

Reduced Melatonin Secretion Drives Association between Night Shift Work and Breast Cancer

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Previous epidemiological studies have suggested that the risk of breast cancer is increased by 35-80% among nightshift workers compared to dayshift working peers, with greater risk among those who work more frequent shifts throughout a greater number of years. Night shift work has also been associated with increased risk of endometrial, prostate and colon cancers. Specifically, it is hypothesized that exposure to light at night may increase breast cancer risk by suppressing the normal nocturnal production of melatonin, a neurohormone with direct oncostatic properties, and/or by increasing production of reproductive hormones since melatonin has also been implicated in regulating the pituitary release of gonadotropins and simulating ovarian estrogen production. However, these mechanisms have not been comprehensively examined in populations of actual nightshift workers, and previous studies have generally relied on a single measure of melatonin at one point in time.

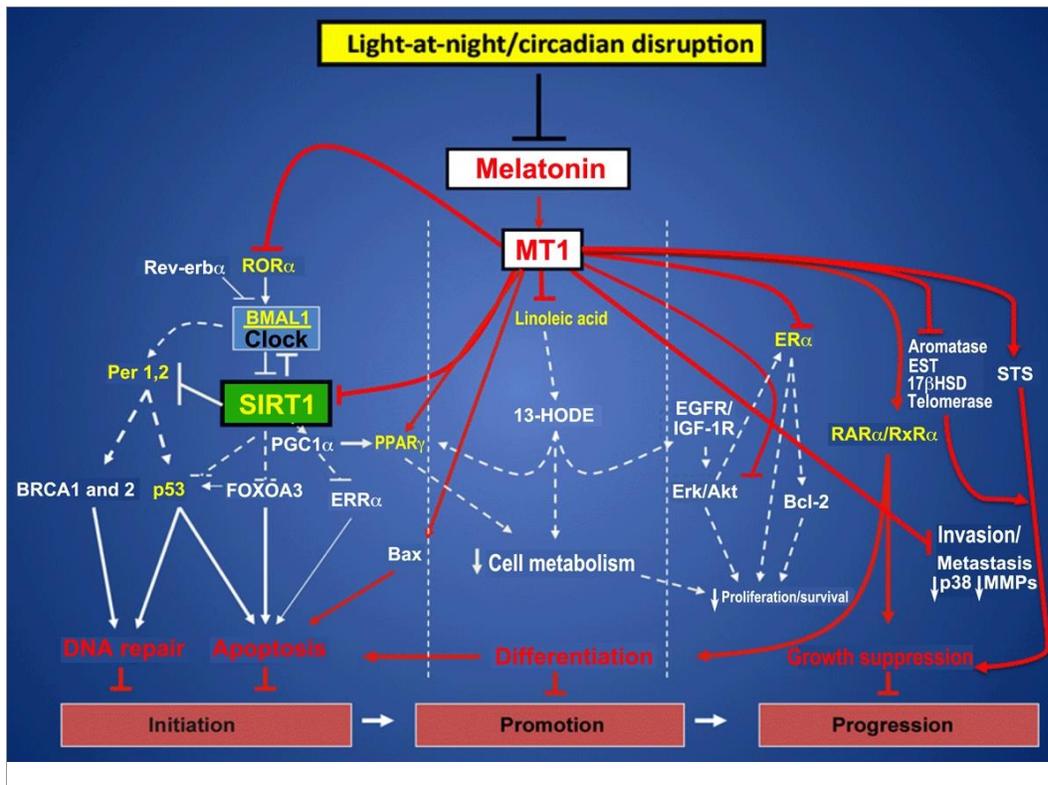
Therefore, in an effort to elucidate the mechanisms underlying the increased risk of breast cancer observed among nightshift workers, Dr. Scott Davis, Public Health Sciences Division, and colleagues were recently the first to measure urinary 6-sulfatoxymelatonin, the most common melatonin metabolite, in addition to luteinizing hormone (LH), follicle-stimulating hormone (FSH) and estrogens (estrogen conjugate, E1C) at multiple time points throughout the course of a typical work day and subsequent sleep period in 172 nightshift and 151 dayshift-working nurses. Women were 20-49 years of age and measures were taken during the early to mid-luteal phase of their menstrual cycle.

Urinary 6-sulfatoxymelatonin levels were 62% lower (mean 18.1 vs. 35.3 ng/mg creatinine, $p < 0.0001$), while FSH was 62% higher (6.1 vs. 4.6 ng/mg creatinine, $p < 0.01$) and LH was 58% higher (1.8 vs. 1.2 ng/mg creatinine, $p < 0.01$) during the daytime sleep of nightshift workers relative to the nighttime sleep of dayshift workers. Even during a subsequent night off, 6-sulfatoxymelatonin remained significantly lower (-42%, $p < 0.0001$) in nightshift compared to dayshift workers. Nocturnal melatonin levels were 69% lower (mean=14.9 ng/mg creatinine, $p < 0.0001$), while FSH and LH were 35% (mean 5.8 ng/mg creatinine, $p < 0.05$) and 38% (mean 1.7 ng/mg creatinine, $p < 0.05$) higher, respectively, during nighttime work relative to nighttime sleep in dayshift workers. However, no

differences in E1C levels were detected between groups, suggesting that the direct oncostatic effects of melatonin, rather than elevated reproductive hormones, are the primary mechanism driving the increased breast cancer risk among female shift workers.

Given that work at night is widespread phenomenon, further studies on the impact of various shift schedules and routines on physiological and circadian rhythms of workers in real-world environments will be required to provide evidence-based recommendations for prevention. To date, preventive effects of melatonin supplementation on breast cancer risk have not been clearly documented.

[Davis S, Mirick DK, Chen C, Stanczyk FZ. 2012. Night shift work and hormone levels in women. *Cancer Epidemiology, Biomarkers & Prevention*, doi:10.1158/1055-9965.EPI-11-1128.](#)



Source: Blask et al. *J Pineal Res.* 2011; 51:259–269.

Impact of the nocturnal circadian melatonin signal (via the mt1 receptor) and its disruption by exposure to light at night on molecular/endocrine and dietary/metabolic regulatory mechanisms governing breast cancer initiation, growth promotion and progression.