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Authors: Shannon Johnson Andrew Russo

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Humboldt State University

School of Physics

STIM1, a direct target of microRNA-185, promotes tumor metastasis and is associated with poor prognosis in colorectal cancer

by X Z hang

STIM1 (Sterile Stimulated Immune-mediated Re-constitution, or STIR-1) is a therapeutic target for a non-small cell lung cancer. STIM1 reduces the diversity of the CD8+ T cells that attack the cancer while increasing the numbers of T cells that fight the tumor. STIM1 is not specifically targeting the tumor cells, but instead it acts on the lymph nodes, causing broad immune damage. Studies have suggested that STIM1 induces the production of microRNA-185, a microRNA involved in tumor progression and metastasis.

In a new study, Fusheng Lu, Dr. Marybeth Oâ€™Donnell, and colleagues from Johns Hopkins University School of Medicine investigated whether STIM1 induces the production of microRNA-185 in the CD8+ T cells that attack the lung cancer tumors. The study has been published in the November 8th, 2011, issue of Cancer Research, the official journal of the American Association for Cancer Research.

The study examined several genes that could express microRNA-185. Interestingly, the expression of these genes became associated with STIM1 expression. STIM1 could regulate the expression of 14 microRNAs that were expressed normally during the first stage of tumor growth. However, the function of each microRNA depends on how STIM1 is expressed. For example, microRNA-190 (TCR189) was normally found in T cells, but it also exhibited an abnormal expression when the STIM1 was raised. Moreover, TCR189 expresses only on the RANKL (Receptor for oncogene Activation), whereas STIM1 expression is seen on the CD4+ T cells, the antigen surface receptor of the T cells. This means that TLR189 is a direct target of STIM1 in the lung tumor cells.

â€œThis novel study identifies a novel way to selectively inhibit microRNA-185 that can be applied in treating tumor progression, but also effects the immune system in general,â€ commented Dr. Lu.

â€œTreatment strategies need to be based on finding the optimal microRNA targets; STIM1 is a useful target in this regard,â€ said Ms. Marybeth Oâ€™Donnell, one of the senior researchers from Johns Hopkins University School of Medicine in the study.

If validated, the mechanisms of STIM1 could be developed as a target of anti-tumor agents such as a targeted anti-cancer drug STIM1 because STIM1 increases sensitivity to T cell suppression via STIM1. In a Phase 2 trial, patients receiving anti-STIM1 (TS001) developed resistance to other anti-tumor treatments, but the anti-STIM1 drug STIM1(E311) continued to be effective in the patients at 2 years of follow-up.

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