

Connexin 43 and Ewing Sarcoma: Stay Tuned

Marilyn M. Bui¹, Damon Reed² and David L. Becker³

¹ Moffitt Cancer Center

Received: 11 February 2013 Accepted: 4 March 2013 Published: 15 March 2013

Abstract

To the editor: In our study¹ published in Sarcoma in 2011, we found that Connexin 43 (Cx43) was frequently (78

Index terms— Connexin 43 and Ewing Sarcoma: Stay Tuned Marilyn M. Bui ? , David L. Becker ? & Damon Reed ? o the editor: In our study¹ published in Sarcoma in 2011, we found that Connexin 43 (Cx43) was frequently (78%) expressed in the 36-Ewing sarcoma (ES) patient tissue microarray specimens. Most interestingly, a higher level of Cx43 overexpression was correlated with adverse clinical outcome and shorter survival regardless of tumor stage, location, tumor size and clinical management. Positive score of Cx43 was significantly correlated with reduced overall survival ($p=0.02$). The average positive Cx43 scores for patients alive and dead at 3 years was 46.08 and 96.98 ($p=0.004$) at 5 years was 46.06 and 96.43 ($p=0.02$) respectively. Recently, a study published in Biochimicaet Biophysica Acta² demonstrated that expression level of Cx43 was repressed by EWS-FLI1, Cx43 gene expression was associated with the gap junction intercellular communication changes and Cx43 inhibits ES growth via modulation of cell proliferation via p27. Surprisingly, ES overexpression of Cx43 reduced tumor growth and was associated with better survival. Although these two studies show different prognostic values regarding to Cx43 and ES, both confirm that Cx43 has a potential role in ES tumorigensis and prognosis. While there is a larger effort to study the association of Cx43 with other cancers such as carcinoma, melanoma and hematopoietic malignancy, the need for further studies of Cx43 and ES cannot be overemphasized. ES is the second most common bone tumor in children and adolescents and also can arise in the soft tissue. If the tumor is not metastatic, with surgery, chemotherapy and radiation therapy, patients have a 75% chance of 5-year survival. However, there is only 20% 5-year survival for metastatic ES. Drs. Becker and Mendoza-Naranjo have preliminary data showing that Cx43 is largely up-regulated in a panel of metastatic/chemoresistant ES compared to primary ES cell lines which would support the clinical association we found in our work. In addition, the silencing of Cx43 reduces tumor growth and survival in metastatic ES cells. More effort should be invested to investigate the biology of Cx43 and ES, especially for metastatic ES. The ultimate hope is to discover potential novel targeted therapy that can improve the outcome of this devastating disease. We are looking forward to more exciting results in this field. We are hopeful and stay tuned. ¹

¹Connexin 43 and Ewing Sarcoma: Stay Tuned

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