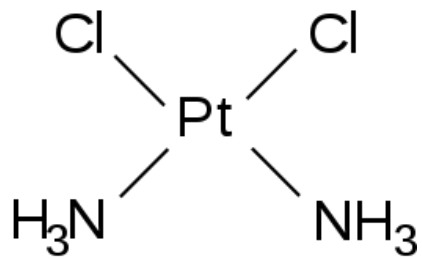


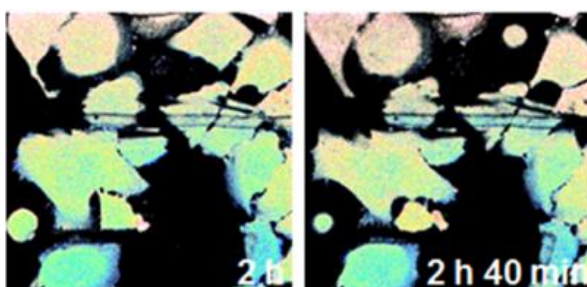
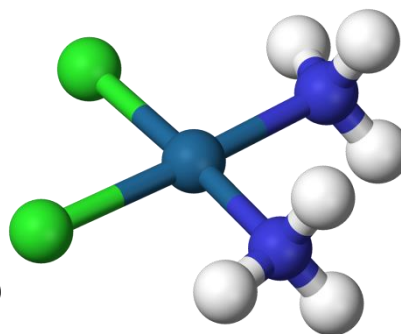
Research (What is it about?)	Unknown biochemistry of the well known anti-cancer drug
UNN authors	<i>Lukina M., Dudenkova V.</i>
We find (The result)	It is shown that the action mechanism of one of the main anti-cancer drugs – <i>cisplatin</i> – is expressed in cell cytoplasm <i>acidification</i> . The ability of cell to maintain alkaline medium defines its further fate: division or death
Abstract	<p><i>Cisplatin</i>, cisplatinum, or <i>cis</i>-diamminedichloroplatinum, is a well-known chemotherapeutic drug. It is effective against various types of cancers but it is possessed of many serious side effects what influences the strategy of its application. While knowing its action mechanism this strategy may be more effective. In particular resistance to this drug remains a major obstacle in chemotherapy.</p> <p>It is generally accepted that the cytotoxicity of cisplatin is determined primarily by its DNA adducts. DNA damage arrests the cell cycle, inhibits transcription, and initiates cell death. However, recent studies suggest that cisplatin has multiple cellular targets beyond nuclear DNA. Consequently, cell response to cisplatin cannot be fully described in terms of only DNA adduct formation, but can include multiple drug-induced physiological changes. Uncovering the mechanism and targets of cisplatin action can be a key to the understanding of its cytotoxicity and resistance and leads to the development of new therapeutic strategies.</p> <p>The use of <i>genetically encoded acidity sensors</i> allowed us to show for the first time that cisplatin induces <i>acidification of the cytoplasm</i> early after the treatment. We revealed <i>in vitro</i> that a capacity of cells to recover and maintain alkaline balance after the initial acidification is the crucial factor in mediating the cellular decision to survive and proliferate at a vastly reduced rate or to undergo cell death. We showed <i>in vitro</i> that acidification occurs after prolonged therapy, and this, likely, favors metabolic reorganization of cells.</p> <p>A metabolic shift from glycolysis towards oxidative metabolism accompanied the cisplatin-induced inhibition of cancer cell growth <i>in vitro</i> and <i>in vivo</i>.</p>

Representative articles 2017-2018, quartiles	1. <i>Shirmanova M.V., Druzhkova I.N., Lukina M.M., Dudenkova V.V., Ignatova N.I., Snopova L.B., Shcheslavskiy V.I., Belousov V.V., Zagaynova E.V.</i> Chemotherapy with cisplatin: insights into intracellular pH and metabolic landscape of cancer cells <i>in vitro</i> and <i>in vivo</i> . <i>Sci. Reports.</i> 7 :8911 (2017).	Q1
Q-index (Qi) for the result		4
high blue		

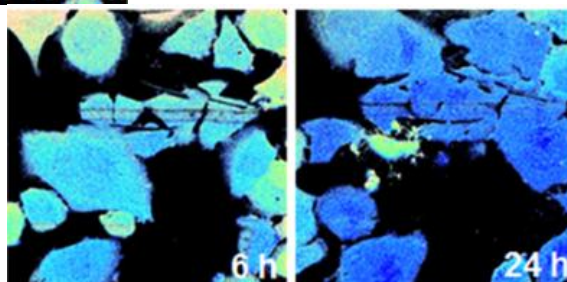
In collaboration	Privolzhsky Research Medical University, Nizhny Novgorod 603005, Russia Shemyakin–Ovchinnikov Institute of Bioorganic Chemistry RAS, Moscow 117997, Russia Becker & Hickl GmbH, Berlin 12277, Germany
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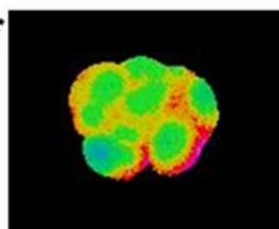
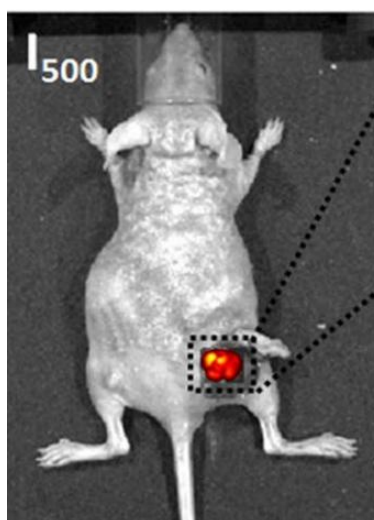
Cis-diamminedichloroplatinum (*cisplatin*)



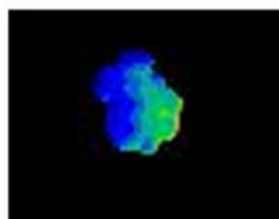
The dynamics of acidification and death in cell ensemble under the action of cisplatin.



Fluorescent visualization of tumor



Without treatment



Cisplatin therapy