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عنوان المشروع باللغة العربية - Title of the proposed project in Arabic	تأثير التآزر من الميلاتونين وفيتامين D على التعبير الجيني لل P-53 في خطين سرطان الثدي الخلية
Title of the proposed project in English	Synergistic Effect of melatonin and Vitamin D on the gene expression of P-53 in two breast cancer cell line
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التخصص الدقيق للمشرف الرئيس - Specialty of PI	assistant Professor
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المدة المتوقعة لإنجاز البحث منذ الحصول على موافقة عمادة الدراسات - (العليا) بالشهور - Expected time in month to finish	12 months
Abstract of the proposal (No more than 200 words)	Melatonin is the hormone produced by pineal gland, which is thought to control the sleep is directly related to circadian activity through supra-chiasmatic nucleus. In the last few years a number of studies related to disruption of melatonin's circadian profile by exposure to light at night time has been described to play an important role in initiation, promotion and

progression of breast cancer [1,2,3,4].

Research suggests also that women with low levels of vitamin D have a higher risk of breast cancer. Vitamin D may play a role in controlling normal breast cell growth and may be able to stop breast cancer cells from growing.

The study by Imtiaz ., S et al (2012)[5,6] showed a strong correlation between the vitamin D deficiency and the prevalence of breast cancer in the females. The exact relationship of the effect of melatonin and vitamin D at the genetic and molecular level are still unknown. There is a need to explore the full therapeutic potential of these sunshine hormones on the pathophysiology of breast cancer is worth pursuing.

The aim of the present study is to determine the apoptotic effect of melatonin and vitamin D in breast cancer lines.

Hypothesis of the proposal

Melatonin and vitamin D should have the therapeutic potential in the treatment of breast cancer.

Specific objectives

To set up the tissue culture lab and facility for our masters and post graduate study

To enable the students to learn novel and updated cutting edge techniques in research to enable them to compete at international levels

To build up the image of our Biochemistry department by introducing new and latest research technology such as using Li-COR for imaging and western blots.

Methodology & Major Techniques to be used

Methodology:

Breast cancer line MCF-7 and MDM cultures cells will be set up as follows

1. Control cultures without any treatment
2. Cultures treated with different doses of melatonin (10, 50,100ng/ml) and 2.5µg/ml of D3).
3. cultures treated with melatonin alone
4. cultures treated with vitamin D alone

Following assessment parameters will be employed..

- To assess cell viability by trypan blue method.
- To assess the LDH activity in the different cultures.(by kit)
- to calculate cell proliferation by MTT assay.(by kit)

- Sequencing of P53 gene from two cell lines
- Quantitative evaluation of Gene expression of p53 by RTPCR in
- Assessment of Caspase activity in different treatment groups.(by kit)
- Quantitative evaluation of Protein expression of P53 by western blot and by in cell –western using Li-COR odyssey machine.
- Statistical analysis of the results.

Availability of Samples

Yes

Availability of Chemicals

Yes

Availability of Instruments

Yes

Ethical Approval

Not needed

Recent References

1. Saggi S, Rehman H, Abbas ZK, Ansari AA. Recent incidence and descriptive epidemiological survey of breast cancer in Saudi Arabia. Saudi Medical Journal. 2015;36(10):1176-1180. doi:10.15537/smj.2015.10.12268.
2. Touitou Y, Reinberg A, Touitou D. Association between light at night, melatonin secretion, sleep deprivation, and the internal clock: Health impacts and mechanisms of circadian disruption. Life Sci. 2017 Mar 15;173:94-106. doi: 10.1016/j.lfs.2017.02.008. Epub 2017 Feb 16. Review. PubMed PMID: 28214594.
3. Van Dycke KC, Rodenburg W, van Oostrom CT, van Kerkhof LW, Pennings JL, Roenneberg T, van Steeg H, van der Horst GT. Chronically Alternating Light Cycles Increase Breast Cancer Risk in Mice. Curr Biol. 2015 Jul 20;25(14):1932-7. doi: 10.1016/j.cub.2015.06.012
4. Shiu SY, Leung WY, Tam CW, Liu VW, Yao KM. Melatonin MT1 receptor-induced transcriptional up-regulation of p27(Kip1) in prostate cancer antiproliferation is mediated via inhibition of constitutively active nuclear factor kappa B (NF-κB): Potential implications on prostate cancer chemoprevention

and therapy. *J Pineal Res.* 2013;54:69–79

5. Imtiaz S, Siddiqui N, Raza SA, Loya A, Muhammad A. Vitamin D deficiency in newly diagnosed breast cancer patients. *Indian Journal of Endocrinology and Metabolism.* 2012;16(3):409-413. doi:10.4103/2230-8210.95684.

6. Edwin O. Quisbert -Valenzuela¹ and Gloria M. Calaf¹. Apoptotic effect of noscapine in breast cancer cell lines. *International journal of oncology* 4 2666 8: 2666-2674, 2016DOI: 10.3892/ijo.2016.3476