OPEN ACCESS Freely available online

Journal of Cell Signaling

Commentary

Impact on Stress Signaling Networks of Sphingolipid in Tumor Cells

Amoozgar Svendsen*

Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA

DESCRIPTION

Different tumor ablation therapies, carried out by direct applications of local acute trauma-inducing shock to the targeted lesion with the purpose of its rapid *in situ* annihilation, play increasingly important roles in interventional oncology. These therapies include ones that use high hydrostatic pressure, photothermal, cryoablation, microwave, or radiofrequency energy delivery, non-thermal light (photodynamic therapy), or exposure to an electric field. The weakening of proteostasis caused by a buildup of misfolded/damaged proteins is a common harm caused in tumor cells treated with ablation treatments. Affected cells see this as a trauma that is frequently brought on by thermal or oxidative stress and endangers the integrity and homeostasis at the affected spot. These kinds of stress activate evolutionary well-preserved canonic defense systems based on cellular stress signalling network, which operate to restore the balance of the cell's metabolic activity. In order to activate or inhibit specific biochemical processes, they converse the incoming signal (the appearance of a stressor molecule) onto downstream effector molecules. The purpose of this commentary is to underline those intracellular signalling pathways that are active impact the fate of tumor cells that are involved and, ultimately, how well treatments work.

The stress signalling network is made up of interconnected intracellular signal transduction pathways that offer defense mechanisms for reducing stress challenge, which are expressed as adaptive responses designed to ensure reestablished homeostasis and the survival of affected cells. This is accomplished either by enhancing stress resistance or by lessening the impact of stress with increasing tolerance. The former is achieved by improving the removal of primary stressor molecules that have been produced, whereas the latter is accomplished by minimizing stress damage (for example, by increased protein folding capacity). While the first response to stress trauma is activated to aid the cells in protecting themselves from the insult and recovering from it, the cellular signalling cascades are redirected towards self-destructive programmes leading to cell death or elimination through immunological rejection.

The stress signalling network's signal transduction cascades can be divided into four categories:

- Correcting modifications to gene and protein expression that are intended to halt overall protein synthesis while increasing the expression of proteins that relieve stress, such as protein chaperons and folding enzymes. Heat Shock Response (HSR), Unfolded Protein Response (UPR), Integrated Stress Response (ISR), and antioxidant response are the most well-known of these cell autonomous pathways.
- The involvement of the Sterol Regulatory Element-Binding proteins (SREBs) pathway, which mediates the metabolism of cholesterol and fatty acid metabolism regulation together with the related caspase-1 activity, in order to repair damaged cellular membranes in order to maintain cell integrity.
- Enhancing the ER-Associated protein Degradation response (ERAD), autophagy, as well as apoptosis and other cell death signalling cascades in the elimination of permanently damaged proteins and cells.
- Immunogenic cell death induction and subsequent immune eradication cascades.

UPR/ISR sensor kinases *PERK* and *IRE1,* transcription factor *HSF1* of HSR, and oxidative protein-folding controlling enzyme Protein Disulfide Isomerase (PDI), which actively participates in the UPR and antioxidant response, all play important pro-survival roles in adaptive stress response pathways. Selective inhibitors of these signalling components significantly lower the survival of tumor cells subjected to ablation therapies and may be applied in the clinic to enhance the effectiveness of tumor therapy with these methods.

Cross-talk with the signalling nodes controlling the fundamental cellular metabolism, such as c-Jun Amino-terminal Kinase (JNK) and p38 Mitogen-Activated Protein Kinase (MAPK), further fine-tunes the adaptive stress responses. In turn, the MAPK activity controls the expression of significant master nuclear transcription factors, like *STAT3* and *HIF-1*, allowing them to play crucial roles in the stress response. The effects of *HIF-1* activity on angiogenesis, glucose metabolism, and cell survival have a significant impact on tumor growth. *STAT3* encourages angiogenesis, cell survival, and immunosuppression by similarly altering the tumor microenvironment. In our experiments, the effects of particular *STAT3* and *HIF-1* inhibitors on tumor cells subjected to PDT (as an example of ablation therapy) were

Correspondence to: Amoozgar Svendsen, Department of Radiation Oncology, Massachusetts General Hospital and Harvard Medical School, Boston, MA, USA, E-mail: asvendsen@harvard.edu

Received: 21-Jul-2022, Manuscript No. JCS-22-19303; **Editor assigned:** 26-Jul-2022, PreQC No. JCS-22-19303 (PQ); **Reviewed:** 09-Aug-2022, QC No. JCS-22-19303; **Revised:** 16-Aug-2022, Manuscript No. JCS-22-19303 (R); **Published:** 23-Aug-2022, DOI: 10.35248/2576-1471.22.07.299

Citation: Svendsen A (2022) Impact on Stress Signaling Networks of Sphingolipid in Tumor Cells. J Cell Signal. 7:299

investigated. NSC 74859, a benzoic acid derivative that specifically inhibits *STAT3* activation, dimerization, and DNA-binding activity, and LW6, an aryloxyacetylaminobenzoic derivative that facilitates *HIF-1* degradation, were both put to the test. Both inhibitors dramatically decreased the survival of tumor cells treated with PDT at dosages that displayed no discernible harm when used alone. The pro-survival function of *STAT3* and *HIF-1* in cells responding with PDT-mediated stress is revealed by this research. Their inhibitors are excellent candidates for use as adjuvants in PDT and other ablation therapies to enhance the therapeutic results. Importantly, cells treated with PDT and exposed to the ceramidase inhibitor LCL521 showed an even greater loss in survival. According to studies, sphingolipid activity plays a significant role in cellular stress signalling. Due to their influence on the genes regulating the metabolism of these lipids, PDT and other stress-inducing treatments have been demonstrated to have a significant impact on the sphingolipid profile in treated tumors.