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Differential Regulation of *BBC3*/PUMA and *PMAIP1*/Noxa by Ionizing Radiation: A Role for p53

O. A. Kuchur[a], *, P. D. Kuchur[a], D. O. Kuzmina[a], A. V. Zavirsky[b], and A. A. Shtila[a, c]

[a]*Chemistry and Biology Cluster, ITMO University, Saint-Petersburg, 197101 Russia*

[b]*Kirov Military Medical Academy, Saint-Petersburg, 194044 Russia*

[c]*Blokhin National Medical Research Center of Oncology, Moscow, 115478 Russia*

**e-mail: kuchur@scamt-itmo.ru*

The transcriptional factor p53 is a key sensor of ionizing radiation. A plethora of p53 regulated genes include *BBC3* and *PMAIP1* that encode the pro-apoptotic proteins PUMA and Noxa, respectively, as well as the cell cycle inhibitor *CDKN1A*/p21. The balance of these mechanisms is decisive for the fate of irradiated cells. Using the human colon carcinoma cell line HCT116 (wild type p53) and its isogenic subline HCT116p53KO (non-functional p53) we here demonstrate that therapeutic doses of γ-irradiation predominantly induced *BBC3*/PUMA and *CDKN1A*/p21 but not *PMAIP1*/Noxa in a p53-dependent manner. A bioinformatics analysis of the full-length genome sequences identified a striking difference between the predicted p53 binding motifs in the *BBC3* and *PMAIP1* genes. Our results are applicable for the design of targeted tools aimed at p53-dependent activation of pro-apoptotic genes along with the limitation of the cell cycle arrest in irradiated tumor cells.

Keywords: p53, PUMA, Noxa, p21, ionizing radiation, tumor cells, radiosensitivity, cell death