

Review

Joseph Youkhanna, Joan Syoufjy, Mary Rhorer, Oyebola Oladeinde and Reema Zeineldin*

Toward nanotechnology-based solutions for a particular disease: ovarian cancer as an example

Abstract: Recent nanotechnology research has been enhancing or creating new applications that have the potential to advance the diagnosis or therapy of diseases. These contributions to the field of nanomedicine have so far been focused on creating the new technologies rather than focusing on particular diseases in order to improve their outcomes. For the latter to occur, we recommend the following: (1) creation of interdisciplinary research funding that awards collaborations between biological, medical, clinical, and pharmaceutical scientists with their colleagues in engineering, physics, and chemistry, (2) increasing the training of bio- and medical students in the field of nanotechnology, and (3) focusing on specific diseases for creating nano-based solutions. In this review, we focus on ovarian cancer as an example of a disease that could benefit from advances in nanotechnology to enhance its understanding, diagnosis, and therapy. We also stress the need to train biological, medical, clinical, and pharmaceutical students in the field of nanotechnology with presenting results on such training in USA pharmacy schools.

Keywords: diagnosis; nanotechnology; ovarian cancer; pharmaceutical; PharmD students; therapy; training.

*Corresponding author: Reema Zeineldin, Department of Pharmaceutical Sciences, MCPHS University, 19 Foster Street, Worcester, MA 01608, USA, e-mail: reema.zeineldin@mcpchs.edu
Joseph Youkhanna, Joan Syoufjy, Mary Rhorer and Oyebola Oladeinde: Department of Pharmaceutical Sciences, MCPHS University, 19 Foster Street, Worcester, MA 01608, USA

1 Introduction

Research in the nanomedical field has been on the rise resulting in advances that are potentially useful for developing new diagnostic technologies and new therapies, but mostly, they are not focused toward particular diseases. Part of this problem is due to lack of training of personnel in the biomedical and health fields in the

field of nanotechnology. Another reason for this problem is the lack of coordinated efforts that promote interdisciplinary collaborations that focus on disease-oriented nanosolutions.

The purpose of this review is to present the steps needed to move into practice the idea that nanotechnology should be disease-oriented (Figure 1). We present how nanotechnology can improve understanding, diagnosing, and treating a particular disease with using ovarian cancer as an example. We also evaluate the training of biomedical scientists and present potential solutions to enhance their participation in multidisciplinary research.

2 Nanotechnology to improve understanding of ovarian cancer progression

Ovarian cancer is the leading cause of death from a gynecologic malignancy in the USA [1–3]. Ovarian cancer has always been thought to originate in the ovarian surface epithelium (OSE); however, recently, evidence points to either originating from the fimbria of fallopian tubes for high-serous-grade ovarian cancer or the OSE for low-grade invasive tumors [4–7]. The main problems of ovarian cancer's poor prognosis have been its late diagnosis, when it has already metastasized to other organs, and relapse due to resistance to therapy. The first line chemotherapy for ovarian cancer is usually a combination of platinum- and taxane-based agents. However, resistance to both and, in particular, to platinum is common and is associated with relapse and recurrence of the disease. Some of these problems hindering eradicating ovarian cancer may be resolved if more nanotechnology efforts are directed toward understanding the mechanism of its progression, enhancing its early diagnosis, improving its therapy, and overcoming resistance. Recent developments in the nanotechnology field are helping us understand certain characteristics of

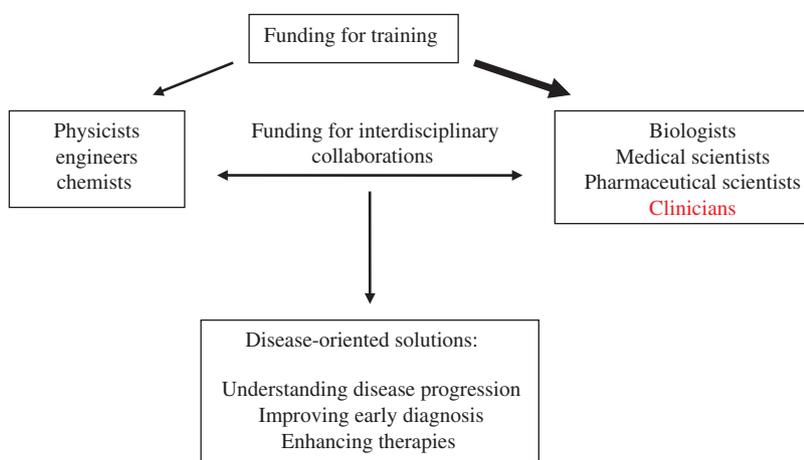


Figure 1 Schematic of steps needed for heading toward nanotechnology-based solutions for a particular disease.

ovarian cancer cells, such as variation of cells' elasticity associated with sensitivity or resistance to therapy, affected cell-cell adhesions, and improving detection of ovarian cancer stem cells and circulating tumor cells. We will address each of these points separately and present how nanotechnology could improve our understanding of ovarian cancer progression and enhance its diagnosis and therapy.

2.1 Evaluate ovarian cancer origin and staging

Recently, it became clear that ovarian cancer may arise from either the fimbria of fallopian tubes or the OSE. High-grade serous ovarian carcinoma originates in the fimbria of fallopian tubes and is characterized by *p53* inactivations [8–10]. In contrast, low-grade serous carcinomas seem to originate in the OSE or fallopian tubes and are characterized by mutations in *K-RAS*, *B-RAF*, and *PTEN* [8, 10–12].

The question to consider here is, can nanotechnology help identify for each patient the origin of her disease. The importance of answering this question is that it may help to determine the extent and the stage of the disease and potentially evaluate its response to therapy. In addition, this will facilitate better understanding of the mechanisms of ovarian cancer progression. To identify the origins of ovarian cancer, some efforts may be directed to create multimarker screening devices that are capable of evaluating simultaneously several markers of OSE or fallopian fimbria or even evaluate intracellular gene mutations or gene expression to understand the progression of the disease and potential response to therapy.

2.2 Probing ovarian cancer cells with atomic force microscopy for elastography

Certain nanotechnology applications may help us determine the changes in the mechanical properties of ovarian cancer cells during disease progression as they become more motile or resistant to chemotherapy. A variety of biophysical techniques such as membrane stretching, atomic force microscopy, optical traps, micropipette aspiration, particle tracking rheometry, magnetic twisting cytometry, optical tweezers, and various biophysical techniques in nanotechnology make use of ferromagnetic or superparamagnetic beads to attach to ovarian cancer cell receptors [13–18]. This allows for twisting and stretching of the cell, which provides a way to better understand the mechanical properties by which these cells progress.

A recent study evaluating cell stiffness using atomic force microscopy (AFM) found that invasive ovarian cancer cells are less stiff than the ones with lower invasive potential [19] or benign cells [20]. Also, they are more viscous than benign cells [20]. Furthermore, results showed that decreasing the organization of actin had a much greater effect on decreasing the elasticity and viscosity of a cell compared to decreasing the microtubule organization, the effect of which was insignificant [21]. It was concluded that the measurement of cell stiffness was a more sensitive measurement in determining the potential of cells to undergo metastasis when compared to examining the cell structure or epithelial characteristics (from determining the level of E-cadherin, cortical actin, and vimentin expression in certain ovarian cancer cells) [20, 21]. Stiffness measurements by AFM is helping better understand the mechanisms at work in tumor progression, at the

physical and molecular level, thus, providing the clinical means that will determine the potential of cells to become metastatic. AFM was also used to differentiate between the nanomechanical properties of cisplatin-resistant and cisplatin-sensitive cells [22]. Only cisplatin-sensitive cells exhibited increased stiffness that was dose-dependent [22]. This research may help understand the mechanisms of drug resistance in relation to remodeling of the cell architecture.

2.3 Ovarian cancer specialized cells

There is evidence for the existence of certain rare cancer cells in ovarian cancer, including cancer stem cells (CSCs) and circulating tumor cells (CTCs) [23]. CSCs in ovarian cancers are heterogeneous and resistant to therapy and are capable of giving rise to similar cells or more differentiated ones [23–27]. CSC isolation and enrichment is based on expression of specific cell markers [24, 28]. Nanotechnology has the potential to improve our understanding of CSCs' heterogeneity through cellular biomarkers screening, which may help resolve the origins of ovarian cancer whether it is OSE or fallopian fimbria. Furthermore, labeling CSCs with magnetic nanoparticles or quantum dots allows their *in vivo* tracking for the purpose of studying their migration and contribution to disease progression [29]. Another potential nanotechnology contribution could be targeting CSCs through their specific cell markers with nanocarriers loaded with cytotoxic agents. Potential targets within the CSCs could include the epigenetically modified regulatory elements or microRNAs [30].

The other type of rare cells is ovarian circulating tumor cells (CTCs), which are hard to detect. Nanotechnology could improve the detection of these cells; for example, recently, a novel microfluidic chip-based micro Hall made it possible to detect rare ovarian CTCs in the presence of immense numbers of blood cells and unbound reactants [31]. The magnetization properties and the bio-orthogonal chemistry of magnetic nanoparticles make it possible to detect biomarkers, epithelial cell adhesion molecule, and specific receptors of any individual cell [31]. The techniques and methods mentioned above provide a less expensive way in the diagnosis of rare cancer cells in clinical settings. Several microfluidic platforms or immunomagnetic particles employing recognition of CTCs' markers have been created to detect or enrich for CTCs in cancers, and the reader is referred to a recent comprehensive review on this topic [32].

2.4 Other possibilities

Another nanotechnology contribution that may help study specific ovarian cancer cells from ascitic fluid is the ability to selectively remove them using magnetic nanoparticles [33, 34]. Nanotechnology may help understand ovarian cancer cell adhesions by using specific surface topographies that have nanoscale features or certain functional groups in order to evaluate interactions of ovarian cancer cells or ovarian CSCs with these surfaces, which may be designed to simulate mesothelial cells. For example, such surfaces that had immobilized E-cadherin or fibronectin on substrates have been used with other cell types [35], and they could easily be used with ovarian cancer cells. The value of this is to create simplified models with isolated molecules to understand interaction events that usually lead to adhesion of ovarian cancer cells to the mesothelial lining of the peritoneum, which precedes their invasion and metastasis.

3 Nanotechnology for ovarian cancer diagnosis

Late diagnosis of ovarian cancer is a serious problem as most women do not get diagnosed with the disease early enough to treat it. Instead, most are diagnosed when they are already at advanced stages (III or IV), when the disease has already spread to other organs. Early diagnosis of ovarian cancer will lead to immediate therapy and improved survival rate [1]. Nanotechnology could serve the early diagnosis of ovarian cancer by improving either screening of biomarkers or imaging techniques. Our purpose is to give a general overview on the possibilities where nanotechnology may enhance diagnosis of ovarian cancer; for more details, the readers are referred to our recent review on this topic [36].

3.1 Biomarker screening in ovarian cancer

Combining transvaginal sonography and serum marker CA125 (MUC16) has been the main modality studied so far for diagnosing ovarian cancer [1]. Recent advances in proteomics and genomics led to identification of additional diagnostic or prognostic biomarkers including genes, proteins, and metabolites [1, 37, 38]. Nanotechnology contribution to this area is mainly through creating new platforms to assess, simultaneously, hundreds of biomarkers in small volumes of samples. These

platforms may include microfluidics or functionalized nanoparticles that adsorb to low abundance or low molecular weight biomarkers as summarized by Kim and coworkers [36].

3.2 Imaging of ovarian cancer

Recent improvements in existing imaging techniques are due to the use of nanomaterials in these techniques. An example of this is using in sonography lipid- or polymer-based microbubbles that contain contrast agents in what is referred to as contrast-enhanced ultrasound (CE US) [39–41]. The microbubbles may be targeted to specific cell markers such as vascular endothelial growth factor (VEGF) receptor, integrins, or P-selectin, which enables imaging at the vasculature or inflammation sites [42–47]. The half-life of the microbubbles is increased by functionalization with polyethylene glycol (PEGylation). CE US has been used in ovarian cancers to assess microvascular changes, which helps differentiate between benign and malignant cancers [48–50]. The advantages of this imaging technique include the early detection of neovascularities at metastatic sites and monitoring of the response to anti-angiogenic therapy in cancers [41, 51, 52].

Many nanomaterials have unique characteristics that enabled various modes of imaging including molecular and/or multimodal imaging in addition to enabling imaging techniques that were not previously in use. Molecular imaging techniques target particular cancer-associated cell markers either on the cell surface or intracellular markers such as intracellular signaling molecules or may even target gene expression [53–55]. Examples of such markers in ovarian cancer are folate receptor α and CA125. Multimodal or multiplexed imaging results from combining more than one imaging technique simultaneously for the early detection and to obtain information about the cancer localization and metastasis [56]. Moreover, multimodal imaging enables examining molecules within distinct cellular events simultaneously and in real time. Another advantage of nanoparticles is that they are multifunctional, so they can be functionalized with various moieties including targeting ligands, imaging agents, and more than one therapeutic agent. This characteristic of combining an imaging agent and a therapeutic agent allows for simultaneous diagnosis and therapy while following the patients' response to therapy through imaging, which is referred to as theranostics.

Some examples of the newer deep-tissue imaging techniques that employ nanomaterials and that were not previously in use are surface-enhanced Raman

spectroscopy (SERS)-based imaging and photoacoustic imaging (PAI). In SERS-based imaging, metallic nanoparticles such as gold and silver act as amplifiers to produce strong Raman spectrum [57, 58]. In PAI, carbon nanotubes and gold nanoshells are used [59–63] with non-ionizing near-infrared (NIR) light, which results in the generation of ultrasound waves that are collected and converted to electrical signals [63–67]. Furthermore, nanotechnology has been enhancing the sensitivity of magnetic resonance imaging (MRI) through the use of gadolinium-based nanoparticles or iron oxide nanoparticles as contrast agents [68, 69]. Using liposomes, micelles, or dendrimers as carriers of these contrast agents reduces the direct toxicity of contrast agents [70–79]. In addition, iron oxide has been used for molecular imaging to detect various cancer-specific cell markers such as folate receptor α , integrins, and transferrin receptor [68]. All the above improvements in imaging techniques are due to the unique optical characteristics of nanomaterials, and they could be employed for the diagnosis of ovarian cancer.

4 Nano-based ovarian cancer therapy

The treatment of ovarian cancer usually involves cytoreductive surgery followed by the standard first-line chemotherapeutic combination regimen of platinum- and taxane-based drugs [37, 80, 81]. Many ovarian cancer patients suffer from recurrence of ovarian cancer, and they become resistant to therapy and incurable [1–3, 37, 81]. Newer directions in ovarian cancer therapy may target the tumor microenvironment, e.g., use anti-angiogenic or immunomodulatory therapeutic agents [82–85]. Nanotechnology has the potential to enhance ovarian cancer therapy in many ways including enhancing intraperitoneal (IP) therapy, employing targeted nanocarriers, overcoming resistance, and introducing new modes of therapy as summarized in the following sections.

4.1 Nano has the potential to enhance IP therapy and reduce toxicity

Although IP therapy alone or in combination with intravenous (IV) therapy has better efficacy than IV therapy alone, the toxicities associated with it have been limiting its use in patients [86]. This is an area where nanotechnology could contribute through reducing toxicities of cytotoxic agents through being encapsulated within nanocarriers.

Furthermore, recent studies demonstrate that IP administration of some nanocarriers resulted in their accumulation in the peritoneum including paclitaxel-loaded nanoparticles [87] and iron oxide nanoparticles [88]. This is a promising finding, but it may be nanoparticle-dependent.

4.2 Targeted nanocarrier therapies in ovarian cancer

The multifunctionality of nanocarriers makes them ideal for decorating with targeting moieties to ovarian cancer cells while at the same time being loaded with more than one therapeutic agent or even with therapeutic and imaging agents for theranostic value. The readers are referred to a recent review for more details on potential cell markers being targeted, such as VEGF, folate receptor α , mucins and other receptors in addition to presenting studies on the various types of nanocarriers being evaluated for this purpose [36].

4.3 Overcome resistance to chemotherapy in ovarian cancer

4.3.1 The mucin barrier

The presence of mucins (MUC) including CA 125 (MUC16) is a characteristic of epithelial ovarian cancers. Mucins are large extracellular proteins that carry oligosaccharide glycosylations serving to protect the cell and regulate the microenvironment at the cell surface. It has been determined that aberrant mucin expression occurs in ovarian tumors; the most notable being MUC1, MUC4, MUC5AC, MUC13, and MUC16 [89, 90]. Aside from screening purposes, mucins have been shown to form a physical barrier that hinders chemotherapeutics' access to cells in many carcinomas, such as pancreatic and breast cancers [91, 92]. It appears that large penetration force is required for penetration of the tip of atomic force microscope for multidrug resistance ovarian cancer cells when compared to the same cells after inhibition of glycosylation that resulted in a reduced density of mucins [93]. This confirms that mucin forms a physical barrier to chemotherapy.

In ovarian cancer, specifically, mucins have been linked to peritoneal metastasis through the interaction with mesothelin on the peritoneal lining as well as inhibiting the normal immunological response of natural killer (NK) cells that results in lysis of ovarian cancer cells, thus, leading to tumor progression [94–96]. Treatment of ovarian cancer by targeting the mucin barrier could improve the

chemotherapeutic response of cancerous tumor cells. It was suggested that nanotechnology may be incorporated into this type of treatment by coupling anti-mucin radio-labeled antibodies with liposomes and other nanoparticles to improve the response in treating resistant tumor cells through increased tumor uptake and chemotherapy retention [90]. Moreover, nanotechnology could improve the penetration of the mucin barrier if nanoparticles are loaded with enzymes that specifically digest mucins or interfere with their gene expression.

4.3.2 Spheroids penetration

Ovarian cancers usually shed cells in the form of single cells or multicellular aggregates (MCAs) or what is referred to as spheroids. These spheroids may attach to the mesothelial lining of the peritoneum to initiate secondary tumors in adjacent organs [97–99]. They are resistant to radiation- and chemotherapy and contribute to relapse in treatment [99–102]. Improved penetration of these spheroids has been recently reported using carbon nanotubes [103]. This finding shows great promise for carbon nanotubes, or perhaps rod-shaped nanomaterials, in improved uptake and penetration by these aggregated cells, which could potentially enhance their response to therapy and which remains to be explored further.

4.4 New modes of therapy and other possibilities

Newer modes of therapy are emerging due to special characteristics of nanomaterials. For example, photodynamic therapy uses a selective wavelength of light to irradiate targeted photosensitizing nanomaterials that have been administered locally or systemically. The form of radiation most commonly used to heat the nanoparticles is NIR tuned to a wavelength between 650 and 900 nm [104]. When irradiated, the nanomaterials absorb the radiation, generating heat and causing apoptosis of the cells that have internalized the nanomaterials. This form of cell killing is commonly referred to as photothermal ablation. Among the nanomaterials that have been studied and proven to be effective photosensitizers are gold nanoparticles and carbon nanotubes [105–109]. These nanomaterials, along with magnetic nanoparticles that have photo- or magnetothermal characteristics, could be useful in combining imaging with ablation therapy to monitor responses to individualized therapies.

Additional new strategies for improved ovarian cancer therapy may employ enzyme-triggered drug release where enzymes within the tumor environment may hydrolyze the nanocarrier to trigger drug release at the tumor site [110]. In the case of ovarian cancer, phospholipases and metalloproteases that exist at the cancer microenvironment [111–113] could be employed for such a mechanism of drug release.

5 Training bio- and medical specialists in the field of nanotechnology

We presented above the possibilities where nanotechnology could improve research and therapy of a disease using ovarian cancer as an example. There is a great need to move from trying new nanotechnologies with cell systems or animal models that happen to be available to researchers to doing research that is more focused on particular diseases. For that purpose, interdisciplinary collaborations are needed between engineers, physicists, and chemist with their colleagues in the bio/medical/clinical and pharmaceutical sciences. However, for this to actually happen, the latter scientists must be trained in the field so that they can shift their research from focusing on evaluating toxicities of nanomaterials into nanotechnology-based research that focuses on finding solutions for specific diseases.

Currently, education and training of a new generation of nanotechnology-trained personnel with various specializations does not seem to meet the future workforce needs within the United States, Europe, or the world [114–116]. Since the emergence of nanotechnology, there has been an emphasis on the importance of educating students studying engineering, physics, chemistry, and material science on the topic to provide the labor force that is needed to push forth industrial advancement [114, 117, 118]. In contrast, educating students within the biological, medical, pharmaceutical, clinical, or health science fields on the topic has been lagging or even hardly mentioned in literature.

Currently, the vision of education on nanotechnology focuses on using degrees in traditional disciplines and adding an option for a minor, concentration, or certificate in nanotechnology [115]. These programs attract mainly nonbiology and nonmedical students because they are offered by nonbio- or nonmedical departments such as chemistry, physics, or engineering departments.

Recently, Duncan and Gasper (2011) critically evaluated the clinical relevance of preclinical and clinical studies in the field of nanotechnology [119]. One of their conclusions was that although nanotechnology has great potential in contributing to nano-based therapies and diagnostics, such successful disease-specific contributions may be possible through interdisciplinary collaborations [119]. This translates to collaborations not only between engineers, physicists, and chemists but also with biological, biomedical, clinical, and pharmaceutical scientists.

We sent a survey to pharmacy schools within the United States to evaluate if the topic of nanotechnology is taught to pharmaceutical science graduate students and to Doctor of Pharmacy (PharmD) students. The survey instrument consisted of six questions regarding nanotechnology (Table 1) and was approved by the authors' Institutional Review Board (IRB) with an exempt designation. Forty-three (43.4% response rate) pharmacy schools responded to the survey (Table 1). Several pharmacy schools (20 out of 43) volunteered unsolicited information about which courses taught a section on nanotechnology.

As shown in Table 1, only four (9.3%) pharmacy schools offer a stand-alone elective course on nanotechnology to PharmD students. On the other hand, 29 (67.4%) schools offer the topic as part of another course. Nonetheless, those 29 schools were among 33 schools that indicated that students had only a brief exposure to the topic. According to the extra information volunteered by responding schools, when this topic is taught as part of another course, that course is either a core course like pharmaceuticals or biopharmaceuticals or an elective such as advanced or novel drug delivery systems, biotechnology, or pharmacogenomics. Several schools volunteered information that such teaching is at an introductory level and is for part of a lecture or two rather than a stand-alone topic.

Among the schools that offer graduate studies (27 schools), we found that 81.5% (22 out of 27 schools) offer a brief exposure to the topic of nanotechnology, while 7.4% (2 out of 27 schools) do not. Only 33% of the schools with graduate programs (9 out of 27) offer the topic as a stand-alone graduate course. Table 1 shows the detailed responses of pharmacy schools regarding the graduate curricula. The number of schools that offered to graduate students a stand-alone course on nanotechnology was not statistically different from those that did not.

In addition, we evaluated the association between groups (PharmD curriculum and graduate curriculum) and the outcomes (yes and no answers) by forming a 2×2

Table 1 Responses of surveyed pharmacy schools.^a

Question	Response (%)			NR ^c	p-Value ^d
	Yes	No	N/A ^b		
PharmD curriculum					
1. Is nanotechnology taught as a stand-alone course to PharmD students, e.g., an elective?	4 (9.3%)	39 (90.7%)	0	0	<0.001
2. Is nanotechnology included as a topic as part of other offered courses?	29 (67.4%)	14 (32.6%)	0	0	0.022
3. Do PharmD students get a brief exposure to the topic of nanotechnology?	33 (76.7%)	9 (20.9%)	1 (2.3%)	0	<0.001
Graduate curriculum					
1. Is nanotechnology taught as a stand-alone course to graduate students, e.g., an elective?	9 (20.9%)	14 (32.6%)	17 (39.5%) ^e	3 (7.0%)	0.297
2. Is nanotechnology included as a topic as part of other offered courses?	20 (46.5%)	4 (9.3%)	16 (37.2%) ^e	3 (7.0%)	0.001
3. Do graduate students get a brief exposure to the topic of nanotechnology?	22 (51.2%)	2 (4.7%)	16 (37.2%) ^e	3 (7.0%)	<0.001

^aThis survey was sent via email to 99 pharmacy schools throughout the USA that were affiliated with the American Association of Colleges of Pharmacy (AAPC) in 2011 and that had the Dean’s contact information readily available through each school’s website.

^bN/A, not applicable. Several Pharmacy schools responded with “not applicable” when answering the questions in relation to graduate program because these schools do not have a graduate program.

^cNR, no response.

^dp-Value from χ^2 -test for each question (null hypothesis: yes=no).

^eSeveral of the responding pharmacy schools answered N/A (not applicable) to the survey as 16 schools do not offer a graduate program in pharmaceutical sciences.

contingency tables for each question (Table 2). We found that only for question 1, on a stand-alone course, the p-value was <0.005 indicating that stand-alone courses on nanotechnology seem to be more prevalent in pharmaceutical science graduate programs rather than PharmD programs.

Overall, this survey demonstrated that most pharmacy schools do not have an established stand-alone course of education in the field of nanotechnology. On the other hand, ~77% of the responding schools indicated that PharmD students get exposed briefly to the topic within one to two lectures. Our findings for the graduate program also showed that one-third of pharmacy schools have a stand-alone course, while the majority teaches it as part of another course or teach it briefly. This survey demonstrates that there is more inclination for the graduate program than the PharmD program to teach nanotechnology as a stand-alone topic. This may be explained by the involvement of graduate students in research contributing to nano-based pharmaceuticals. On the other hand, 77% of the schools that graduate pharmacists with a PharmD degree only briefly expose their students to the topic of nanotechnology. Around 20% in 2007 (predicted 50% in 2020) pursue clinical residencies [120] where they interact with patients while

being consulted on treatments and/or design of clinical trials. This subgroup represents clinicians who lack sufficient training in the field of nanobiotechnology and who could benefit from such training in order to be involved in multidisciplinary collaborations for disease-specific nanosolutions. We suspect that similar limited nanotechnology-educational trends exist among other bio, medical, and clinical fields worldwide; although we are not aware of studies that evaluate this.

Table 2 Contingency tables comparing the responses for PharmD with graduate student curricula.

	PharmD curriculum	Graduate curriculum	p-Value ^a
Question 1 responses			
Yes	4	9	0.008
No	39	14	
Question 2 responses			
Yes	29	20	0.250
No	14	4	
Question 3 responses			
Yes	33	22	0.303
No	9	2	

^ap-Value from Fisher’s exact test for each question (null hypothesis: yes for PharmD=yes for graduate).

6 Summary and future directions

There is a need to create interdisciplinary collaborative opportunities to direct the field of nanotechnology into a direction of research that is disease-oriented rather than material-oriented and, thus, accelerate specific disease needed solutions. Currently, there is a deficit in providing training funding for bio- and medical students (majors: biology, medicine, pharmacy, dentistry, optometry, imaging) at BS, MS, and doctoral levels. A real need for funding exists at the postbaccalaureate level for training basic and clinical scientists who may collaborate with their colleagues in other fields to advance the disease-focused nanotechnologies for the purpose of curing diseases. Funding for this purpose could be set specifically for setting up and for attending

nanotechnology courses, virtual labs, wet labs, and summer internships. Furthermore, there is a current deficiency in the training of biological and medical scientists in the field of nanotechnology. Thus, funding is needed to train the future trainers possibly through summer internships or workshops. In addition, in order to promote interdisciplinary collaborations, then, funding for nano-solutions for specific diseases may be needed. Reviewers of these grants ought to be a combination of disease and nano specialists.

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Joseph Youkhanna received his Doctorate of Pharmacy degree in 2011 at MCPHS University. He obtained his undergraduate studies at Wayne State University in Detroit, MI. He worked closely with Dr. Reema Zeineldin for 1 year researching on teaching the expanding field of nanotechnology. Joseph is currently a staff pharmacist at Walgreens Pharmacy in Detroit, MI, USA.



Joan Syoufjy received her Bachelor Degree (BS) in Molecular Biology at the University of Michigan (US) in 2008. Then, she pursued her Doctor of Pharmacy degree (PharmD) at the MCPHS University where she started to work with Dr. Zeineldin to discover ways to incorporate methods of teaching Nanotechnology to PharmD students. Her interest in Nanotechnology provoked her to continue her education in Nuclear Pharmacy, which involves the preparation of radioactive medicine to help diagnose and treat specific diseases. She is currently employed with CVS/Pharmacy as a pharmacist in charge in Detroit, MI, USA.



Mary Rhorer received her Doctor of Pharmacy degree in May 2013 at MCPHS University in Worcester, MA, USA. Her research work with Dr. Zeineldin has focused on ovarian cancer therapy and nanotechnology. She is currently a clinical pharmacy resident in Albany, VA, Medical Center and she plans to specialize in Oncology Pharmacy.



Oyebola Abiodun Oladeinde received his “Laurea” degree in Chemistry in 2009 at Morgan State University. After graduation, he obtained a cancer research trainee award (CRTA) to join the Center for Cancer Research, Chemical Biology Laboratory at the National Cancer Institute, Frederick, MD, where he studied in the group of Dr. Larry Keefer (2009). In May 2013, he received his Doctor of Pharmacy degree at MCPHS University, where his research project involved the application of nanotechnology-based drug delivery against ovarian cancer resistant to current chemotherapy. He is currently a community pharmacist at Walgreens Pharmacy.



Reema Zeineldin received her PhD in Biomedical Sciences from the University of New Mexico (UNM) where her work focused on understanding the progression of ovarian cancer. During her post-doctoral training, she did research on biosensing in the Department of Chemical and Nuclear Engineering at UNM. She is currently an Associate Professor at MCPHS University teaching PharmD students and performing research that focuses on nano and bio integrations for biosensing and for the therapy of ovarian cancer.