Proteasome inhibitors

Proteasome inhibitors suppress the growth of some tumors. Currently, ***bortezomib*** is used clinically for the treatment of multiple myeloma, or mantle cell lymphoma. The effect on other tumors is being tested.

– Further reading: *Proteasome inhibitors / history*

Although there have already been hundreds of studies devoted to the effects of ***bortezomib*** on the whole organism and on cell cultures, we still do not know why this drug preferentially kills cancer cells and allows healthy cells to live. What is certain is that proteasome inhibition represents a simultaneous intervention in a huge number of cellular events at once. In different tumor cell lines, this drug induces different changes *in vitro*.

– Further reading: *Proteasome inhibitors / studies*

Disadvantages of the therapy

Unfortunately, ***bortezomib*** has some drawbacks: it is **given by injection** and is not very effective against many types of tumors. It generally does not work against solid tumors. Even multiple myeloma cells usually develop resistance to it over time. There is therefore an obvious demand for additional proteasome inhibitors that could bring more benefits to oncology patients and new profits to pharmaceutical companies. **Second-generation 20S proteasome inhibitors** are currently being developed.

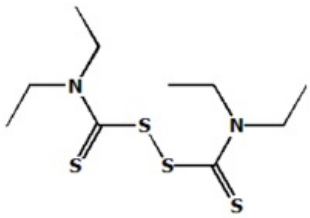
– Further reading: *Proteasome inhibitors / second generation*

Antabuse / Disulfiram

So far, an exotic possibility to influence the ubiquitin-proteasome system is the **inhibition of deubiquitinases**. In 2007, Poh1 was proposed as one of the promising targets of antitumor therapy. It is a deubiquitinase that cleaves a polyubiquitin chain from a protein bound to the 26S proteasome[1].

The use of a drug that has been used for decades in the **treatment of alcoholism** is being considered. Antabus® (disulfiram) can inhibit Poh1 and other JAMM domain DUBs. An overview of the entire issue can be found in the publication [2]. The actual inhibitor is most likely ***dithiocarb***, a **metabolite of disulfiram**, in a complex with copper.

– Further reading: *Proteasome inhibitors / disulfiram (Antabuse)*



Disulfiram (Antabuse) structure

References

Related articles

- Proteins
- Degradation of proteins
- Ubiquitination
- Deubiquitination
- Ubiquitin-proteasome system / history
- Proteasome
- Translation

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