In our war against cancer, the role of alternative medicine has become more and more important. Throughout the world, scientists are discovering from old medicinal plants new properties that hold great promises for cancer prevention and treatment.

One such Chinese medicinal plant, the "Thunder God Vine" (Tripterygium wilfordii Hook F.) is found to possess properties that can target some tumor-specific proteins, causing cancer cell death and leading to suppression of cancer growth.

This ivy-like vine which belongs to the Celastraceae family has always been known for its anti-inflammatory effects and has been used as a natural medicine in China for hundreds of years. It has been effectively used in the treatment of autoimmune diseases (rheumatoid arthritis, systemic lupus erythematosus), asthma, and chronic inflammation. In some cases, side effects have been reported. In the past two decades, the Thunder God Vine has been investigated for its effect in combating cancer. There are more than 100 natural compounds found in the Thunder God Vine, and many have been tested for anticancer activities. Celastrol, a natural quinone methide friedelane triterpene, is an active compound extracted from the root bark of this medicinal plant.

In cancer patients certain activities of a large protein complex, called the proteasome, are abnormally high. The function of the proteasome in a normal cell is to degrade unneeded or damaged proteins by a chemical reaction. But if the activity of the proteasome is too high, which is the case in cancer patients, tumor suppressor proteins get degraded, leaving cancer free to grow. This is a vicious cycle in a cancer cell. An inhibitor of the proteasome, therefore, should have potential anticancer effect.

Most recently, we reported that celastrol, the natural compound...
extracted from the root bark of the Thunder God Vine, is a selective proteasome inhibitor with potent anticancer activity. This finding was published last year in Cancer Research, a prominent scientific journal in the cancer field.

Our laboratory experiments show that celastrol has a powerful inhibitory effect on purified human and animal proteasome, and on proteasome in human prostate cancer cells and tumors that were grown in nude mice. Celastrol potentially and preferentially inhibits the specific proteasome activity that promotes cancer growth. Further lab experiments using nude mice demonstrated that proteasome inhibition in vivo by celastrol is accompanied by significant cancer cell death (apoptosis) and tumor growth inhibition.

The special chemical structure of celastrol, called aromatic ketone carbons (as indicated in the below picture), allows it to bind tightly to a specific amino acid of the proteasome, causing proteasome inhibition and therefore inducing cell death in cancer.

We reported in the Cancer Research article that celastrol inhibits the proteasome activity in both androgen receptor-negative and androgen receptor-positive prostate cancer cells. As a result, the levels of several natural tumor suppressor proteins increased, accompanied by suppression of androgen receptor protein expression (which is a cell death inhibitor) and induction of cell death. Daily treatment of human prostate tumor-bearing nude mice with celastrol for up to 31 days resulted in significant inhibition (65%-93%) of the tumor growth. Multiple assays using the animal tumor tissue samples from both early and end time-points demonstrated in vivo inhibition of the proteasomal activity and induction of cell death after celastrol treatment. Our results demonstrate that celastrol is a natural proteasome inhibitor that has a great potential for cancer prevention and treatment. Antitumor activity of celastrol was also observed in a breast cancer mouse model. Celastrol inhibited 60% tumor growth in breast cancer xenograft.

Tumors rely on new blood vessels that sprouted in and around them to grow and to travel to different sites of the body, a process called tumor metastasis. The process by which new blood vessels emerge is called angiogenesis. Celastrol was found to be a potent inhibitor of tumor angiogenesis and metathesis. By shrinking the blood vessels of the cancer tumor, it inhibits the tumor’s growth and makes it hard to metastasize.
Celastrol’s anti-inflammatory property is surprisingly versatile in fighting human diseases. Besides shrinking the tumor and the vessels that feed cancer, celastrol is found to block neuronal cell death in cultured cells and in animal models, thereby indicating its potential use in treatment of cancer and neurodegenerative diseases such as Alzheimer’s disease.

As with many promising complementary medicines in treating cancer and other devastating human diseases, there are many challenges to be met before celastrol can be safely used on patients. Among them, is to find natural and/or synthetic analogs that have the same potency but less toxicity and therefore reduced side effects. Another task is to study the effect of celastrol at a very low dose in combination with chemotherapy or radiotherapy. It is expected that inhibition of the proteasome activity by celastrol will sensitize tumor cells to these therapies. Regardless of these challenges, the recent research results on celastrol and other compounds from Chinese medicinal plants did help to illuminate the bright future of cancer prevention and treatment.