# Exposure to dim light at night may make breast cancers resistant to chemotherapy

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For rats bearing human breast tumors, exposure to dim light at night made the tumors resistant to the standard breast cancer chemotherapy doxorubicin, but giving the rats a melatonin supplement during the dim-light exposure at night prevented resistance development and promoted tumor regression, according to data presented at the 13th Annual AACR International Conference on Frontiers in Cancer Prevention Research, held Sept. 28–Oct. 1.

"Using our rat model of breast cancer, we recently reported [see July 25, 2014, news release] that exposure to dim light at night made human breast tumors resistant to the antihormone breast cancer drug tamoxifen," said Steven M. Hill, PhD, professor of structural and cellular biology and the Edmond and Lily Safra chair for breast cancer research at Tulane University School of Medicine in New Orleans. "In this new study, we find that the same is true for doxorubicin, the most commonly used anticancer chemotherapy drug in the world.

"Although our research is very promising, it is not at a point where we can make recommendations to breast cancer patients taking either tamoxifen or doxorubicin about melatonin supplementation," continued Hill, who is also director of the Tulane Center for Circadian Biology. "Instead, because melatonin is produced by our bodies at a very specific time of day, exclusively during darkness at night, we can recommend that patients follow a natural light/dark cycle as much as possible, try to sleep or stay in a completely dark room during the night, and/or use a sleep mask. Taking melatonin supplements at the wrong time of day would potentially disrupt the natural melatonin cycle, which may, in itself, impair breast cancer responsiveness to tamoxifen and doxorubicin."

For the study, Hill and colleagues analyzed rats exposed to 12 hours of normal light followed by 12 hours of dim light. Half of the rats received melatonin supplementation during the dim-light period (nighttime). Tumor growth in rats that did not receive nighttime melatonin supplementation was 2.8-fold faster compared with tumor growth in rats receiving nighttime melatonin supplementation. In addition, tumors in rats that did not receive nighttime melatonin supplementation were completely resistant to doxorubicin, whereas tumors in rats given nighttime melatonin supplementation were sensitive to doxorubicin and regressed rapidly.

According to Hill, the researchers identified two potential molecular mechanisms by which exposure to dim light at night might cause the observed doxorubicin resistance. "When we analyzed tumors from rats that did not receive nighttime melatonin supplementation, we detected substantially increased levels of two enzymes that break down doxorubicin to a less active form and significantly elevated levels of membrane proteins that transport doxorubicin out of cells, compared with tumors from rats receiving nighttime melatonin supplementation," said Hill.

"Tumors from rats receiving nighttime melatonin supplementation had lower levels of these enzymes and transporters," Hill continued. "So we think that melatonin helps maintain high levels of active doxorubicin in the cancer cells, whereas suppression of circadian melatonin production by exposure to light at night has the opposite effect."

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