# Knocking Out Survival Protein Could Aid Leukemia Treatment

23 April 2007

An effective way to fight leukemia might be to knock out a specific protein that protects cancer cells from dying, a new study shows. The findings suggest that a drug that can block this “survival protein” might on its own be an effective therapy.

But such a drug used in combination with several existing drugs might also offer an effective one-two punch against drug-resistant forms of chronic lymphocytic leukemia (CLL) and acute lymphoblastic leukemia (ALL). The two forms of cancer kill about 20,500 Americans yearly.

The survival protein is called Mcl1. It usually helps keep normal cells healthy and is involved in the development of the components of the immune system, but it can also help prolong survival of cancer cells.

Cells with an overabundance of the protein are also more resistant to anticancer drugs such as rituximab, which has revolutionized the treatment of certain chronic and acute leukemias.

The study by researchers at the Ohio State University Comprehensive Cancer Center is published online in the journal *Clinical Cancer Research*.

“Our findings demonstrate that Mcl1 may be an effective target for drugs directed against CLL and ALL,” says principal investigator John C. Byrd, professor of internal medicine and director of the hematologic malignancies program at Ohio State's James Cancer Hospital and Solove Research Institute.

“These results give us a rationale for lowering the amount of this protein in CLL cells and suggest that this should enhance the action of rituximab and perhaps other agents as well.”

Rituximab is an antibody-based drug that targets CLL and ALL cells and causes the cells to self-destruct.

“We've shown that knocking down Mcl1 can, by itself, cause CLL cells to die, and that this effect might enhance the activity of rituximab,” says first author Rehan Hussain, a postdoctoral fellow with Ohio State's Comprehensive Cancer Center.

Byrd, Hussain and their collaborators conducted this research using cancer cells from 17 CLL patients and ALL cell lines grown in the laboratory.

The investigators placed molecules called small interfering RNA (siRNA) inside the cells and found that the tiny molecules greatly reduced the amount of the survival protein, causing many of the cells to die. The effect was the same even in cells that came from patients with advanced cancer or from patients with tumors that resisted conventional treatment.

When the researchers treated cells with both siRNA and the drug rituximab, the combination killed significantly more leukemia cells than the drug alone.

Overall, says Byrd, “Our data indicate that specifically targeting Mcl1 might be effective in the treatment of CLL, particularly when combined with rituximab.”

Source: Ohio State University