Negative Pressure Wound Therapy: Cancer Metastasis Stimulated by HIF-1ALPHA Regulated MALAT1 and SOX Cooperation

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Negative-pressure-wound-therapy (NPWT), a wound-closure technique used following tumor resection has been suggested to promote metastasis. As this claim isn't well established and the molecular mechanism is elusive, NPWT still remains widely utilized. Novel interactions between noncoding-RNAs (i.e. MALAT1) and transcription-factors (i.e. SOX) may reveal this missing link in metastatic physiology. This study's objectives were to investigate (1)NPWT-specific MALAT1-SOX cooperation and activation of metastatic genes, (2)the effect of NPWT-induced wound healing factors (i.e. HIF-1α) on metastatic MALAT1-SOX cooperation, and (3)the precise role of MALAT1-SOX cooperation in negative pressure (NP)-induced cancer migration. NPWT increased RT-qPCR expression of MALAT1 and SOX(2,5,9) by over two-fold ($p<0.01$). Upon NPWT, MALAT1 uniquely bound to and regulated expression of SOX(2,5,9) ($p<0.05$), increasing expression of downstream metastatic Wnt genes (61-68%; $p<0.05$). Also, upon NPWT, HIF-1α stimulated MALAT1-SOX expression (65-77%; $p<0.05$) and binding (52-81%), highlighting NPWT-specific HIF-1α activation of MALAT1-SOX cooperation and subsequent metastasis. NP-induced migration of cancerous cells was significantly diminished upon decreased MALAT1-SOX binding. Thus, NPWT-induced HIF-1α expression activates MALAT1-SOX cooperation to further induce metastasis. This study, for the first time, establishes and brings awareness to the detrimental effects of NPWT on cancer patients and delineates a novel underlying molecular pathway for NPWT-induced metastasis. Future investigations involve interrupting MALAT1-SOX binding, through specific drug-mediated inhibition of the MALAT1 promoter. This would prevent metastatic progression and allow for NPWT to remain a viable treatment option.

Awards Won:

Fourth Award of $500