

## LETTER TO THE EDITOR

**LED light between Nobel Prize and cancer risk factor**

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Are light and illumination just a matter of energy efficiency? Should we ignore the importance of light as an environmental signal to the physiological and immune systems in our body? The answer is NO, as light is an important signal for entraining the biological clock and calendar information in terrestrial mammals, including humans. The 2014 Nobel Prize in Physics was given jointly to Isamu Akasaki, Hiroshi Amano and Shuji Nakamura “for the invention of efficient blue light-emitting diodes (LEDs) which has enabled bright and energy-saving white light sources”. While the most positive feature of LED lighting is reduced energy consumption (Crawford, 2009), there is growing evidence suggesting a negative association between the promising technology and human health problems, particularly increased cancer incidences (Falchi et al., 2011; Haim & Portnov, 2013).

In our modern lifestyle, most of the new electrical devices we use include LED in their screens or the operation light indicator and many find their ways into the bedrooms of the youth that are exposed to this illumination during their sleep, when actually they had to be in the dark and produce the neuro-hormone melatonin. The nocturnal synthesis of melatonin is highly sensitive to artificial light-at-night (ALAN) exposure of any spectral composition (Brainard et al., 1997; Hanifin et al., 2006; Thapan et al., 2001). However, results of several studies revealed a wavelength-dependent decrease in pineal melatonin production (Cajochen et al., 2011; West et al., 2011; Zubidat et al., 2011). Blue LED illumination, which emits light at the short end of the visual spectrum (440–480 nm), has been demonstrated to be the most effective frequency for melatonin suppression compared with conventional lighting technologies (Falchi et al., 2011; West et al., 2011). Finally, looking directly to the source of LED illumination can severely damage retinal cells (Chamorro et al., 2013).

Fluorescent and white LED illuminations that emit short wavelength are utilized in the treatment of seasonal affective disorder (Glickman et al., 2005; Nelson, 2005). Nevertheless, melatonin strongly regulates numerous vital functions including antioxidant, antiaging and most relevant anti-oncogenic properties (Srinivasan et al., 2011). Consequently, melatonin suppression by short-wavelength ALAN is highly expected to compromise human health, including risk for cancer (Erren et al., 2008; Leonardi et al., 2012; Schwimmer et al., 2014).

Several epidemiological and experimental studies have recurrently suggested a potential role of melatonin in the treatment of cancer (Mediavilla et al., 2010; Srinivasan et al., 2008). Reduced levels of melatonin in women exposed to ALAN during night work and sleep deprivation are associated with an increase in breast cancer risk (Davis et al., 2001; Schernhammer et al., 2001; Viswanathan et al., 2007). Furthermore, melatonin treatment was found to protect against prostate and breast cancers in several animal models (Bartsch & Bartsch, 1981; Haim et al., 2010; Schwimmer et al., 2014; Shah et al., 1984; Tamarkin et al., 1981). The protective features of melatonin against carcinogenic activity are varied and include inhibition of cell proliferation, induction of apoptosis, enhancing anti-tumor immune responses and inhibition of cancer cell metabolism (Blask et al., 2005; Proietti et al., 2013; Srinivasan et al., 2008). The cellular mechanism by which melatonin contributes to cancer prevention is not entirely known, but regulating epigenetic remodeling of oncogenes is increasingly being suggested (Mediavilla et al., 2010). DNA methylation is a common and an important epigenetic pathway for regulating gene expressions in response to environmental signals (Jaenisch & Bird, 2003). The genome of cancer cells have been demonstrated to present aberrant DNA methylation in tumor

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suppressor genes and metastatic genes that are responsible for mediating carcinogenic activity from early to terminal stages of tumor progression (Day & Bianco-Miotto, 2013; Hattori & Ushijima, 2014; Xiang et al., 2013). In a recent review, we have suggested a possible mechanism for ALAN-induced cancer development (Haim & Zubidat, 2014). Accordingly, the ALAN-induced melatonin suppression stimulates oncogenes and inhibits tumor suppressor genes by genomic regulation of aberrant DNA methylation resulting in tumor progression.

No doubts that ALAN caused the most dramatic environmental change in the last decades and satellite images of human activity increasingly show more places worldwide are illuminated with an increase in light intensity, known today as light pollution. The American Medical Association (AMA) in 2012 passed a resolution with regard to light at night as a source of pollution, as it suppresses melatonin production and interrupts with our sleep and daily rhythms (AMA, 2012). Furthermore, they call upon developing new technologies for illumination. We assume that they were aware of the problematic issues of LED illumination. Although the association between ALAN and cancer development remains controversial, the current evidence from epidemiological (Kloog et al., 2008; Wang et al., 2013; Yang et al., 2014) and experimental (Blask et al., 2009; Schwimmer et al., 2014; Wu et al., 2011) studies regarding the negative effect of light pollution on human health is worrying greatly. Therefore, further studies are warranted in order to characterize the ALAN spectral threshold for triggering carcinogenetic activity and to implement effective countermeasures for reducing any potential side effects of the novel lighting technology such as filtering the emitted short wavelength.

While the LED technology is currently being viewed as a huge step in cost-efficient solution for lighting systems, and the authors of this article congratulate the winners of the Nobel Prize in Physics in 2014 for their achievement, the new innovation is likely to impose public health risks reflected in increased short-wavelength emissions. LED technology as a source of illumination in public spaces is under discussion and, unquestionably, we need more research in order to suggest a smart use of this technology. As chronobiologists, we cannot ignore the impact of the novel illumination on public health. We do not want to live under darkness but as the AMA calls (AMA, 2012), we should look for healthy illumination that does not interfere with our biological clock, considered as a musical conductor in charge of synchronizing our daily rhythms, just like musical instruments in an orchestra.

#### DECLARATION OF INTEREST

The authors report no conflicts of interest.

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