

## How to reduce side effects of cancer drugs?

### Abstract (600 word limits)

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**Statement of the Problem:** Asparaginase-based drugs are highly successful (up to 97%) against childhood acute lymphoblastic leukaemia (ALL), however, they occasionally induce a serious side effect Acute pancreatitis (AP) that often forces to discontinue the treatment. AP is a potentially deadly disease with no specific therapy in the clinic. Previous investigations into the mechanisms of AP (recently reviewed in Petersen et al 2021) established that intracellular ATP loss is a crucial factor exacerbating calcium overload and necrosis. We have recently reported that glucose metabolism and hence ATP production are severely inhibited under AP conditions. Severe ATP loss and calcium overload potentiate each other leading to massive necrosis.

We have suggested supplementing glucose with galactose and found both significant and substantial reductions of all crucial hallmarks of asparaginase-induced AP in vitro and in vivo.

**Conclusion & Significance:** Galactose as an oral supplement effectively protects pancreas in different models, including asparaginase-induced mouse model of AP. Galactose supplementation has been shown also to increase ATP levels in control cells, suggesting that its use is not limited to AP cases. Available data suggest that galactose oral supplementation can be used to reduce side effects of asparaginase-based drugs for ALL and potentially other cancer drugs where ATP loss and necrosis limit their therapeutic potential.

### Biography (200 word limit)

Oleg Gerasimenko is a Reader at Cardiff School of Biosciences, Cardiff University, UK. Fellow of The Physiological Society, UK. Received his PhD from Bogomoletz Institute of Physiology Ukrainian Academy of Science in 1991. Lecturer from 2000 and Reader from 2005 at The University of Liverpool, UK. He has published 93 papers in reputed journals (8474 citations by Google Scholar, h-index 47). Has been serving as an Editorial board

member of several journals: Scientific Reports, Cells and Pflügers Archiv - European Journal of Physiology.

#### References (With Hyperlink)

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