extra-lysosomal proteolytic pathways and it is involved in the removal of inflammatory proteins, cell cycle regulators, oxidized and misfolded proteins.

The modulation of the proteasome functionality represents an established target in a number of pathologic conditions such as cancer, neurodegenerations and inflammation.

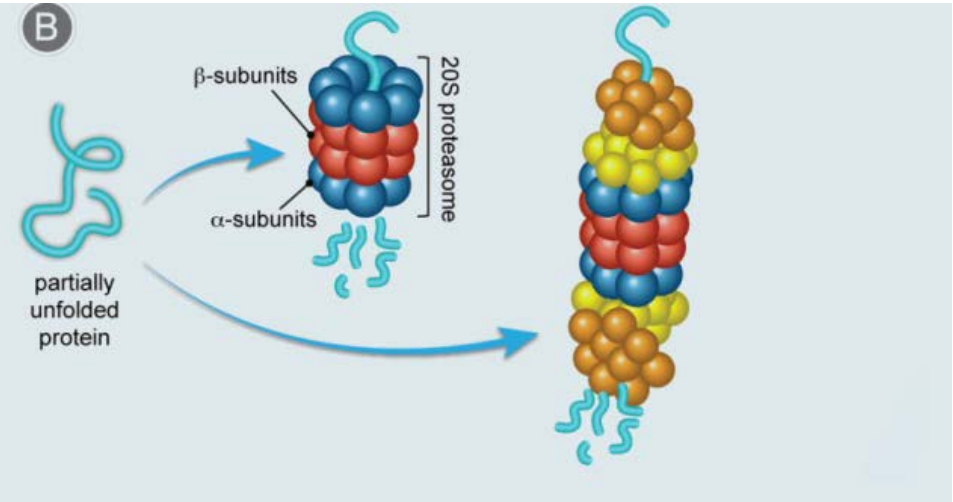


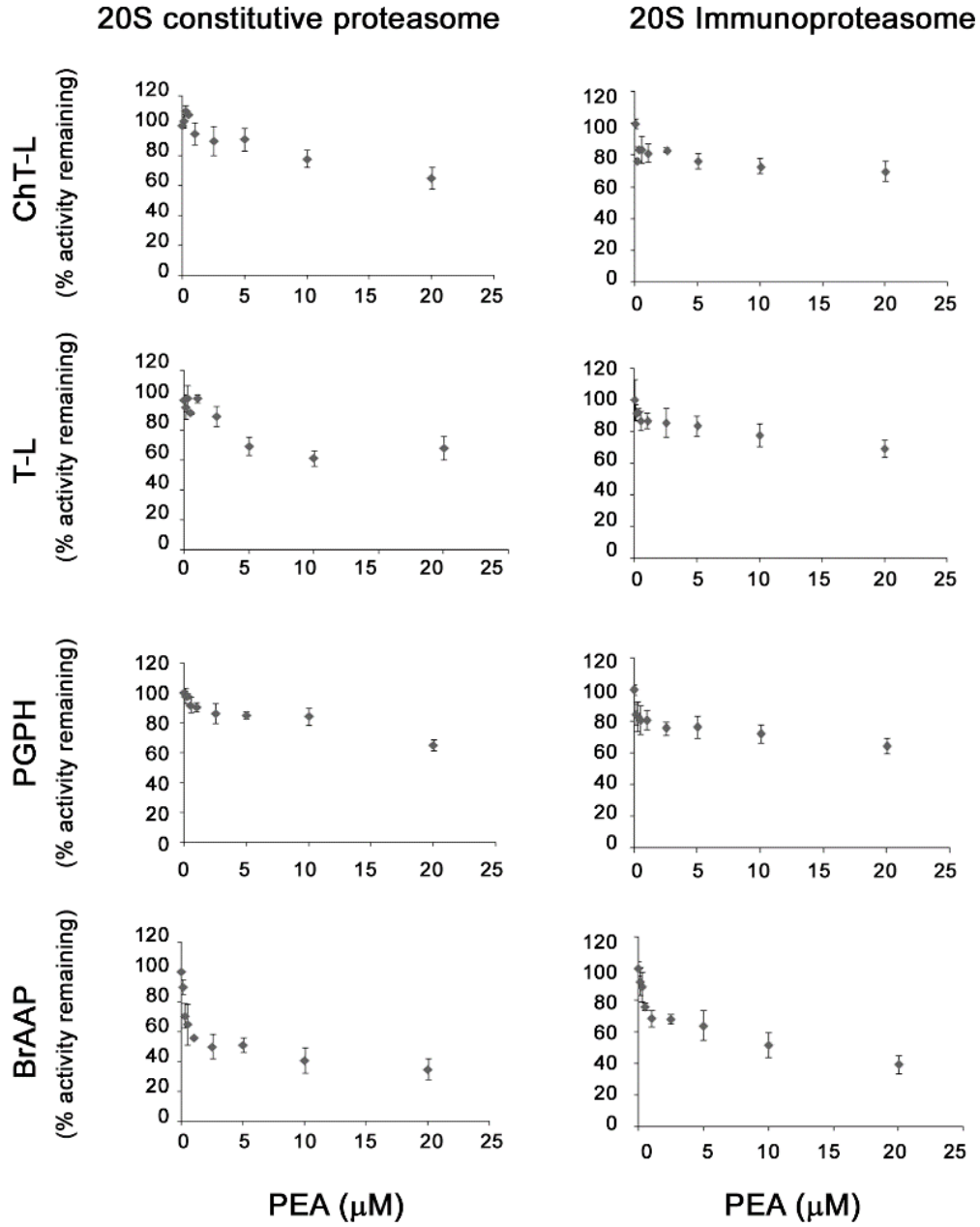
AIM of the STUDY

The cytotoxic effect of PEA on tumor cells via proteasome inhibition has been explored:

- At first, we studied the effect of different concentrations of PEA on isolated constitutive and immuno-proteasomes.
- Successively, human cervical carcinoma cells were chosen as a model to measure PEA effect on tumor cell viability.
- The effect of PEA on the proteolytic activities of cellular proteasomes was evaluated and the expression level of several proteasome substrates were determined.
- Additionally the apoptotic pathway has been explored

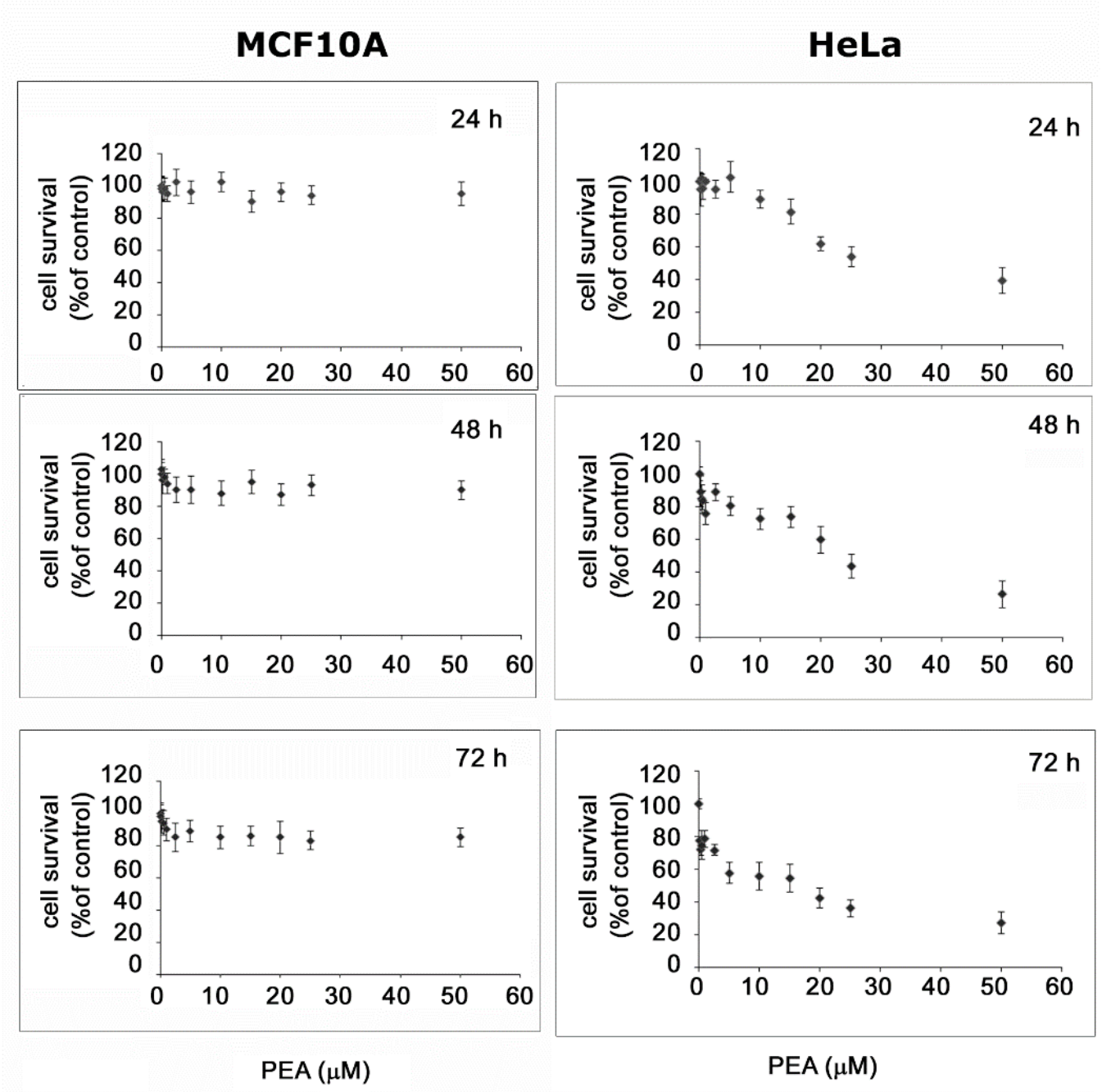
20S proteasomes activities are inhibited *in vitro in the presence of PEA*



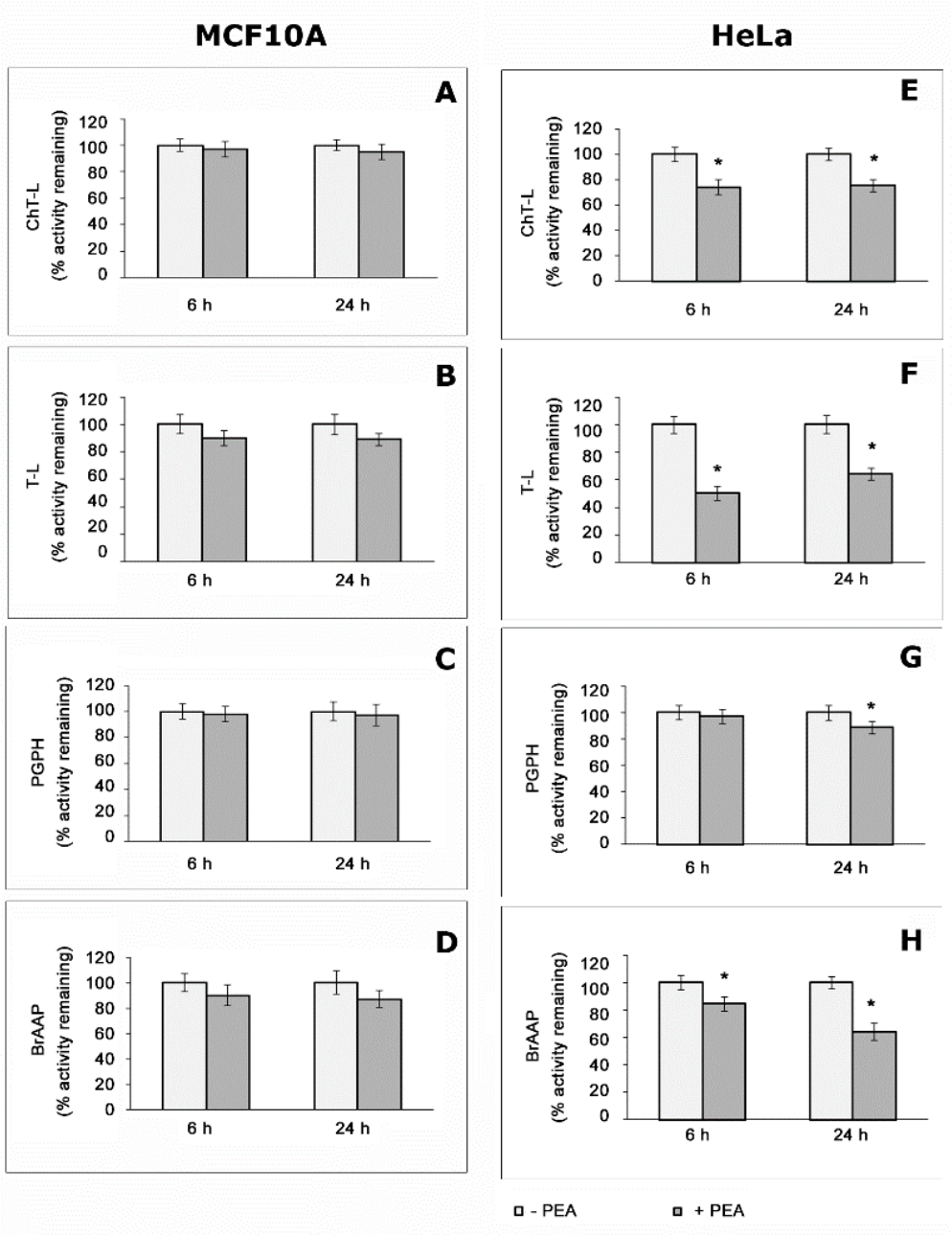


PEA cytotoxicity on tumour cells:

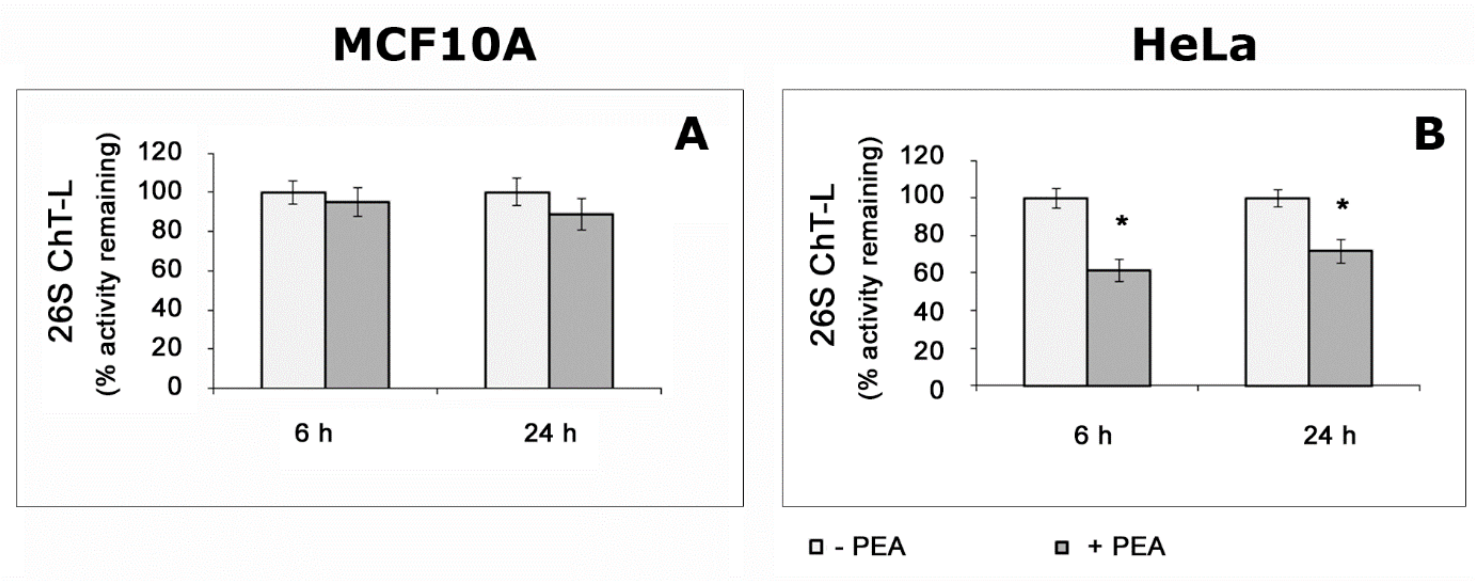
HeLa cells viability decreased upon PEA exposure

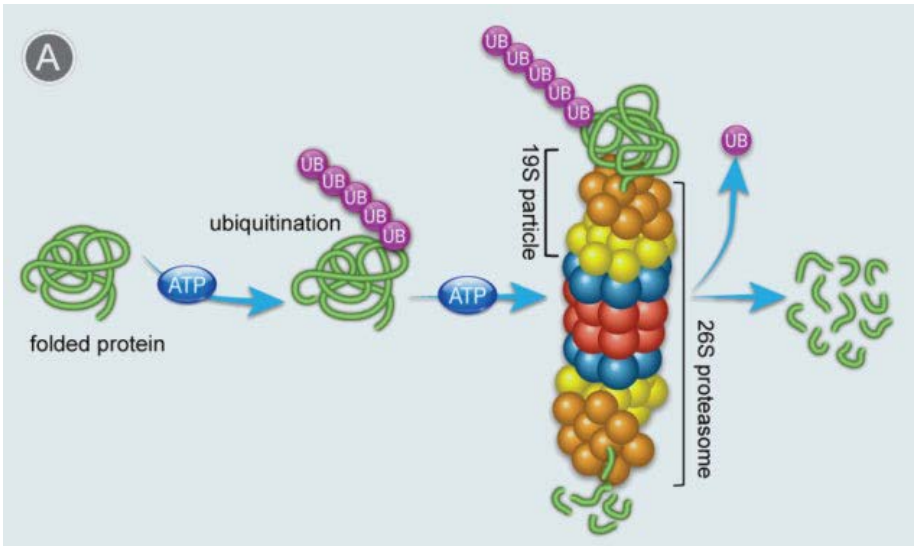


Inhibitory effects of PEA on tumour cells proteasomes

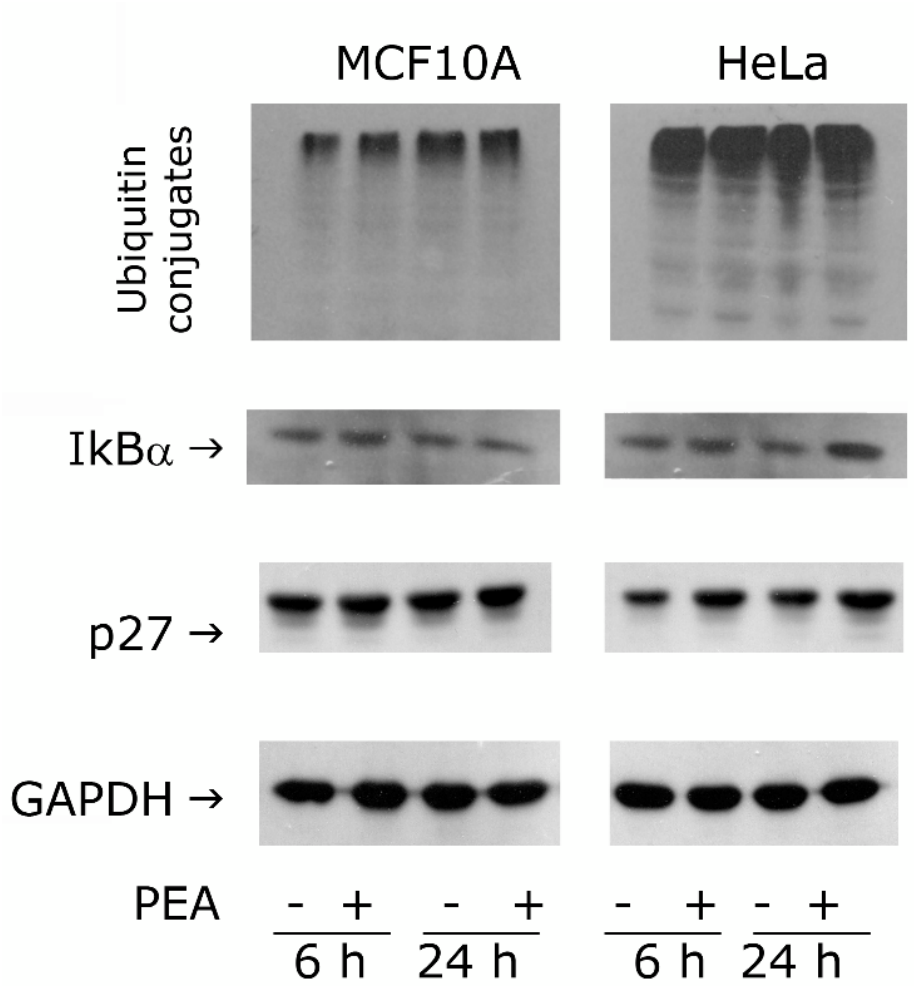


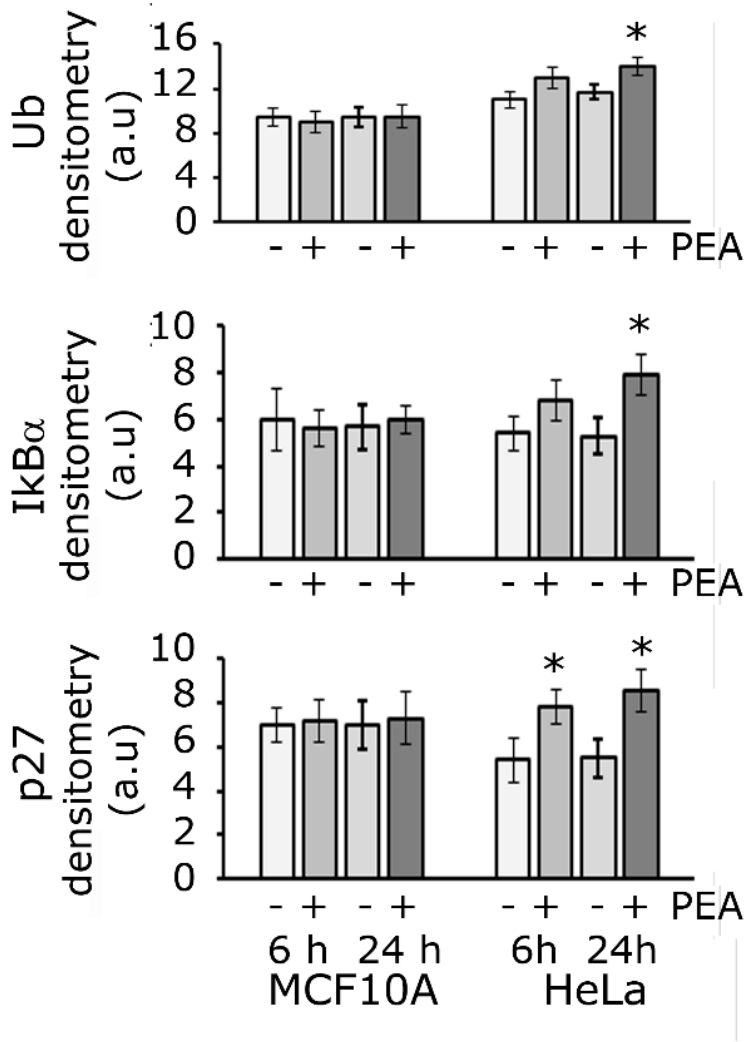
26S proteasome ChT-L activity is inhibited by PEA in HeLa cells



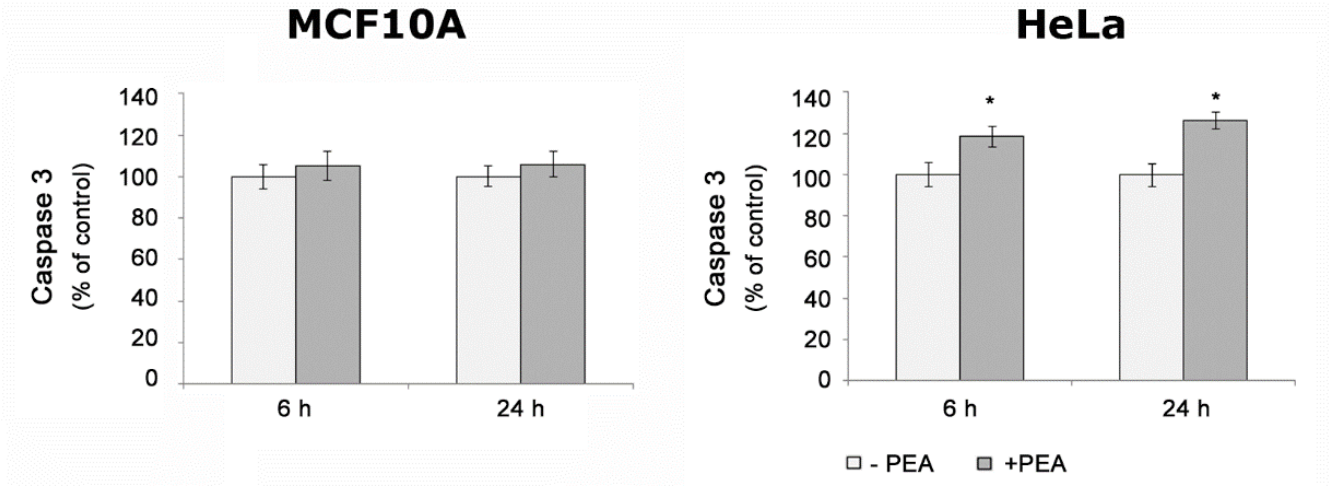


PEA-dependent proteasome inhibition





PEA triggers apoptosis in tumour cells



Conclusions

- An additional mechanism of PEA action is described, precisely the induction of proteasome inhibition.
- PEA can affect tumor cells survival through the activation of apoptosis.
- This finding could represent an important preliminary step in considering PEA as a possible anti-cancer drug, however further studies are needed to better explore the involved pathways