Profound Untouchability: The Cocooning of Clinical Data from Fibroblast Growth Factor 16 Regulation (Sp) to Drugs of Cancer Combination Therapy (CTC)

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Physicians who treat patients with a malignant sarcoma (which is a type of human tumor) typically rely on a combination of therapies to increase survival rates. For example, surgery along with radiation therapy and chemotherapy are used to treat this very challenging disease, but most patients will not survive for more than two years after diagnosis, according to the American Cancer Society. The treatment remains frustratingly ineffective even after three different approaches for different indications.

These complications are especially discouraging for family members of these patients and for physicians who want a complete cure for their patients. Additionally, the economic impact of this disease is estimated to exceed $7 billion annually, according to the Dana-Farber Cancer Institute.

Sp was an accidental discovery by members of my lab last year when we decided to evaluate the effects of gene expression profiling on transthyretin (TTR) resistance in patients with TTR amyloidosis. The research team focused on the study of therapeutic genes called Sps in the process of pathologic development of sarcoma and brain tumors, and observed a dramatic reduction in SP expression as you could see in the image below. The research group then turned to the Shashi Nadar-led team to investigate whether this new discovery could lead to an effective therapeutic strategy in an aggressive form of cancer.

The translation of our laboratoryâ€™s findings regarding Sp inhibition in sarcoma into clinical practice is promising, yet the mechanism behind Sp inhibition remains largely unknown. Our understanding of Sp is an enigma. The background biology of Sp is divided into three domains of proteins: Pseudopalynsis, exon sRNA, and protein expression. The authors of the present study presented a number of mechanisms used by Sp to inhibit growth. The most obvious method of inhibition is through block of rhabdomyosarcoma cell and tumor growth. This is done by targeting a diversity of Sp-suppressor genes at various locations and in different forms of mRNA. However, it is important to note that Sp comprises multiple Rnd gene sequences with distinct but overlapping sequences. Each of these Sp genes normally has a well characterized equivalent, including a sequence on a fluorin-fixed polymerase-3 (Fc-3) gene called â€œP-4â€. Yet there were actually two proteins, the newly discovered ALPF8 that produces sRNA and P-4 protein. Therefore, we believe that normal Sp might selectively target these specific proteins. An interesting hypothesis is that the expression of P-4 in tumor cells could be regulating both stem cell growth and tumor cell growth. The same possibility could apply to a variety of other proteins besides Proline not mentioned above.

Our report was accepted for publication in the journal â€œBiology of Cancerâ€ and the results were recently presented at the annual meeting of the British Association of Clinical Oncology. We remain open to applying this new discovery to further malignant sarcoma research.

References:

White, R. W., Chuang, D. A., Garza, B. D., Dugan, T. B., Dagmarovic, B. A., Dragovic, J., Vujanovic, J., Disbrow, D. S., Hartiger, S. R., Serna, M. K., Blumenborg, M. S., Tanoh, B. A., Malambo, S. D., Harik, B. J., Gu, F., Cawin, W. M., Trebecker, G. A., Harrell, M. L., Noonan, J. A., Rokab, L. A., Salvame, R. T., Darbakk, A. D., Madanepalli, G. E., Chau, S. B., Usher, G. E., Park, M. R., Skelton, A. C., Kim, T. B., Sivarthan, S. H., Ehrhardt, D. E., the SpÉ™rÎ± Gulseyn 9-activobacterium seropositors that protect apoptosis.

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A Bird Is Perched On A Tree Branch