



Evaluation of serum IgE, TNF alpha at patients with genital warts, Iraq

Nisreen Kaddim Radi ^{1*}, Ihsan Jara Atiyah ², Samerh Shaker Hamood ¹

¹ College of science for Women, University of Babylon, Babil, IRAQ

² F.I.B.M.S of D.V, Imam Sadiq teaching hospital, IRAQ

*Corresponding author: nesreenzain.83@gmail.com

Abstract

Condylomata acuminata also known as genital wart result from the infection with human papilloma viruses particularly HPV type 6 & 11. Thirty three samples (blood and skin tissue) were accumulated from patient with genital warts (females) whom visit dermatology department of Hilla hospital/Iraq, with thirty three sera gathered from healthy persons act as control group. The diagnosis was achieved via dermatologist and by applied in situ hybridization (ISH) test to detect HPV types 6 & 11. The estimation of IgE and TNF α levels at patient sera were done by using ELISA test. The result show that About 92% of patient with genital wart donated appositve result to the infection with HPV type 11 and 6, and there were significant increasing in IgE levels at patients sera compared with control group Mean \pm S.E [202.36 \pm 10.16, 24.12 \pm 1.68 IU/ML] and also TNF α show increasing in their level at patients sera compared with control groups Mean \pm S.E [68.18 \pm 1.72, 46.68 \pm 1.13 pg/ml].

Keywords: genital wart, IgE, in situ hybridization, females, HPV, ISH

Radi NK, Atiyah IJ, Hamood SSH (2020) Evaluation of serum IgE, TNF alpha at patients with genital warts, Iraq. Eurasia J Biosci 14: 3101-3106.

© 2020 Radi et al.

This is an open-access article distributed under the terms of the Creative Commons Attribution License.

INTRODUCTION

The term genital wart is refer to Benign projection appear as tiny wart like tumors at the genital tract, but, sometimes lesions changes to malignant alteration leading for dangerous tumors developing (Fleischer et al. 2001. Cates 1999).

About 95% of cervical carcinoma caused by HPV especially types 18 and 16 at infection percent about 50% while HPV types 6 and 11 resulted in less malignant tumors at 14% of infection rate (Batista, et al. 2010. Markowitz, et al. 2014. Tying, 2000. Lombard, et al. 1998) The favored technique using for detection of HPV infection were polymerase chain reaction (PCR) and hybridization (ISH), usual checking of anomalous cervical histology like Pap smear still the frequently practical and laboratory method that are used for detection cervical cancer in all the world. many deaths are even now recorded every year, In spite of, the screening programs achievement (Evans, Aliesky, & Cooper, 2003. Evans, Aliesky, & Cooper, K. 2003. Bryan, et al. 2006. Poljak, et al. 2012; Roudgarmi, & Farahani, 2016).

The chiefly trouble deceit with the analysis of Pap smear abnormalities as the technique. need skilled dermatologist, and the result Show extremely changeable false-negative rate. Consequently, therapy choice are typically approved at delayed stage of the infection with genital wart and This is the majority reason in charge of mortality because of cancer in developed

countries. (Cuzick, Meijer, & Walboomers, 1998. Cuzick, et al. 2012).. gE antibodies (Immunoglobulin E) recognized as antigen-specific which activate the allergic responses. IgE have a vital role in immediate hypersensitivity as well as IgE work to protect immunity anti parasites and intracellular pathogen like viruses, in addition to controlling homeostasis of mast cell. (Burton, & Oettgen, 2011). interferon's (IFNs) are generally divided into two class. The first is I IFNs which identified as viral IFNs also consist of IFN- α , IFN- β , and IFN- ω . The second class IFN is recognized as IFN- γ (immune IFN), Tumor necrosis factor (TNF) is considered as pro inflammatory cytokine which in charge of many functions, Like causing of cytolysis for specific tumor cell lines.

The activation of macrophages, natural killer cells, T and B lymphocytes, astrocytes, smooth muscle cells, endothelial cells, some tumor cells, and epithelial cells resulting in the production of TNF- α (Clark, 2007. Roff, Song, & Yamamoto, 2014. Katze, He, & Gale, 2002). TNF is regard as a central cytokine in acute viral diseases, especially diseases resulted from the infection with influenza virus, and Ebola virus, dengue virus (Aggarwal, 2003). the aim of this study was to investigate HPV types which causes genital warts

Received: June 2019

Accepted: March 2020

Printed: September 2020

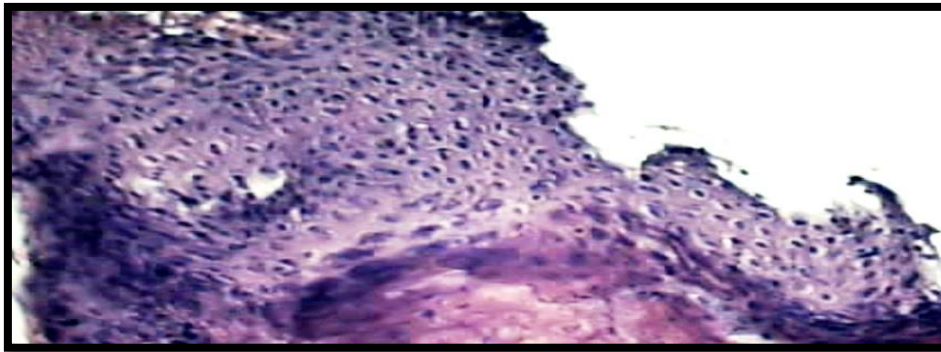


Fig. 1. Section of human lesion with genital wart display koilocytes cells contain peri nuclei ends (Haematoxylin and eosin 4x)

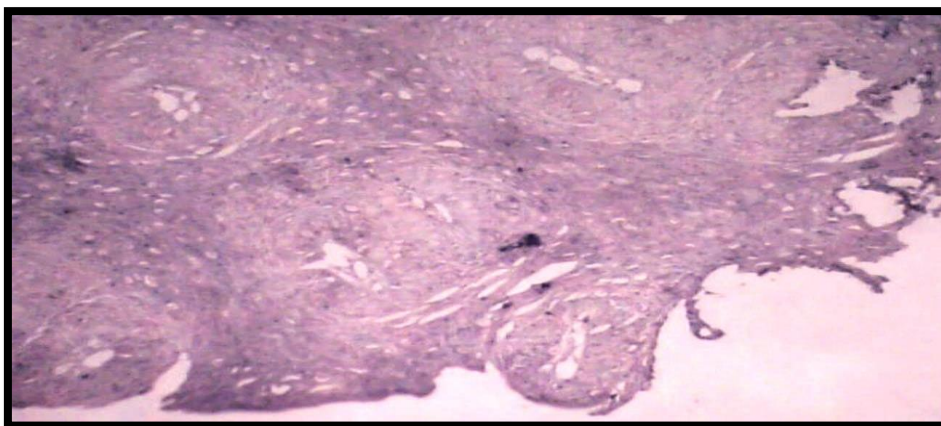


Fig. 2. Section of wart lesion give positive result for (ISH) in situ hybridization d to detect Human papilloma virus type 6,11 (purple color dot)

infection in thirty three females of Hilla city/Iraq and to evaluated some immunological markers like TNF α and IgE at patient sera.

MATERIAL AND METHODS

In our study Thirty three samples (skin tissue and blood) were accumulated from patient contaminated with genital wart which visit Public Hilla hospital, Babylon/ Iraq, with thirty three sera gathered from healthy people play as control group. The examination of viral types was carried by dermatologist and assured by using ISH test (Maxim Biotech, Inc., USA) to identify papilloma virus types at patient with genital warts,mean while the estimation of IgE level was done by using ELISA test (abcam.USA) and (Elabscience) for estimation of TNF α at patients sera whom infected with skin warts.

Sectioning of Skin lesion and preparing slides

Wart lesions were put in a plane tube contain formalin 10%, after that it were placed in paraffin. Then tissue block were transected through microtome to (4 μ m) thin sections, and fixed on a slides to subjected for pigmentation by hematoxylin and eosin stained slides

method (Bancroft, & Stevens, 1982. Cribier, Scrivener, & Grosshans, 2001).

In situ hybridization method

In situ hybridization was done according to the manufacturer's leaflet company (Maxim Biotech, Inc., USA)(Ali, Al Alwan, & Al Alwany, 2014).

RESULTS

Histological Examination

Histological finding of genital wart reveled that Presences of overexcited (multi) granular layer, papillomatous and perinuclear vacuolated cell known as koilocytes **Fig. 1.**

From (**Fig. 2**) show about 92% of patient with genital warts give positive result for ISH test which denoted as purple colors in the skin tissue fixed slide.

Mean Difference of TNF α and IgE Concentration between Patients and control group.

Table 1 revealed the Mean Difference of TNF α and IgE. Concentration between Patients' and control group. There was significant Mean Difference of IgE Concentration by Patients 'sera, with $p \leq 0.05$.

Table 1. The relation between TNF α and IgEcon.at patients sera and control group

Parameters	Control (Mean \pm S.E)	patients (Mean \pm S.E)	P-value of groups
IgE IU/ml	1.68 \pm 24.12	10.16 \pm 202.36	<0.001*
TNF pg/ml	46.68 \pm 1.13	68.18 \pm 1.72	<0.001 *

t-test.

*P \leq 0 .05. S.E: Standard error

DISCUSSION

In the last few years we had used HPV DNA examination as an extra investigative method in cervical tumors survey resulted from The strong connection among viral integration with invasive carcinoma (Wright, et al. 2004. Ronco, et al. 2010. Sankaranarayanan, et al. 2009). In situ hybridization (ISH), is a straight signal recognition test, contain the benefit of protecting the morphologic framework of DNA signals for Human papilloma virus (Bryan, et al. 2006). HPV Host defense is complex, Examination of diseases in patient have strict clinical presentation reveled the host defense and immune system stimulation, Advance study of severe and recalcitrant warts determine immune mechanisms which control one of our long-associated fellow visitors of HPV. (Turner, Chen, Krewski, & Ghadirian, 2006. Wang, & Diepgen, 2005).

the majority frequent reasons of allergic signs is ingrained in an unusual inflammatory reaction to usually harmful exogenous particles. T-helper type 2 (Th2) cells stimulated the production of IL4, IL5, IL13 which interceded production of mucus, development of eosinophil, and stimulation of allergen-specific IgE through Bcells (Akdis, 2006). the activation of IgE receptor signaling pathway took place when the IgE interacted with allergens. (Kanehisa, et al. 2010). In the development stages of cervical cancer, the reactions of immune system correlated to allergies would work to excluded HPV infection earlier then viruses be able to set up persistent infection(Castaing, et al. 2005. Burnet, 1957). Up controlling of TNF creation has been concerned in a range of human infection involved major depression Alzheimer's illness (Swardfager, et al. 2010). cancer (Locksley, Killeen, & Lenardo, 2001. Dowlati, et al. 2010. Victor, & Gottlieb, 2002). and inflammat(Castaing, et al. 2005).ory bowel disease (Brynskov, et al. 2002).

TNF play important role in the regulation and inhibition of intracellular pathogens: it induced

employment of inflammatory cells to infection region, as well as induced the creation and the protection of granulomas to control the infection. Besides that, TNF immediately trigger macrophages, and next phagocytose along with pathogens killing. many studies have been discovered that Inflammatory cytokines, similar to tumor necrosis factor, are active mediators of the innate antiviral immune reaction. An eventual study by Scott et al(Gately, et al. 1998. Scott, et al. 2013. Moscicki, Schiffman, Kjaer, & Villa, 2006). revealed a important contrary connection between clearance period of HPV occurrence especially high-risk types infections and elevated levels of IL-12 and TNF- α calculated in cervico vaginal lavage specimen through a multiplex immune tests. The opposite connection of HPV clearance time by elevated levels of IL-12 and TNF- α can indicate macrophage induction and follow-on inflammation. Tissue damage resulting from chronic inflammation can support cellular alteration resulting in malignancy. (Mantovani, Allavena Sica, & Balkwill, 2008).

Extra studies recorded to the infection with HR or else of violent genotypes belong to HPV could produce cell transformation so as to resist growth inhibition mediated by TNF α . this results appeared to be owing from reduced expression or damage the receptors of TNF α on the cell infected with HPV (Govan, Constant, Hoffman, & Williamson, 2006. Simoes, et al. 2005) In opposite of that results,there were another studies Song et al. (Song, et al. 2007. Nicol, et al. 2005). Denoted that TNF α and IL-10 levels un seed to associate with cervical malignancy following the infection with HPV. Still, showed (Nicol, Fernandes, & Bonecini-Almeida, 2005.Zahraa et al. 2017. Nisreen et al. 2017.Nisreen 2017. Ali et al. 2017. Nisreen Shaima Israa 2017). that the transformation of epithelial cells in cervix had a reduction ability to express TNF α in addition to recommended that the expression losing in cervical cancer cells could have changed the microenvironment of the tumor as well as thereby assisted ongoing growth of tumor.

ACKNOWLEDGEMENTS

We gratefully acknowledge the all kind of technical supports from the Department of Biology, College of science for Women, University of Babylon.

REFERENCES

- Aggarwal, B. B. (2003). Signalling pathways of the TNF superfamily: a double-edged sword. *Nature reviews immunology*, 3(9), 745-756.
- Akdis, M. (2006). Healthy immune response to allergens: T regulatory cells and more. *Current opinion in immunology*, 18(6), 738-744.

- Ali H., Sabreen A., Nisreen K., Hawraa S., AfafK S(2017).. Molecular Study for Recurrent Spontaneous Abortions (RSA): the role of HSV, B19, and CMV Markers and Polymorphisms in TLR-3 associated with BOH. *International journal of chmechial tech*; 10: 422-428
- Ali, S. H. M., Al Alwan, N. A., & Al Alwany, S. H. (2014). Detection and genotyping of human papillomavirus in breast cancer tissues from Iraqi patients.
- Bancroft, J. D., & Stevens, A. (1982). *Theory and Practice of Histological* 2nd edition Churchill living ston. Edinburgh, London, 622.
- Batista, C. S., Atallah, Á. N., Saconato, H., & da Silva, E. M. (2010). 5-FU for genital warts in non-immunocompromised individuals. *Cochrane Database of Systematic Reviews*, (4).
- Brown, D. R., Schroeder, J. M., Bryan, J. T., Stoler, M. H., & Fife, K. H. (1999). Detection of multiple human papillomavirus types in Condylomata acuminata lesions from otherwise healthy and immunosuppressed patients. *Journal of clinical microbiology*, 37(10), 3316-3322.
- Bryan, J. T., Taddeo, F., Skulsky, D., Jansen, K. U., Frain, B. M., Qadadri, B., & Brown, D. R. (2006). Detection of specific human papillomavirus types in paraffin-embedded sections of cervical carcinomas. *Journal of medical virology*, 78(1), 117-124.
- Bryan, J. T., Taddeo, F., Skulsky, D., Jansen, K. U., Frain, B. M., Qadadri, B., & Brown, D. R. (2006). Detection of specific human papillomavirus types in paraffin-embedded sections of cervical carcinomas. *Journal of medical virology*, 78(1), 117-124.
- Brynskov, J., Foegh, P., Pedersen, G., Ellervik, C., Kirkegaard, T., Bingham, A., & Saermark, T. (2002). Tumour necrosis factor α converting enzyme (TACE) activity in the colonic mucosa of patients with inflammatory bowel disease. *Gut*, 51(1), 37-43.
- Burnet, M. (1957). Cancer—a biological approach: III. Viruses associated with neoplastic conditions. IV. Practical applications. *British medical journal*, 1(5023), 841.
- Burton, O. T., & Oettgen, H. C. (2011). Beyond immediate hypersensitivity: evolving roles for IgE antibodies in immune homeostasis and allergic diseases. *Immunological reviews*, 242(1), 128-143.
- Castaing, M., Youngson, J., Zaridze, D., Szeszenia-Dabrowska, N., Rudnai, P., Lissowska, J.,... & Navratilova, M. (2005). Is the risk of lung cancer reduced among eczema patients?. *American journal of epidemiology*, 162(6), 542-547.
- Cates Jr, W. (1999). Estimates of the incidence and prevalence of sexually transmitted diseases in the United States. *American Social Health Association Panel. Sexually transmitted diseases*, 26(4 Suppl), S2-7.
- Clark, I. A. (2007). How TNF was recognized as a key mechanism of disease. *Cytokine & growth factor reviews*, 18(3-4), 335-343.
- Cribier, B., Scrivener, Y., & Grosshans, E. (2001). Molluscum contagiosum: histologic patterns and associated lesions: a study of 578 cases. *The American journal of dermatopathology*, 23(2), 99-103.
- Cuzick, J., Bergeron, C., von Knebel Doeberitz, M., Gravitt, P., Jeronimo, J., Lorincz, A. T.,... & Szarewski, A. (2012). New technologies and procedures for cervical cancer screening. *Vaccine* 30 (Suppl 5): F107–F116.
- Cuzick, J., Meijer, C. J., & Walboomers, J. M. (1998). Screening for cervical cancer. *The Lancet*, 351(9113), 1439-1440.
- Dowlati, Y., Herrmann, N., Swardfager, W., Liu, H., Sham, L., Reim, E. K., & Lanctôt, K. L. (2010). A meta-analysis of cytokines in major depression. *Biological psychiatry*, 67(5), 446-457.
- Evans, M. F., Aliesky, H. A., & Cooper, K. (2003). Optimization of biotinyl-tyramide-based in situ hybridization for sensitive background-free applications on formalin-fixed, paraffin-embedded tissue specimens. *BMC Clinical Pathology*, 3(1), 2.
- Fleischer Jr, A. B., Parrish, C. A., Glenn, R., & Feldman, S. R. (2001). Condylomata acuminata (genital warts): patient demographics and treating physicians. *Sexually transmitted diseases*, 28(11), 643-647.
- Gately, M. K., Renzetti, L. M., Magram, J., Stern, A. S., Adorini, L., Gubler, U., & Presky, D. H. (1998). The interleukin-12/interleukin-12-receptor system: role in normal and pathologic immune responses. *Annual review of immunology*, 16(1), 495-521.
- Govan, V. A., Constant, D., Hoffman, M., & Williamson, A. L. (2006). The allelic distribution of-308 Tumor Necrosis Factor-alpha gene polymorphism in South African women with cervical cancer and control women. *BMC cancer*, 6(1), 24.
- Kanehisa, M., Goto, S., Furumichi, M., Tanabe, M., & Hirakawa, M. (2010). KEGG for representation and analysis of molecular networks involving diseases and drugs. *Nucleic acids research*, 38(suppl_1), D355-D360.

- Katze, M. G., He, Y., & Gale, M. (2002). Viruses and interferon: a fight for supremacy. *Nature Reviews Immunology*, 2(9), 675-687.
- Locksley, R. M., Killeen, N., & Lenardo, M. J. (2001). The TNF and TNF receptor superfamilies: integrating mammalian biology. *Cell*, 104(4), 487-501.
- Lombard, I., Vincent-Salomon, A., Validire, P., Zafrani, B., De la Rochefordiere, A., Clough, K.,... & Sastre-Garau, X. (1998). Human papillomavirus genotype as a major determinant of the course of cervical cancer. *Journal of clinical oncology*, 16(8), 2613-2619.
- Mantovani, A., Allavena, P., Sica, A., & Balkwill, F. (2008). Cancer-related inflammation. *nature*, 454(7203), 436-444.
- Markowitz, L. E., Dunne, E. F., Saraiya, M., Chesson, H. W., Curtis, C. R., Gee, J.,... & Unger, E. R. (2014). Human papillomavirus vaccination: recommendations of the Advisory Committee on Immunization Practices (ACIP). *Morbidity and Mortality Weekly Report: Recommendations and Reports*, 63(5), 1-30.
- Moscicki, A. B., Schiffman, M., Kjaer, S., & Villa, L. L. (2006). Updating the natural history of HPV and anogenital cancer. *Vaccine*, 24, S42-S51.
- Nicol, A. F., Fernandes, A. T. G., & Bonecini-Almeida, M. D. G. (2005). Immune response in cervical dysplasia induced by human papillomavirus: the influence of human immunodeficiency virus-1 co-infection-review. *Memorias do Instituto Oswaldo Cruz*, 100(1), 1-12.
- Nisreen K. (2017). Estimation of Fas Ligand Protein (FASL) in patients with varicella zoster virus in Hilla/Iraq. *Pakistan of journal Biotechnology*. 14 (4) 707- 709.
- Nisreen K., Sama J., Shireen S., Oruba K., Zahraa I.(2017).. Immunological Study for Patient with Verruca Vulgaris and Verruca Plana Caused by HPV in Hilla/ Iraq.: *Journal of Global Pharma Technology*. 09(9):63
- Nisreen K., Shaima A., Israa A.(2017). Evaluation of CD4 and CD8 in Patients Infected with Genital Wart Caused by Human Papilloma Virus in Babylon Province/Iraq. *Journal of Global Pharma Technology*. 12(09):372-375
- Poljak, M., Cuzick, J., Kocjan, B. J., Iftner, T., Dillner, J., & Arbyn, M. (2012). Nucleic acid tests for the detection of alpha human papillomaviruses. *Vaccine*, 30, F100-F106.
- Roff, S. R., Song, E. N., & Yamamoto, J. K. (2014). The significance of interferon- γ in HIV-1 pathogenesis, therapy, and prophylaxis. *Frontiers in immunology*, 4, 498.
- Ronco, G., Giorgi-Rossi, P., Carozzi, F., Confortini, M., Dalla Palma, P., Del Mistro, A.,... & Naldoni, C. (2010). Efficacy of human papillomavirus testing for the detection of invasive cervical cancers and cervical intraepithelial neoplasia: a randomised controlled trial. *The lancet oncology*, 11(3), 249-257.
- Roudgarmi, P., & Farahani, E. (2016). Characterization of Sand Dunes to Detect the Sand Source and their Stabilization, Abardej, Iran. *International Journal of Geography and Geology*, 5(1), 1-9.
- Sankaranarayanan, R., Nene, B. M., Shastri, S. S., Jayant, K., Muwonge, R., Budukh, A. M.,... & Chinoy, R. (2009). HPV screening for cervical cancer in rural India. *New England Journal of Medicine*, 360(14), 1385-1394.
- Scott, M. E., Shvetsov, Y. B., Thompson, P. J., Hernandez, B. Y., Zhu, X., Wilkens, L. R.,... & Goodman, M. T. (2013). Cervical cytokines and clearance of incident human papillomavirus infection: Hawaii HPV cohort study. *International journal of cancer*, 133(5), 1187-1196.
- Simoes, R. T., Gonçalves, M. A. G., Donadi, E. A., Simoes, A. L., Bettini, J. S. R., Duarte, G.,... & Soares, E. G. (2005). Association of tumor necrosis factor α -2 and α -8 microsatellite alleles with human papillomavirus and squamous intraepithelial lesions among women in Brazil. *Journal of clinical microbiology*, 43(8), 3932-3937.
- Song, S. H., Lee, J. K., Seok, O. S., & Saw, H. S. (2007). The relationship between cytokines and HPV-16, HPV-16 E6, E7, and high-risk HPV viral load in the uterine cervix. *Gynecologic oncology*, 104(3), 732-738.
- Swardfager, W., Lanctôt, K., Rothenburg, L., Wong, A., Cappell, J., & Herrmann, N. (2010). A meta-analysis of cytokines in Alzheimer's disease. *Biological psychiatry*, 68(10), 930-941.
- Turner, M. C., Chen, Y., Krewski, D., & Ghadirian, P. (2006). An overview of the association between allergy and cancer. *International journal of cancer*, 118(12), 3124-3132.
- Tyring, S. K. (2000). Human papillomavirus infections: epidemiology, pathogenesis, and host immune response. *Journal of the American Academy of Dermatology*, 43(1), S18-S26.
- Victor, F. C., & Gottlieb, A. B. (2002). TNF-alpha and apoptosis: implications for the pathogenesis and treatment of psoriasis. *Journal of drugs in dermatology: JDD*, 1(3), 264-275.
- Wang, H., & Diepgen, T. L. (2005). Is atopy a protective or a risk factor for cancer? A review of epidemiological studies. *Allergy*, 60(9), 1098-1111.

- Wright, T. C., Schiffman, M., Solomon, D., Cox, J. T., Garcia, F., Goldie, S.,... & Saslow, D. (2004). Interim guidance for the use of human papillomavirus DNA testing as an adjunct to cervical cytology for screening. *Obstetrics & Gynecology*, 103(2), 304-309.
- Zahraa I., Zainab A., Nisreen K., Tsahel H., Abeer F.(2017). Investigation of Oxidative Stress in Patient with Varicella ZosterVirus (VZV) Infection. *Journal of Global Pharma Technology*.2017; 10(9):94-97.
- Zehbe, I., Hacker, G. W., Su, H., Hauser-Kronberger, C., Hainfeld, J. F., & Tubbs, R. (1997). Sensitive in situ hybridization with catalyzed reporter deposition, streptavidin-Nanogold, and silver acetate autometallography: detection of single-copy human papillomavirus. *The American journal of pathology*, 150(5), 1553.

www.ejobios.org