Scientists identify molecular factors involved in regulating tumor-causing transcription factors

Authors: Johnny Clements Lisa Brennan Steven Buckley Angel Hamilton Anne Morris

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California Polytechnic State University-San Luis Obispo

School of Chemistry

A team of scientists from the University of British Columbia has determined that a type of transcription factor and mechanisms are at work at the molecular level that regulate tumor-causing transcription factors associated with bone cancer. The research, reported online Dec. 21 in the Proceedings of the National Academy of Sciences (PNAS), may serve as a foundation for developing novel therapeutics to target this cancer.

â€œCancer cells are long-lived, mobile and grow fast â€“ characteristics that make them increasingly difficult to beat,â€ says senior author Jeff Murray, PhD, a researcher at the UBC Cancer Research Centre and the School of Population and Public Health. â€œThe fact that we have been able to identify and quantify the molecular factors involved in proliferation of tumor cells allows us to identify the regulatory changes within a cell that may be driving the immune response to cancer cells, ultimately providing insight into our approaches to cancer treatment.â€

Murray, who is also an associate professor at the UBC Department of Clinical Pharmacology and Physiology, and a member of the UBC/Ulsan Cancer Institute, will present a more detailed summary of the findings at the Christmas meeting of the American Association for Cancer Research in San Francisco on Dec. 27.

The researchers were able to establish the specific molecular interaction between a transcription factor and the cell pathway governing inflammation by looking at the secretion of a transcription factor from circulating tumor cells. In acute lymphoblastic leukemia, as in other forms of cancer, an abnormal activation of inflammatory cells called CRF4 leads to the development of tumors. CRF4 regulates transcription factors and, by analyzing the fact that an inactive transcription factor called Gpp-InU12u1 acted in synergy with a high transcription factor called Ki55ub, the team was able to identify the molecular interplay between transcription factors and the occurrence of leukemic cells. They determined that this particular transcription factor, in turn, is identified by other leukemia and other cancer cell-cell infiltrating tumor cells.

The researchers then used this insight to identify the transcription factors activating the protein CRF4 in the diseased bone marrow of mice. They found that the transcription factors associated with this leukemia, Ki55ub and Gpp-InU12u1, are responsible for suppressing DNA repair, which is essential to repair the genomic damage done by cell-signaling molecules such as CRF4. These transcription factors suppress the apoptosis of fast-growing tumor cells and, ultimately, provide the growth signals necessary for tumor cell proliferation and spreading. Because most cancer treatments inhibit apoptosis, they result in failure to kill the cancer cells. They also suggest that targeting the RID, nuclear receptor and CRF4 pathways may be ways to kill fast-growing cancer cells.

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Other authors of the PNAS article include lead author Gayathri Chadalapaka, BSc and PhD candidate; Tao Zhang, BSc; Rudyard Smith, PhD, and Tsun-Ming Kim, postdoctoral fellow; Siu-Mei Lam, Gail Windmiller, and Edward Han, MD, PhD; Tsai-Yuan Zhang, PhD; Andrew Wilson, PhD; Trie Yee and Alok Parida, BSc; and Stephen Safe, PhD.

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A Brown And White Bird Sitting On A Wooden Bench