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A lethal cancer knocked down by one-two drug punch

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In the battle against cancer, allies can come from unexpected sources. Research at The Jackson Laboratory has yielded a new approach to treating leukemia, one that targets leukemia-proliferating cells with drugs that are already on the market.

Jackson Adjunct Professor Shaoguang Li, M.D., Ph.D., who now has a laboratory at the University of Massachusetts Medical School in Worcester, led a research team that identified a gene involved with the inflammatory response that could hold the key to treating or even preventing chronic myeloid leukemia (CML), a lethal cancer.

In research published in the journal *Nature Genetics,* the researchers also showed that an asthma medication for human patients is an effective treatment for CML in mice.

The gene, Alox5, processes essential fatty acids to leukotrienes, which are important agents in the inflammatory response. But according to the researchers, Alox5 has a more sinister side. It is vital to the development and maintenance of cancer stem cells.

Cancer stem cells are slow-dividing cells that are thought to give rise to a variety of cancers, including leukemia, and to be critical for maintaining them. Researchers theorize that cancer stem cells must be targeted for effective treatment of many cancers, but direct evidence is still lacking.

The researchers found that CML did not develop in mice without Alox5

because of impaired function of leukemia stem cells. Also, Alox5 deficiency did not affect normal stem cell function, providing the first clear differentiation between normal and cancer stem cells.

Li also treated mice with CML with Zileuton, an asthma medication that inhibits the Alox5 inflammation pathway, as well imatinib, commonly known as Gleevec, the most effective current leukemia medication. Imatinib effectively treated CML, but Zileuton was more effective. The two drugs combined provided an even better therapeutic effect.

The Jackson Laboratory is seeking patent protection on the novel approach to treat CML that Li and colleagues have demonstrated.

The exact mechanism for the Alox5 gene in regulating the function of leukemia stem cells but not normal stem cells needs further study, but it appears that the two types of stem cells employ different pathways for self-renewal and differentiation. The findings provide a new focus of study into how leukemia stem cells are distinct from normal stem cells and how they can be targeted in cancer therapies. A future clinical trial targeting Alox5 will provide the first anti-stem cell strategy in cancer therapy. It is likely that other cancer stem cells will have specific pathways that also differentiate them from their normal stem cell counterparts.

Source: Jackson Laboratory