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The effect of Daunorubicin on lysosomal capacity in cancer cells

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The main reason for the failure of chemotherapy for cancer patients is the emergence of resistance to various drugs (MDRs). Cancer cells with MDR phenotype are characterized by insensitivity to the anticancer drugs that are structurally unrelated and have a different mechanism of action. One possible mechanism of MDR is the lysosomal sequestration of hydrophobic weak-base drugs (a number of anticancer drugs), which leads to reduced availability of the drug at the target site. It was reported that incubation of cells with low concentrations of hydrophobic weak-base drugs for several day's results in extensive biosynthesis of lysosomes what further increased drug resistance. Here we studied the effect of three-day incubation with daunorubicin (50 nM DNB) on the lysosomal capacity of human leukemic cells K562. DNB-treated cells showed increased lysosomal capacity as judged from the increased staining with lysosomotropic probe. Similarly, LC/MS/MS analysis of extracts from DNB incubated cells revealed increased lysosomal accumulation of tyrosine kinase inhibitors (TKI) compared to uninfluenced cells. These results together indicated the expansion of the lysosomal compartment in response to DNB treatment. We also addressed the question, whether lysosomal expansion is associated with lysosomal biogenesis. However, western blot analysis of lysosomal protein expression (LAMP1, LAMP2 and ATPase subunit V) did not show any change in DNB-treated cells. The cell cycle analysis and cell morphology examination showed that DNB induces cell cycle arrest in the G2/M phase of the cell cycle. Such cells doubled the DNA content, and also roughly doubled the number of other organelles, including lysosomes. In conclusion, our data show that cell pretreatment with DNB does not lead to biogenesis of lysosomes but it is associated with cell cycle modulation.

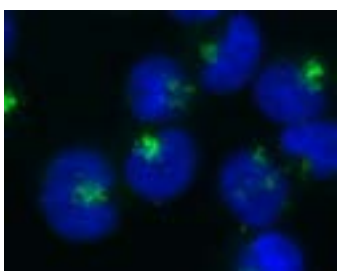

Fig 1: Control

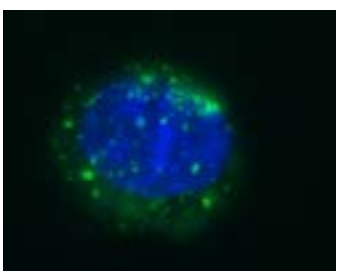

Fig 2: 50nM DNB; 3days

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Biography

Nikola Pastvova is pursuing her PhD in the Institute of Anatomy at Palacky University in Olomouc. Meanwhile, she is the first author of one paper in *International Journal of Molecular Sciences*. In 2016, she took part in a conference in Lugano, Switzerland. Her research is focused on the study of multidrug resistance of cancer cells.

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