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<AT>Metabolic pathway of 4-pyridone-3-carboxamide-1β-D-ribonucleoside and its effects on cellular energetics

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**<ABS-HEAD>Abstract**

<ABS-P>**4-pirydone-3-carboxamide-1β-D-ribonucleoside (4PYR) is an endogenous nucleoside that could be converted to triphosphates, diphosphates, monophosphates and an analogue of NAD – 4PYRAD. Elevated level of these compounds were observed in chronic renal failure, cancer and active HIV infection. However, little is known about the effect on cell functionality and the metabolic pathways. This study tested effects of 4PYR in different cell types on nucleotide and energy metabolism and clarified enzymes that are involved in conversions of 4PYR.**
<ABS-P>**We found that human neuroblastoma cells, human malignant melanoma cells, human adipose-derived stem cells, human bone marrow-derived stem cells, human dermal microvascular endothelial cells and human embryonic kidney cells, were capable to convert 4PYR in to its derivatives. This was associated with deterioration of cellular energetics. Incubation with 4PYR did not affect mitochondrial function, but decreased glycolytic rate (as measured by extracellular acidification) in endothelial cells. Silencing of adenosine kinase, cytosolic 5'-nucleotidase II and nicotinamide nucleotide adenylyltransferase 3, blocked metabolism of 4PYR. Incubation of endothelial cells with 4PYR decreased AMP deaminase activity by 40%.**
<ABS-P>**The major finding of this paper is that human cells (including cancer type) are capable to metabolise 4PYR that lead to deterioration of energy metabolism, possibly as the consequence of inhibition of glycolysis. This study identified also that several enzymes of nucleotide metabolism could also be involved in conversions of 4PYR.**
<KWD>Abbreviations: A375, human malignant melanoma cells; ADA, of adenosine deaminase; AK, adenosine kinase; AMPD, AMP deaminase; CD 31, platelet endothelial cell adhesion molecule; CD44, CD44 antigen; CD 45, receptor, type tyrosine-protein phosphatase; CD73, 5'-nucleotidase; CD 90, Thy-1 membrane glycoprotein; CD 105, endoglin; CHRF, chronic renal failure; cN-IA, cytosolic 5'-nucleotidase IA; cN-IB,cytosolic 5'-nucleotidase IB; cN-II, cytosolic 5'-nucleotidase II; cN-IIIA, cytosolic 5'-nucleotidase IIIA; cN-IIIB, cytosolic 5'-nucleotidase IIIB; 2-DG, 2-