Pseudomonas aeruginosa Exotoxin T (ExoT): A Viable Cancer Therapeutic

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Abstract:

Breast cancer is the most frequently occurring cancer in women with one in eight women in the United States expected to be diagnosed with breast cancer during their life. This high rate of incidence makes breast cancer the leading cause of mortality from cancer in women. Treatments for most patients include a combination of surgery, chemotherapy, hormone therapy, ionizing radiation or administration of biologicals (e.g. herceptin). However, these treatments often fail and a significant number of women are faced with the prospect of metastatic disease. Despite significant improvements in the treatment of metastatic breast cancer, the 5-year survival rate is still less than 50%. Chemotherapy is the most common approved therapy for metastatic breast cancer but it frequently fails to provide long-term control of breast cancer. Innovative therapies are needed to successfully treat primary breast tumors and prevent breast tumor metastases. We hypothesize that Pseudomonas aeruginosa Exotoxin T possesses unique properties that make it an ideal candidate to be used alone or in combination therapy to eradicate and prevent breast cancer metastases. These properties include: (1) its potent cytotoxicity against highly resistant and metastatic cacer cells; (2) its ability to prevent Apoptotic Compensatory Proliferation Signaling; (3) its anti-proliferative impact on various tumor cells; (4) its ability to inhibit tumor cell migration; and (5) its potential to induce durable and systemic anti-tumor immunity.

Biography:

Dr. Shafikhani is an Associate Professor in the Department of Medicine, Division of Hematology, Oncology, and Cell therapy at Rush University Medical Center. Dr. Shafikhani's group is interested in understanding how the presence of tumor and infection lead to a state of immune-confusion affecting both anti-tumor and anti-bacterial immune defenses. His group is also interested in developing bacterial toxins as effective anti-cancer therapeutics. His group is also interested in innate immune dysregulation that renders diabetic wounds vulnerable to infection.

Publication of speakers:

1. Kaminsky, A., Gupta, K., Goldufsky, J., and Shafikhani, S.H. (2018). The GAP domain of ExoS is necessary and sufficient to induce intrinsic apoptosis. Sci Rep. 2018 Sep 19;8(1):14047.
2. Gupta, K., Goldufsky, J., Wood, S., Tardy, N., Moorthy, G. S., Gilbert, D. Z., Zayas, J. P. Hahm, E., Altintas, M. M., S., Reiser, J., and Shafikhani, S.H. (2017) Apoptosis and compensatory proliferation signaling are coupled by CrkI-containing microvesicles. Developmental Cell, Jun 19;41(6):674-684.
3. Wood, S., Goldufsky, J., Bello, D., Masood, S, and Shafikhani, S. H. (2015) Pseudomonas aeruginosa ExoT induces mitochondrial apoptosis in target host cells in a manner that depends on its GAP domain activity. J Biol Chem. 290:29063-73.

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