

# NANOSCIENCE AS AN ADVANCED TECHNOLOGY IN THE FIELD OF OVARIAN ONCOLOGY

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**Abstract:** Nanotechnology does provide us with the space to improve the cancer prevention efficacy by using advanced techniques like precision medicine, successive and confined screening techniques. Still, for many cancer types, new approaches for treating established disease are required, especially for treating ovarian cancer, which requires a targeted drug therapy. There has been a burgeon effort to prevent and detect cancer, especially in the field of Ovarian cancer via various inventions and scientific developments. Nanoscience and Nanotechnology, to this context has a pivotal role to play in the treatment of ovarian cancer. This compact communicative review describes the evolution and the trending nanotechnology deployed to curb ovarian cancer.

**Keywords:** ovarian cancer, nanotechnology, nanotherapy

## 1. BACKDROP

The need for an enhanced technology to curb cancer can be evident from the statistics [1] which indicate the rising cancer occurrences coupled with an increased mortality rate. Cancer is one of the leading causes of deaths worldwide with an estimated 7.6 million individuals lost each year and accounting for 13% of all deaths [2]. Several reports have predicted that the cancer related deaths will go up to 13.1 million by the end of 2020, and this is because cancer is not a single disease in which particular virus/bacteria affects the immune system [3].

Instead it is a combination of several diseases related with each organ system. To combat this burgeoning of the mortality statistics, technological innovations are needed to enhance along with human behaviour changes. Several vaccines were developed to cure cancer caused by the Human papilloma virus by enhanced drug delivery and precision medicine. But in the course of this technological era, these vaccines got more efficient by the incorporation of nanotechnology to it. Nanotechnology does provide us with the space to improve the cancer prevention efficacy by using advanced techniques like precision medicine, successive and confined screening techniques. Still, for many cancer types, new approaches for treating established disease are required, especially for treating ovarian cancer, which requires a targeted drug therapy; nanotechnology has been the most modern tool to develop the same [4].

## 2. OTHER THERAPIES

To this context, although the traditional chemotherapy has been a successful to some extent, the process still remains an imperfect diagnosis treatment its poor bioavailability, high-dose requirements, adverse side effects, low therapeutic indices, development of multiple drug resistance, and non-specific targeting [5-10]. And because of this non-specific domain, the cost of the treatment automatically rises. The main driving force in the development of Nanotechnology is to successfully overcome these problems of non-specific targets' and carry drugs to the desired sites of therapeutic action while reducing adverse side effects and making the entire process economical.

## 3. NANOTECHNOLOGY AND NANOTHERAPY

Nanotechnology has redesigned several aspects to the existing challenges in treating the Ovarian Cancer detection along with providing with precision therapeutics technological treatments. Nanotechnology improves the untraced biomarkers creating new possibilities to enhance imaging and personalized care. Furthermore, the low dissolution factor [11] of the chemotherapeutic drugs can be over mined by the usage of nanotechnology especially in treating ovarian cancer which relies highly on the amount of the aqueous solubility, thus reducing the side effect along with the adverse pharmacogenomic effects [12].

The effects of nanotechnologies have also revealed treating ovarian cancer through various others chemotherapeutic agents such as the nitric oxide therapy, genetic and phototherapy using siRNA. The most important of all is that nanotechnology will help to suppress the disadvantages which platinum and paclitaxel [13] had over the drug delivery pathway for treating ovarian cancer. Some drugs such as the pegylated liposomal [14-15] doxorubicin are already being used to cure ovarian cancer and are expected to evolve further in these coming decades benchmarking upon the effectiveness and the price. A subclass of nanotechnology is Nanotheranostics which provides heterogeneity, drug resistances and recurrences within the affected Cancerian cells [16]. Recent studies using curcumin has proved to be an effective agent for gene therapy in the purview of ovarian cancers which offers high selectivity along with the combined therapeutics resistances [17].

While nanotechnology can be implied to isolate the blood circulating cancer cells by plugging in the target particle, the same technology can be implemented in case of ovarian cancer to cure advanced stages of cancer and even stage III metastasis [18-20]. Additionally, these technologies can help to identify the cancerous cell and assist to modify it by providing chemo-resistance and recurrences. Ovarian cancer cells like EphA2 have tested to prove the above technology to be true [19].

Recent advancements have converted this technology to isolate the cancer cells by surface modification and probation isolation. Isolating these cells has definitely turned out to be one of the ground-breaking treatments in the field of medical sciences. These approaches aim to affect the cellular marker genes which are controlled by the epigenetic methylations [21] and hence affecting the pharmacokinetics of the micro RNAs associated with cancer mediated cells.

Amidst of it praises, the main disadvantages nanomaterial have is their bio-compatibility. Nanocarriers like quantum dots, metal-ligand bonded nanocarriers or carbon nanotubes possess toxicity to humans since they are not biocompatible and are preferred to be used as ex vivo treatment rather than in vivo therapies [21]. Several pieces of research suggest grafting peroxidases with carbon nanotubes which can make the system biocompatible; however incorporating the grafted agents may decrease the efficiency of the carrier system. The loading charges [22], which a non-grafted nanocarriers possess is much higher as compared to a grafted one, once again questioning the efficiency of the therapeutic pharmacokinetics. For this reason, it is essential to develop a simple structure nanoparticle so that there is viability in terms of reproducibility, control, composition and loading capacities [23].

#### 4. ADDRESSING OVARIAN CANCER VIA INTRAPERITONEAL CHEMOTHERAPY

Intraperitoneal (i.p) chemotherapy is the incorporation of the desired chemotherapeutic agents directly into the peritoneum [24]. Despite this being a proposed theory, the impact might be highly valued since the drug directly works on to the peritoneum tissues which are majorly responsible for the malignant spreads. Tested hypothesis showed that there are few common drawbacks about the Intraperitoneal Chemotherapy administration such as issues and complexities related to peritoneal infusion, lower abdominal pain, fall in the resistance to a high level of drug, and toxicity issues related to the catheter implantation, Intraperitoneal Chemotherapy can be effective to maintain an optimum local drug concentration for a durational period and maximize the loco regional effects on peripheral tumours.

An in situ cross linked hydrogel was fabricated by Sun et al comprising of paclitaxel nano crystals. An anti-solvent temperature induced technology was used to prepare the nano crystals with a particle size of  $258 \pm 28.1$  nm and an inherent potential of  $5.51 \pm 0.42$  mV (zeta) using while hyaluronic acid gel was produced by crosslinking HA-adipic acid dihydrazide (HA-ADH) and HA-aldehyde (HA-CHO) [25-26]. The table 1 demonstrates the composite feature of the developed nano crystals, which showed that these were initially less cytotoxic than the micro particle formed in the SKOV3 cellular atmosphere due to decreased retention of the aldehyde retention. But after a single dose of intraperitoneal drug delivery, the study showed that nano crystals were more toxic than the micro crystals PTX which is an important phenomenon for the destruction of the malignant cells [27].

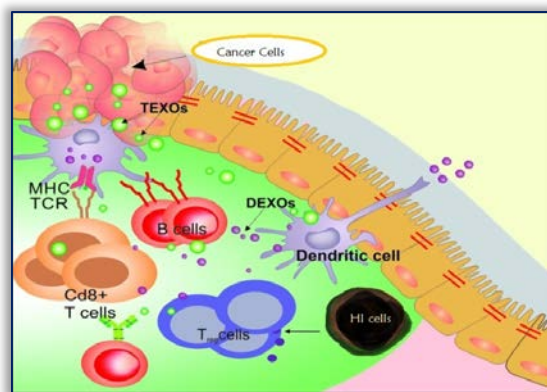


Figure 1- A schematic view of the Intraperitoneal Chemotherapy [26]

Table 1 - Comparative study of Paclitaxel with PTX

Drug	Delivery System	Targeting Ligand	Carrier material	Preparation method	Characterises	Results	Reference
Paclitaxel	Nanoparticle	Follicle-stimulating hormone polypeptide	Hyaluronic acid	Temperature induced crystallization	Particle size: 258.5 nm Zeta potential: 5.51 mV	- Improved cellular uptake - Higher drug concentrations in lymph nodes - Decreased tumor volume - Increased survival time	25
PTX	Micro Crystal	Follicle-stimulating hormone polypeptide	PEG-PLA	Emulsion/solvent evaporation technique	Particle size: 120 - 250 nm Zeta potential: 35 m	- Enhanced interaction with TEM1-positive MS1 cells, - Significant cytotoxicity	26

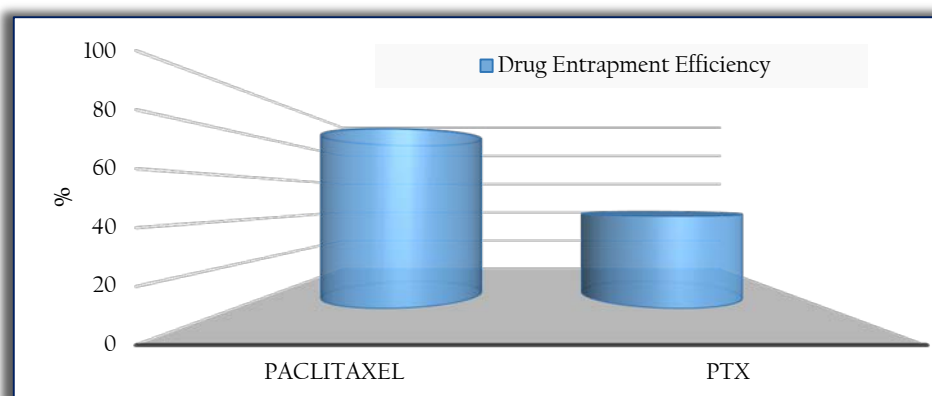


Figure 3- Comparing the Drug entrapment efficiency using Intraperitoneal Chemotherapy

## 5. CONCLUSIONS

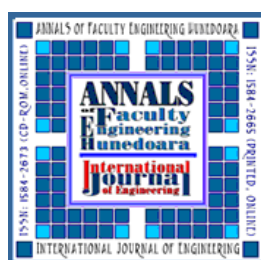
Although it seems that fabricating the design is a herculean task, with recent advancements and developments it is possible to synthesize biocompatible carriers. The number of students opting courses like biotechnology is much less as compared to computer sciences. The result of the same is that we do not produce enough scientists to think about the new synthesis routes and the possibilities. Nanoscience or nanotechnology is not classified as a proper field of engineering making several biologists and chemists diverge away from the field. We need to have more inter-disciplinary classes on these topics which can coalesce amongst themselves to form an entire pivot for a stream. Stress should be made on the technology rather than the associated sciences or the diseases. We can cover several scopes of subjects like polymer science, pharmaceutical science, and material science in this field to strengthen it up giving rise to a proper shape which can mold the problem are addressing.

Nanotechnology is definitely one of the prime paths taken by researchers to accelerate its way to early detection and cure of ovarian cancer. The advancement and the innovation can only be connected to solving the problem if the stream gets a bit more orientation blended with physicist, biologists, chemist, technologists, and pharmaceutics.

## References

- [1] Bellan LM, Wu D, Langer RS. Current trends in nanobiosensor technology. *Rev Nanomed Nanobiotechnol.* 2011;3:229–46.
- [2] Jokerst JV, Raamanathan A, Christodoulides N, Floriano PN, Pollard AA, Simmons GW, Wong J, Gage C, Furmaga WB, Redding SW, McDevitt JT. Nano-bio-chips for high performance multiplexed protein detection: determinations of cancer biomarkers in serum and saliva using quantum dot bioconjugate labels. *Biosens Bioelectron.* 2009;24:3622–9.
- [3] Raamanathan A, Simmons GW, Christodoulides N, Floriano PN, Furmaga WB, Redding SW, Lu KH, Bast RC, Jr, McDevitt JT. Programmable bio-nano-chip systems for serum CA125 quantification: toward ovarian cancer diagnostics at the point-of-care. *Cancer Prev Res (Phila)* 2012;5:706–16.
- [4] Ravalli A, dos Santos GP, Ferroni M, Faglia G, Yamanaka H, Marrazza G. New label free CA125 detection based on gold nanostructured screen-printed electrode. *Sens Actuators B.* 2013;179:194–200.
- [5] Li J, Xu Q, Fu C, Zhang Y. A dramatically enhanced electrochemiluminescence assay for CA125 based on dendrimer multiply labeled luminol on Fe<sub>3</sub>O<sub>4</sub> nanoparticles. *Sens Actuators B.* 2013;185:146–53.
- [6] Hong H, Zhang Y, Sun J, Cai W. Molecular imaging and therapy of cancer with radiolabeled nanoparticles. *Nano Today.* 2009;4:399–413.
- [7] Hahn MA, Singh AK, Sharma P, Brown SC, Moudgil BM. Nanoparticles as contrast agents for in-vivo bioimaging: current status and future perspectives. *Anal Bioanal Chem.* 2011;399:3–27.
- [8] Wu X, Wu M, Zhao JX. Recent development of silica nanoparticles as delivery vectors for cancer imaging and therapy. *Nanomedicine.* 2014;10:297–312
- [9] Maldonado CR, Salassa L, Gomez-Blanco N, Mareque-Rivas JC. Nano-functionalization of metal complexes for molecular imaging and anticancer therapy. *Coord Chem Rev.* 2013;257:2668–88.
- [10] Petersen AL, Hansen AE, Gabizon A, Andresen TL. Liposome imaging agents in personalized medicine. *Adv Drug Deliv Rev.* 2012;64:1417–35.
- [11] Cho EC, Glaus C, Chen J, Welch MJ, Xia Y. Inorganic nanoparticle-based contrast agents for molecular imaging. *Trends Mol Med.* 2010;16:561–73.
- [12] Janib SM, Moses AS, MacKay JA. Imaging and drug delivery using theranostic nanoparticles. *Adv Drug Deliv Rev.* 2010;62:1052–63.
- [13] Mura S, Couvreur P. Nanotheranostics for personalized medicine. *Adv Drug Deliv Rev.* 2012;64:1394–416.
- [14] Fleischer AC, Lyschchik A, Jones HW, Jr, Crispens M, Loveless M, Andreotti RF, Williams PK, Fishman DA. Contrast-enhanced transvaginal sonography of benign versus malignant ovarian masses: Preliminary findings. *J Ultrasound Med.* 2008;27:1011–8.

- [15] Fleischer AC, Lyshchik A, Andreotti RF, Hwang M, Jones HW, Fishman DA. Advances in sonographic detection of ovarian cancer: depiction of tumor neovascularity with microbubbles. *Am J Roentgenol.* 2010;194:343–8.
- [16] Wheatley MA, Lewandowski J. Nano-sized ultrasound contrast agent: salting-out method. *Mol Imaging.* 2010;9:96–107.
- [17] Rapoport N, Gao Z, Kennedy A. Multifunctional nanoparticles for combining ultrasonic tumor imaging and targeted chemotherapy. *J Natl Cancer Inst.* 2007;99:1095–106. 60.
- [18] Rapoport NY, Kennedy AM, Shea JE, Scaife CL, Nam KH. Controlled and targeted tumor chemotherapy by ultrasound-activated nanoemulsions/microbubbles. *J Control Release.* 2009;138:268–76.
- [19] Fleischer AC, Lyshchik A, Hirari M, Moore RD, Abramson RG, Fishman DA. Early detection of ovarian cancer with conventional and contrast-enhanced transvaginal sonography: recent advances and potential improvements. *J Oncol.* 2012;2012:11.
- [20] Xu H, Regino CAS, Koyama Y, Hama Y, Gunn AJ, Bernardo M, Kobayashi H, Choyke PL, Brechbiel MW. Preparation and preliminary evaluation of a biotin-targeted, lectin-targeted dendrimer-based probe for dual-modality magnetic resonance and fluorescence imaging. *Bioconj Chem.* 2007;18:1474–82.
- [21] Kamaly N, Kalber T, Thanou M, Bell JD, Miller AD. Folate receptor targeted bimodal liposomes for tumor magnetic resonance imaging. *Bioconj Chem.* 2009;20:648–
- [22] Wang L, Neoh KG, Kang E-T, Shuter B. Multifunctional polyglycerol-grafted Fe<sub>3</sub>O<sub>4</sub>@ SiO<sub>2</sub> nanoparticles for targeting ovarian cancer cells. *Biomaterials.* 2011;32:2166–73.
- [23] Jemal A, Siegel R, Ward E, Hao Y, Xu J, Thun MJ. Cancer statistics 2009. *CA Cancer J Clin.* 2009;59:225–249. doi: 10.3322/caac.20006.
- [24] Xin Y, Huang Q, Tang JQ, Hou XY, Zhang P, et al. (2016) Nanoscale drug delivery for targeted chemotherapy. *Cancer Lett* 379: 24-31.
- [25] Drbohlavova J, Chomoucka J, Adam V, Ryvolova M, Eckschlager T, et al. (2013) Nanocarriers for anticancer drugs--new trends in nanomedicine. *Curr Drug Metab* 14: 547-564.
- [26] Cai L, Xu G, Shi C, Guo D, Wang X, et al. (2015) Telodendrimer nanocarrier for co-delivery of paclitaxel and cisplatin: A synergistic combination nanotherapy for ovarian cancer treatment. *Biomaterials* 37: 456-468.
- [27] Fan L, Chen J, Zhang X, Liu Y, Xu C (2014) Follicle-stimulating hormone polypeptide modified nanoparticle drug delivery system in the treatment of lymphatic metastasis during ovarian carcinoma therapy. *Gynecol Oncol* 135: 125-132.



ISSN 1584 - 2665 (printed version); ISSN 2601 - 2332 (online); ISSN-L 1584 - 2665

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