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<th>Radiation Response Protein, Sialyltransferase (ST6Gal I)</th>
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Ionizing radiation increases ST6Gal I expression

Sialic acids, nine carbon acidic sugars bearing negatively charged at physiological pH, are known to be ubiquitously expressed on the non-reducing ends of the sugar chains of glycoproteins and glycolipids in tissues. They are known to be key determinants for a large variety of biological processes, including cell-cell communication, immune defense, tumor cell metastasis and inflammation.1 The β-galactoside α(2, 6)-sialyltransferase (ST6Gal I) has been identified as being able to catalyze the α(2, 6)-sialylation of N-acetyllactosamine. Since our previous study indicated that mRNA expression levels of ST6Gal I in the mouse spleen and intestine were increased by whole body irradiation, we confirmed these findings in the mouse spleen system. Induction of ST6Gal I at both the mRNA and protein levels was observed following whole body radiation with a dose of 1 Gy.2 Additionally, induction of other sialyltransferase mRNAs such as ST8Sia I, ST3Gal I, ST3Gal II, ST3Gal III, and ST3Gal IV were also observed in the spleen following irradiation of the mice, suggesting that radiation exposure increased the expression of a variety of sialyltransferase genes.

Sialylation of integrin β1 by irradiation

Recently we identified β-galactoside α(2, 6)-sialyltransferase (ST6Gal I) as a candidate biomarker for ionizing radiation. The expression of ST6Gal I and the level of protein sialylation increased following radiation exposure in a dose-dependent manner. We also found that radiation induced ST6Gal I cleavage and the cleaved form of ST6Gal I was soluble and secreted. Sialylation of integrin β1, a glycosylated cell surface protein, was stimulated by irradiation and this increased its protein stability. Overexpression of ST6Gal I in SW480 colon cancer cells that initially showed a low enzyme activity of ST6Gal I increased the sialylation of integrin β1 and also increased the stability of the protein. Inhibition of sialylation by transfection with neuraminidase or by treatment with short interfering (si) RNA targeting ST6Gal I (Si-ST6Gal I) reversed the effects of ST6Gal I expression. In addition, ST6Gal I overexpression increased oncogenic survival following radiation exposure and reduced radiation-induced cell death and caspase 3 activation. In conclusion, we suggest that exposure to ionizing radiation was found to increase sialylation of glycoproteins such as integrin β1 by inducing the expression of ST6 Gal I, and finally protein sialylation contributed to cellular radiation resistance.

Keywords: ST6 Gal I; sialylation; integrinβ1
radiation exposure and sialylated integrin β1 exhibited in vivo. In this study, ST6Gal I induced radioresistance and when transfection with Neu2, inhibition of radiation-induced cell death was examined. Following co-transfection of ST6Gal I overexpression clones with Si-ST6Gal I inhibited by ST6Gal I overexpression. Furthermore, the additional increased clonogenic survival following radiation and reduced radiation-induced cell death. Caspase-3 activation and PARP cleavage followed by ST6Gal I-mediated. To elucidate whether the radioresistance by ST6Gal I was related to sialylation by ST6Gal I, cells were co-transfected with Neu2 and cell death was examined. Following co-transfection with Neu2, inhibition of radiation-induced cell death and caspase 3 activation by ST6Gal I were reversed, suggesting that the ST6Gal I-induced radioresistance was mediated by protein sialylation. ST6Gal I has been suggested to have an important role in oncogenic transformation and metastasis. Increased expression of ST6Gal I has been observed in colorectal cancer, breast cancer, cervical cancer, and choriocarcinoma. However, elevated ST6Gal I inhibited the formation of a glioma in vivo. Therefore, expression of ST6Gal I may have different effects in different cancer types. However, an altered radiation response by ST6Gal I was never suggested. In this study, ST6Gal I induced radioresistance and when Si-ST6Gal I or neuramidase 2 was co-transfected, the increased radioresistance was abolished, suggesting that ST6Gal I-mediated protein sialylation is involved in the radiation response resistance and protein sialylation enables the cell to resist radiation-induced damage through the inhibition of apoptosis. Ionizing radiation causes cancer and metastasis. Therefore, we are now examining the effects of radiation-induced increases in protein sialylation on adhesion and metastasis using sialylation site mutants of integrin β1. Finally, radiation-induced expression of sialyltransferases includes ST6Gal I. Protein sialylation by ST6Gal I has been frequently shown to be higher in cancer cells, is involved in the protein stability of integrin β1, and provides cellular radioresistance, suggesting that protein sialylation might be a novel target to overcome radioresistance in radiation therapy.

Conclusion

In the present study, we observed that radiation exposure increased the expression of ST6Gal I. Our previous study suggested that mRNA expression of ST6Gal I was induced by exposure to a low dose of radiation, specifically in the spleen and intestine, both radiation-sensitive organs. Here, we elucidated the mechanisms of ST6Gal I in the radiation response. From these results, we found that radiation induced expression of sialyltransferases including ST6Gal I. Protein sialylation by ST6Gal I has been frequently shown to be higher in cancer cells, is involved in the protein stability of integrin β1, and provides cellular radioresistance, suggesting that protein sialylation might be a novel target to overcome radioresistance in radiation therapy.

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References


