UKE Paper of the Month March 2012

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Proteomic profiling of germ cell cancer cells treated with aaptamine, a marine alkaloid with antiproliferative activity

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ABSTRACT: Aaptamine is a marine natural compound isolated from the sponge Aaptos aaptos showing antiproliferative properties via a largely undefined mode of action. We analyzed the effects of aaptamine treatment on the proliferation and protein expression of the pluripotent human embryonal carcinoma cell line NT2. Effects on proliferation, cell cycle distribution, and induction of apoptosis were analyzed. At lower concentrations, including the IC50 of 50 μM, aaptamine treatment resulted in a G2/M phase cell cycle arrest, whereas at higher concentrations, induction of apoptosis was seen. Differentially expressed proteins were assessed by 2D-PAGE and mass spectrometry, followed by verification and analysis of protein modifications of the most significantly up- and down-regulated proteins. Aaptamine treatment at the IC50 for 48 h resulted in an alteration of 10 proteins, of which five each showed up- and down-regulation. Changes in the 2D map were frequently noticed as a result of post-transcriptional modifications, e.g. of the eukaryotic initiation factor 5A (eIF5A). Observed alterations such as increased expression of CRABP2 and hypusination of eIF5A have previously been identified during differentiation of pluripotent cells. For the first time, we describe changes in protein expression caused by aaptamine, providing valuable information regarding the mode of action of this compound.

STATEMENT: *Marine natural compounds are considered a rich source of future drugs. Substances isolated from marine life forms are increasingly being studied with regards to their anticancer activity. Our paper for the first time describes changes observed in cancer cells treated with aaptamine, a marine alkaloid isolated from the sponge Aaptos aaptos. We show that aaptamine exerts growth inhibitory properties in germ cell cancer cells at low concentrations, and induces apoptosis at higher concentrations. Using a proteomics screening approach, we were able to identify pathways involved in the bioactivity of the substance. In particular, we unravel increased hypusination of the eukaryotic initiation factor eIF5A as a prominent feature of aaptamine action*

BACKGROUND: This paper stems from a cooperation between the Pacific Institute of Bioorganic Chemistry (PIBOC), Vladivostock, Russia, and the Department of Oncology of the UKE. The first author, S. Dyshlovoy, has received a DAAD scholarship for a research period at the Laboratory of Experimental Oncology, led by F. Honecker at the UKE. Furthermore, laboratories from the Heinrich Pette Institute and the University of Greifswald were involved in this research project.