MedicalXpress

New research suggests cutting calories may improve response to cancer treatment

August 21 2013

New research suggests that restricting calories for a defined period of time may improve the success of cancer treatment, offering valuable new data on how caloric intake may play a role in programmed cancer cell death and efficacy of targeted cancer therapies. Study results were published online today in *Blood*, the Journal of the American Society of Hematology (ASH).

While previous studies suggest a connection between caloric intake and the development of cancer, scientific evidence about the effect of caloric intake on the efficacy of cancer treatment has been rather limited to date. When humans and animals consume calories, the body metabolizes food to produce energy and assist in the building of proteins. When fewer calories are consumed, the amount of nutrients available to the body's cells is reduced, slowing the metabolic process and limiting the function of some proteins. These characteristics of calorie restriction have led researchers to hypothesize that reducing caloric intake could potentially help inhibit the overexpression of the protein Mcl-1, an alteration associated with several cancers.

"While we know that consuming excess calories is associated with increased cancer risk, far less clarity exists in the scientific literature about how calorie restriction and the body's metabolism can potentially affect the body's response to cancer treatment," said lead study author Jean-Ehrland Ricci, PhD, of the French Institute for Health and Medical Research in Nice, France. "By understanding the link between metabolism and the body's natural cancer suppressors and activators, we

can perhaps improve the efficacy of therapy and improve survival for patients suffering from specific types of cancer."

To better understand how calorie restriction might control the overexpression of Mcl-1 in certain cancers and consequently affect treatment efficacy, Dr. Ricci and a team of researchers conducted a series of experiments in mice developing lymphoma resembling Burkitt's lymphoma and diffuse large B-cell lymphoma, two human cancers of the white blood cells.

The team began by separating the mice into two categories: those who would receive a regular diet and those who would receive a reduced-calorie diet (75 percent of normal intake) for the duration of the experiment. After the mice consumed either a regular or a reduced-calorie diet for one week, researchers then further divided the mice into four groups according to the treatment they would receive for the following 10 days. Of the two groups of mice that received a normal diet, one (the control group) did not receive treatment and the other received treatment with an experimental targeted therapy, ABT-737, designed to induce cancer cell death. Of the two groups of mice who received a reduced-calorie diet, one did not receive treatment and the other received ABT-737. On day 17 of the experiment, both treatment and calorie restriction ended, and mice had access to as much food as they desired.

Following this exercise, investigators observed that neither treatment with ABT-737 nor calorie restriction alone increased the survival of mice over that of the other mice; however, the combination of ABT-737 and calorie restriction did. Median survival was 30 days in the control group that received a regular diet and no treatment, 33 days in mice that received a regular diet and treatment with ABT-737, 30 days in mice that received a reduced-calorie diet without treatment, and 41 days in mice that received a reduced-calorie diet and treatment with ABT-737.

Shortly after this experimental period, investigators also observed that the combination of calorie restriction and ABT-737 reduced the number of circulating lymphoma cells in the mice, suggesting that the combination sensitized the lymphoma cells to treatment.

To further test their observations, researchers conducted several additional laboratory-based analyses, confirming that the cancer-related activity of Mcl-1 had decreased. Next, researchers combined two calorie-restriction mimetics (chemical compounds known to mimic the activity of calorie restriction), 2-deoxy-glucose and lonidamine, with lymphoma cells from the mice and ABT-737 and examined their activity. The team observed that the combination of the calorie-restriction mimetics and ABT-737 successfully blocked the protein translation of Mcl-1, confirming their observations that calorie restriction had indeed led to decreased Mcl-1 expression and had sensitized lymphoma cells to treatment.

"The results of our investigation provide encouraging data that suggest that the combination of a defined period of calorie restriction and targeted therapy may have the potential to increase cancer survival," said Dr. Ricci. "This is just the beginning of our journey to bring these research findings to the clinical setting. We next want to examine what component of a reduced-calorie diet – fats, sugars, or another food compound – influenced the lymphoma cells' improved sensitivity to treatment."

Provided by American Society of Hematology