Spotlight

By Caroline Seydel

Cracking Drug-Resistant Pancreatic Cancer

Banerjee *et al.*
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When a cancer becomes resistant to one drug, patients' lives depend on having a second line of treatment ready to go. Oxaliplatin, though it's been used as the second line against pancreatic cancer, doesn't work as well as had been hoped. In this paper, Banerjee *et al.* set out to determine whether treating cancer cells with a chemical found in soybeans could make them susceptible to death by oxaliplatin. They found that the chemical, called genistein, did make it easier for oxaliplatin to induce apoptosis, which could be good news in the fight against pancreatic cancer.

Most people with pancreatic cancer die within the first year after diagnosis. After several cycles of chemotherapy, the cancer generally becomes drug-resistant. Oxaliplatin, which clinicians turn to as a second line of treatment, causes severe adverse side effects in high doses, but low doses don't do much against the disease. Banerjee *et al.*, investigated whether these drug-resistance cancers could be made sensitive to oxaliplatin. They looked to a soy isoflavonoid called genistein, which has been shown to inhibit cell growth, limit tumor cell migration, and spur cell death.

The researchers treated the resistant cancer cells with genistein to find out whether that would open the door to destruction by oxaliplatin. They found that hitting the cells first with genistein, then with oxaliplatin, killed significantly more cells than either agent alone. Genistein paves the way for oxaliplatin by suppressing NF-kB, thus downregulating a variety of downstream anti-apoptotic genes, including Bcl-xL, BCL-2, survivin, and others. This could mean that genistein's ability to sensitize cancer cells might work in various tumor types. Genistein also selectively targets tumor cells, leaving normal pancreatic cells unharmed. Experiments in mice then showed that the combined treatment shrunk tumors, bolstering the cell culture results and marking genistein as a very interesting prospect for pancreatic cancer treatment.

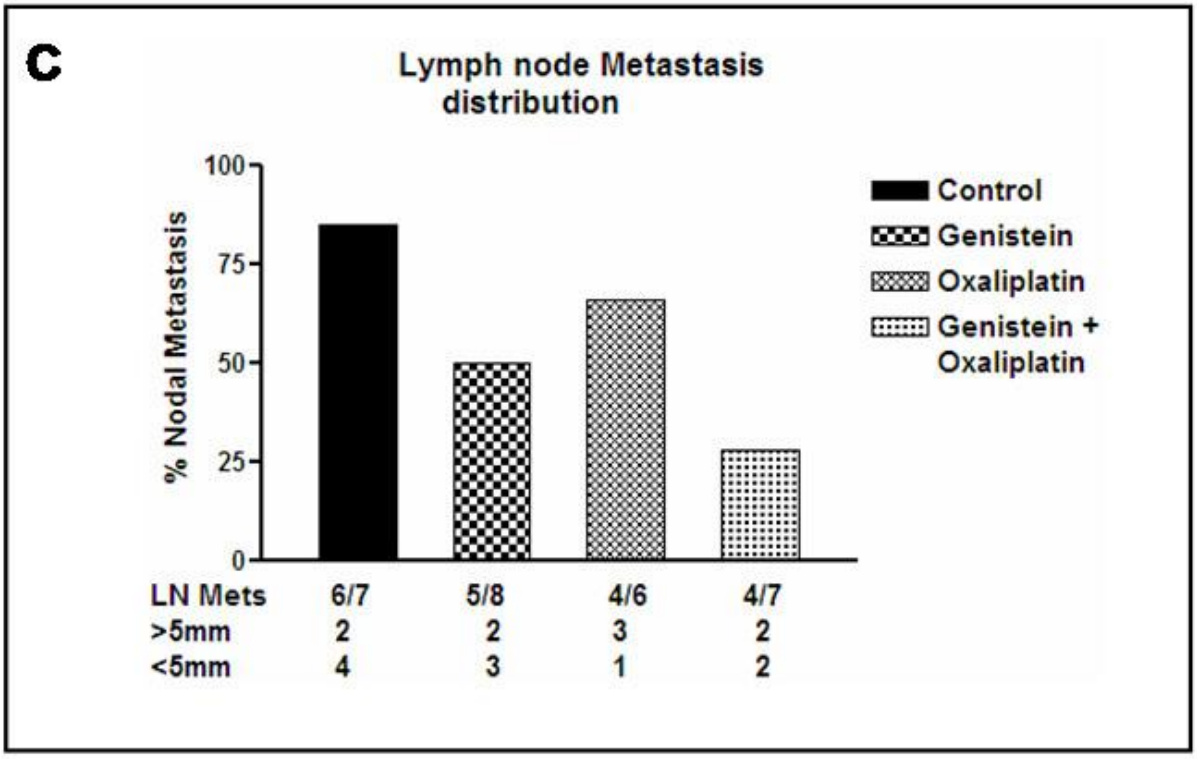

Fig. 5c. Combining genistein and oxaliplatin dramatically reduced metastases