ARTICLES

NGO-ISATION AND THE PLIGHT OF WOMEN IN DEVELOPING NATIONS

Emily Chu

Grade 11, Iroquois Ridge High School, Halton District School Board (Oakville, Ontario), Mentor: Dr. Jaime Llamblas-Wollf (York University)

ABSTRACT

Over the past century, NGOs have been rapidly growing in numbers have become increasingly involved in such health crises as HIV/Aids and Ebola around the world. Many organizations have also been founded to recognize and support oppressed groups in certain countries, one of the most important of these being women. It is undeniable that women of developing nations have been greatly affected by the rise of NGOs, and the ensuing phenomenon of NGO-isation, from increased opportunities for activism, to unsustainable dependencies on nutritional supplements,. This article presents a background of both NGOs and the plight of women in developing nations, as well as attempting to draw a relationship between these two stakeholders in our global society. This article also presents evidence to support the hypotheses that NGOs allow women to become more politically and socially active through government-neutral involvement, but also hinder their health and job prospects by failing to employ local workers and using short-term solutions instead of sustainable ones. Major analysis is conducted on these topics and attempts to determine the correlation between NGOs and their involvement with women in impoverished communities. The article concludes with final comments from the author about their overall experience and thoughts on the issue.

Au cours du précédent siècle, les ONG sont rapidement augmentés en nombre et en implication dans plusieurs pays en développement en conséquence de plusieurs crises de santé telles que VIH / SIDA et Ebola. Plusieurs organisations ont aussi été créés pour donner reconnaissance à certaines groupes dans des pays oppressifs, un des plus importants parmi ces groupes étant les femmes. Il est indéniable que les femmes des pays en développement ont été aidés considérablement par la montée des ONG et le phénomène qui s'ensuit d'ONG-isation. Cet article présente un contexte d'à la fois les ONG et la situation des femmes dans les pays en développement et décrit une proposition de recherche pour tenter de déterminer la relation entre ces deux très importantes parties intéressées dans notre société globale. Cette proposition de recherche décrit ses objectives, buts et hypothèses qui concernent divers aspects de la vie d'une femme et ensuite ça décrit pourquoi ceci est un problème important et comment les données vont être obtenues. L'article conclut avec des commentaires finales de l'auteur à propos de leur expérience générale et leurs pensées concernant le problème.

INTRODUCTION

The topic of this research proposal is the relationship between NGO-isation and women's wellbeing in developing countries. An NGO, or Non-Governmental Organization, is defined as an organization separate from government, and is generally non-profit. Some well-known contemporary NGOs (in the medical/public health field) are Doctors without Borders, The Red Cross/Red Crescent Movement, and Partners in Health. To examine quickly what this type of NGO does, let's look at Doctors Without Borders. This NGO provides emergency health care during things such as armed conflict and epidemics, to countries where their local health systems become overwhelmed. They are a neutral and impartial humanitarian organization that may also assist people who may

face discrimination or neglect from their local health systems. The international component or personality of NGOs can be attributed to the globalization process in the 20th century, as many international problems could not be solved without third party intervention (Dominelli, 2007). They served as an alternative to other governments becoming involved in conflict, as the many wars that took place over the course of the century proved many consequences for neutral countries trying to help. Since several governments were being influenced by international corporations, NGOs arose as a counterbalance factor, working mainly in the fields of humanitarian aid and sustainable development (Bartlett, 2005). The successes of these organizations have led to the arrival of several other

NGOs which have all tried to emulate those of the mid -20th century. Around the world, organizations were created to advocate for almost every cause imaginable. This led to the phenomenon of NGO-isation.

NGO-isation is described as "the transformation of social movements into organizations and the increasing dominance of 'modern' NGOs which emphasize issue-specific interventions and pragmatic strategies with a strong employment focus, rather than the establishment of a new democratic counterculture" (Stubbs, 1997). In short, this movement has greatly changed the way developing nations look at their health systems, and the way citizens receive their health care. In this proposal, I will be focusing on how NGO-isation and its effects affect women and their

RESEARCH OBJECTIVES

These are the objectives of our research: what we want to accomplish, discover, and analyze.

- Collect data from both primary and secondary sources. Interviews will be conducted in specific (affected by both health crises and heavy NGO presence) areas to find out more about how women live their daily lives. For example, Freetown, the capital of Sierra Leone, is a perfect location that involves NGOs in support of the Ebola crisis. This is explained further in the Methodology section.
- 2. Draw interesting and relevant conclusions about the state of women's wellbeing in impoverished countries. Do they suffer more than men? Is their mortality rate higher (especially during childbirth)?
- 3. Draw interesting and relevant conclusions about how NGOs affect local communities in both

HYPOTHESIS AND QUESTIONS

First, it is important to understand the exact role that NGOs play in respective situations. We must clarify their roles in relation to the government and the community, who they are influenced by, and how this consequently affects their relationship with the governments they work with.

Who are the stakeholders within the organizations?
 Who specifically do these organizations affect?
 Do they affect locals and workers as well as governmental organizations?

wellbeing. This research proposal will attempt to look at women socially, biologically, and economically, and attempt to create correlations between their health and the prominence of NGOs in their community. As seen by the works of Ruth Prince, women in Kenya affected by HIV/AIDS, who were generally single, unemployed, or made very little money, depended on NGOs for food supplements for their families. These individual rations were shared amongst families, and created great stress and unsustainability for both the mothers and their families. The critical role women play in their family's lives, from caregiver to main provider, is the reason they are the focus of this article. Therefore, the goal of this research proposal is to discover whether the prominence of NGOs has a positive or negative effect upon women's wellbeing.

- positive and negative ways. For example, does it raise or lower the local unemployment rate?
- 4. Discover correlations between women's prosperity and the presence of NGOs in their communities. Does the increase of NGO presence or involvement correlate with a similar increase in women's employment for example?
- 5. Draw interesting and relevant conclusions about how NGOs affect women in all aspects in their life, whether it is positively or negatively. For example, it may be found that women are offered opportunities to become employed with NGOs, allowing income and quality of life to increase. However, it may also be discovered that women, who are already hungry in their poor socioeconomic conditions, become dependent on insufficient/un-nutritional food supplements.
- Who are these NGOs primarily funded by?
 Does this affect where they put their money and resources due to their donor's interests?
- Are relations with governments neutral or do are they somewhat influenced by political regimes within the nation? How does this affect neutrality and conflict of interests?

There are also many questions surrounding women and their position in this issue. It is important to examine a woman's wellbeing through many perspectives. These

are the questions that need to be answered through the lens of different perspectives:

Social/Political

- Do NGOs give women more power to strive for change? Do they allow women to voice their opinions more and be recognized for their struggles?
- Does it lead to more female representation in government and other organizations?
- Do NGOs enhance or strengthen any present feminist movements?

Biological

- Do NGOs adequately support women in terms of pre-natal and maternal health care?
- Do women benefit from handouts or do they become dependent on unsustainable supplements (in which individual rations are split amongst families), leading to a decrease in their own quality of lives?

Economic

- Does the presence of NGOs enable women to find jobs more easily? Does the presence of NGOs within a community lead to more or less unemployment for women?
- Do NGOs provide any monetary benefits that could be used to supplement or replace income?

After researching more into these questions and the topic in general, these are two hypotheses that were formulated:

- NGOs benefit women in poverty in developing countries in the social and political aspects of their lives. It enables them to voice their opinions that would otherwise be unheard, and NGOs allow them to be protected and become more involved in their communities.
- 2. NGOs hinder the physiological and economic aspects of poor women's lives in developing nations. NGOs do not provide women more opportunities to find jobs, as they do not develop their local economies. They also do not improve facilitative conditions or increase knowledge about maternal health care. Dependency is also a huge factor in this deterioration and can make new mothers dependent on unsustainable supplements.

RATIONALE

In the section above, it is important pose the question of whether women benefit from NGOs or not. There issue has tremendous significance. Women, up until very recently, served a supportive role to men in almost all aspects of their lives. They were relegated to childbearing and providing care and comfort to their partners and their families, forcing them to give up their jobs and live at home. This has led to sexism in the workplace and in society in general. In Western society, much has changed over the past century, as women have been increasingly involved in the workforce and increasingly recognized in politics and the media.

While there is still much ground to cover and glaring inequalities are still present, women of western society have cemented themselves as a powerful civic group, and they continue to gain equality in power and influence. The same cannot be said about women's rights in the rest of the world, particularly in developing countries. Many women in countries like Egypt, Zimbabwe, and Cambodia are still suffering and are not considered anywhere close to equal to men. The work of NGOs, therefore, has the most potential in these regions. Not only are they third-party organizations independent from government influence (in theory, they may be subject to government influence if they receive monetary donations from government agents, leading to a position where they may put their donors interests ahead of the ones they are supposed to serve), they also provide recognition and support for women's groups in places where they generally would be unheard and neglected (Jacobsson, n.d.). However, it is unclear if NGOs provide significant aid to women. or if they actually lessen their quality of lives.

This issue of women and NGOs is extremely pressing and relevant to today's society. Women's issues deserve special attention, especially in countries where women themselves have little to no voice. As seen in Western society, women are crucial to a thriving democracy and society, so it is important that women around the world be supported (Roy, 2015). The involvement of women will pave the way to solving many other social issues, such as education inequality.

Women are the focus of this proposal because of their individual roles and offerings. Not only are they the caregivers and providers for their families, they are also the people in society most affected by rampant

poverty and negative socio-economic conditions. It is worth noting that NGOs are most prominent in areas of need; generally areas of extreme poverty. Women living in these areas are often single mothers, and struggle to find work due to their heavy responsibility of child rearing and caring. An example of this is in Kisumu, Kenya, a community ravaged by HIV/AIDS where most women are single, unemployed or make very little money. There are also many NGOs there, which provide small flour supplements to certain individuals of desperate need (Prince, 2012). When mothers are given this supplement, they often share it with their children and entire families, showcasing how women, and more specifically mothers, put their own needs at risk to help others (Prince, 2012). While not unique to women as a gender, it is more common when most women in developing nations are relegated to caregiving roles, while men work more and may have the income to sustain "middle-class" living (Smith, 2000).

However, NGOs do offer several benefits for women. As NGOs are generally progressive and allow a medium of expression that would otherwise be non-existent, women are given opportunities to participate in activism and community involvement in countries where it would be otherwise dangerous to do so (Jad, 2012). Groups supporting women's rights or feminist movements in oppressive countries are made possible through the existence of NGOs (and are enhanced in non-oppressive but still-developing nations), and this can allow the fight for women's rights to grow and become more recognized within the country (Nazneen, 2009).

The plight of women in developing countries is obvious. While NGOs are designed to help people in need, mostly in developing countries, and for some NGOs specifically women, sometimes the conditions NGOs create when they get involved in a society can have negative repercussions. The purpose of this study is to determine whether the helpful and progressive intentions of NGOs are realized. The main issues that affect women and NGOs are poverty, hunger and malnutrition, sexism, and finally, feminism.

In terms of poverty, many women are single mothers due to the socioeconomic conditions of impoverished communities. They are often forced to work separately from their children in order to provide for them, which neglects their family life, and as a result, family dynamics often suffer. However, they may also be forced to stay at home and care for their families and become

unable to pursue a career. Hunger and malnutrition are also serious issues that greatly affect women. Due to widespread poverty and hunger, mothers often sacrifice their rations of food for their children, so in situations where children are at risk of illness or severe malnutrition, they will starve themselves to provide for them. Also, in developing nations, pregnancy care is not a priority in areas where disease is still rampant, so many women do not get the pre-natal and maternal health care and information they need to take care of themselves. This results in more illnesses in infants, and a higher risk of miscarriage (Davies, 2014).

In many developing nations, women are still oppressed and unable to advocate for their rights. NGOs provide an outlet for this behaviour without repercussions, which is effective in improving and enhancing movements supporting women's rights (Smith, 2000). However, since NGOs utilize a lot of native resources and workers, social issues are carried over. As sexism is an unfortunate part of low socio-economic communities, there is a presence of sexism within the NGOs that become a part of that community, and that is a fundamental issue that will be difficult to change. Although difficult to change, the basic issues of sexism and oppression of feminism is still worth being looked at, as a woman's basic rights are crucial to this study.

Having considered all of this, we must now look towards solutions. If the hypotheses are indeed correct, the way NGOs are run and organized may need to be re-evaluated, and we may need to scrutinize our global relief effort as a whole. Perhaps who they employ, what materials they use, and the sustainability of their remedies are the focus of this reevaluation. It is important that NGOs continue to allow for women to serve as their own activists in their own communities, as sexism is an issue that will continue to exist for many years. However, on the economic and physiological side of the issue, NGOs will need to be reorganized. More focus should be placed on pre-natal health and wellness, to ensure effective motherhood and a decreased infant mortality rate. This is extremely important because this will alleviate some stress from medical centers, and will allow for healthier conditions in child care centers and schools (Chahim, 2013). Mothers will also be less likely to contract potentially life-threatening diseases. Furthermore, NGOs should make a conscious effort to either employ local women. or create opportunities for them, especially in the health

and humanitarian aid sector. Women often take healer or doctoral roles in indigenous or rural communities, and are respected by both locals and outsiders for their methods, as seen by the works of Alicia Giralt and the Mayan-Tz'utujil women of Guatemala. NGOs often take these roles away from women when they integrate into a community, leaving women more economically disadvantaged than before. It is important for NGOs to work with these women, as it will also help them better connect with the community. Through these layered facets and pieces, it becomes apparent that women of impoverished communities and the NGOs that support them could have a mutually beneficial relationship that improves and betters communities as a whole. This is ultimately the goal of our research, and the general movements of both women and NGOs.

METHODOLOGY

Location is critical to collecting the necessary data for this proposal. We need to make sure there is a large enough sample size to accurately study what we are looking for, enough NGO interaction between the community and the government, and all the people affected by the presence of NGOs must be accounted for. As seen in a place like Kisumu, Kenya which had become an epicenter of NGOs and health crises is a good place to collect data. Other examples would include the countries of Sierra Leone or Liberia, which have both recently been affected by Ebola. In response, numerous organizations have become involved in those regions. Sierra Leone's capital, Freetown, would be an effective place to conduct the study due to its high concentration of NGO headquarters, the urban poor, and access to resources.

In terms of collecting data, interviews are the most effective way to do so. Interviewing civilians, the ill, doctors, and government agents (focusing on women of course) will capture some of the perspectives important to this research. Around 20 interviews will accumulate an adequate amount of data necessary for drawing conclusions. The interviews will take place in community centers and will require the presence of a translator. Interviews will give insight into people's perspectives on situations, and will be extremely valuable in trying to figure out how NGOs affect different people differently. Subject matter and questioning will include inquiries on yearly income, number of people in the household, age, involvement

in civic groups, etc. Secondary sources of data will also be used in conjunction with interviews to draw more specific conclusions about women and NGOs. For example, HIV and the Moral Economy of Survival in an East African City by Ruth Prince will be useful in comparing different areas of Africa and the state of wellbeing for women in NGO-driven communities. This text is useful because it contains information about how NGOs influenced the lives of those who suffered from HIV/AIDS. It describes how being sick often reaped benefits from NGOs because they were recognized by an organization that was able to provide them with benefits. This created an odd complex as more people began to identify as HIV positive even if they did not have the disease to try and collect benefits from NGOs. This article provides insight into how NGOs create dependency and unsustainable remedies in communities that result in the worsening of quality of life for the members. It is important and should be looked at when considering the findings from different communities so they can be compared and more accurate conclusions can be drawn.

BIBLIOGRAPHY

- Chahim, Dean, and Aseem Prakash. "NGOization, Foreign Funding, and the Nicaraguan Civil Society." Voluntas VOLUNTAS: International Journal of Voluntary and Nonprofit Organizations (2013): 487-513. Print.
- **2. Davies, Thomas Richard.** NGOs: A New History of Transnational Civil Society. (2014) Print.
- Dominelli, Lena. Revitalising Communities in a Globalising World. Aldershot: Ashgate, 2007. Print.
- **4. Jacobsson, Kerstin.** Beyond NGO-ization: The Development of Social Movements in Central and Eastern Europe. Print.
- **5. Jad, Islah.** "The NGO-isation Of Arab Women's Movements." IDS Bulletin (2012): 34-42. Print.
- 6. Nazneen, Sohela, and Maheen Sultan. "Struggling for Survival and Autonomy: Impact of NGO-ization on Women's Organizations in Bangladesh." Development (2009): 193-99. Print.
- **7. Prince, Ruth.** "HIV and the Moral Economy of Survival in an East African City." Medical Anthropology Quarterly 2012: 534-56. Print.

- **8. Roy, S.** "The Indian Women's Movement: Within and Beyond NGOization." Journal of South Asian Development (2015): 96-117. Print.
- **9. Smith, Bonnie G.** Global Feminisms since 1945: A Survey of Issues and Controversies. London: Routledge, 2000. Print.
- 10. Stubbs, Paul. Social Reconstruction and Social Development in Croatia and Slovenia: The Role of the NGO Sector. Leeds: International Social Policy Research Unit, Leeds Metropolitan U, 1997. Print.

FINAL COMMENTS

Over the past four weeks, I have learned a lot about myself. When I first started this placement I did not expect it to be such an amazing experience, and it is one I will definitely not forget. Not only did I further my skills in research and independent work, I also was able to figure out what issues I was truly passionate about, and writing this research proposal allowed me to delve deep into those topics.

There has never been an experience that has taught me the value of hard work more than this one. Being on my own forced me to make hard decisions like deadlines and deciding which readings to complete first. Of course school involves some organization, but it was through this placement that I was able to learn its true value. I definitely think that this placement has helped me and my work ethics going into grade 12 and especially university. It was also a valuable experience working with Dr. Llambias-Wolff, as he was a university professor that could offer much more insight into the subjects than I could. He chose readings that matched well with my interests, and for that I thank him for making this an enjoyable month. Through the readings, I was able to find out what I liked to research. As Dr. Llambias-Wolff said, it is important to understand the basics of human life and society in order to become a good business person. It was through his mentorship that I was able to thrive and create the research proposal.

Women's rights are very important to me, and I didn't realize this until this placement. Through the readings, I could see how women were taken advantage of and oppressed in third world countries, which saddened me greatly. Although I have experienced some sexism in my own country of Canada, women have much greater freedoms here than in developing nations. I

believe it has been far too long that women have been and continue to be treated secondary in society. NGOs have the power, with their neutrality and influence, to give women voices in places where they would not normally be heard. It is unfortunate to see that some still foster the same sexist sentiments seen throughout the world, and are not encouraging women to pursue equality. This is why this research is significant, because if NGOs today are harming women rather than fostering their growth, we may need to re-evaluate how we run organizations in foreign countries if we want to grow their society.

Of course it is worth noting that I overcame several obstacles over the course of July. Firstly, it was quite a challenge choosing something to write a research proposal about. I was at a stage where I had completed all the readings, but I struggled to find topics that I thought would be broad yet specific enough to find research in. At first I thought simply talking about women's rights was too broad, but it was thanks to a later article which I revisited that I was able to connect the plight of women to NGO-isation, NGO-isation was a topic that I found in many articles, and it was something that was both relevant and interesting to me, so it was perfect. So by revisiting previous articles and making connections, I was able to find an appropriate research topic. Another obstacle I overcame was organizing my thoughts and actions properly. Towards the end of the co-op there were many emails and communication happening between myself and other coordinators. It was important that I stayed on top of all the work that had to be done and all the paper that had to be signed. Unfortunately, because I was working on the research proposal, I missed a deadline for a reflection for my inclass work. Thankfully, I emailed my teacher right away and was able to get things cleared up. Now, I keep a list of everything I have to accomplish in a prioritized fashion to keep me extra-organized.

This paper has allowed me to become much more informed and well-versed in the topics of women's rights and equality. I am very thankful I took this opportunity to pursue this program, because it allowed me to become more introspective on topics that interested me. I was able to see how it was connected to me, and also the world as a whole. I have grown my world sense and view over this summer, and I believe it has benefitted me greatly.

USING NANOPARTICLE-APTAMER BIOCONJUGATES FOR IMAGING AND TREATING PROSTATE CANCER

Timothy Doyle

Grade 12, Bishop Allen Academy, Toronto Catholic District School Board (Toronto, Ontario), Mentor: Dr. Aaron Witham (EBPI)

ABSTRACT

Prostate cancer diagnoses increase each year, and current treatment strategies cause disturbing levels of serious side effects. This has necessitated a search for new strategies to employ more targeted treatments for malignant tissues. One promising alternative therapy is the use of a chemotherapeutic-nanoparticle-aptamer bioconjugate. This method employs aptamers which target over-expressed proteins on cancerous cell surfaces and bind to individual prostate tumour cells with incredible affinity. Once bound, the bioconjugate is taken into the cell where it delivers a toxic payload of chemotherapeutics and destroys the cell by cytotoxic means. The bioconjugate therapy method is specific for cancerous cells which limits side-effects to non-target tissues. Fluorescent properties of some chemotherapeutic components and quantum dot nanoparticles can also provide imaging of these cancerous masses with extreme precision. Successful trials employing aptamers for targeted therapy demonstrate the promise of this technology for future chemotherapeutic applications. Additionally, aptamer conjugates are safer, less expensive, and potentially more effective substitutes to antibody-based targeting methods which are currently being explored as a competing option for this type of treatment.

Les diagnostics de cancer de la prostate augmentent chaque année, et les traitements actuelles qui leurs sont associés sont responsable d'un niveau inquiétant de graves effets secondaires. Cela a nécessité une recherche de nouvelles stratégies dans le traitement plus ciblés des tissus malins. Une thérapie alternative prometteuse se présente dans l'utilisation d'un agent chimiothérapeutique-nanoparticule-aptamer-bioconjugate. Ce procédé engage des aptamères qui ciblent les protéines surexprimées sur la surface des cellules cancéreuses et s'attachent à des individuels cellules tumorales de la prostate avec une affinité épatante. Une fois lié, le bioconjugué s'introduit dans la cellule où il livre une charge toxique de médicaments chimiothérapeutiques ce qui résulte dans la destruction cytotoxique de la cellule cancéreuse. Le procédé de thérapie bioconjugué se dirige vers des cellules cancéreuses ainsi épargnant des effets secondaires le tissu non ciblé. Des propriétés fluorescentes de certains composants chimiothérapeutiques et de nanoparticules de points quantiques aussi aident à fournir des images de ces masses cancéreuses avec une précision importante. Des essais concluants employant des aptamères comme thérapie ciblée distinguent comme prometteuse cette technologie dans des applications chimiothérapeutiques futures. De plus, des conjugués aptamères se sont montrés plus sûrs, moins coûteux, et potentiellement plus efficaces que leurs compétiteurs en traitement à base d'anticorps qui sont actuellement explorés comme option.

INTRODUCTION

Of the approximately 100,000 cases of male cancer diagnoses in Canada each year, 23.9% of these diagnoses will be for prostate cancer, which makes it the most prevalent cancer among Canadian men^[1]. Although methods have been developed to successfully detect and treat prostate cancer initiation and progression, there are several detrimental side-effects that occur at high rates when using these strategies. Some of these effects include impotence, which occurs in approximately 43% of patients, urinary retention in 24% and radiation-induced bowel injury in 1%. Another commonly employed treatment

strategy is the full removal of the prostate gland which results in even higher rates of impotence as well as urinary incontinence^[2]. It is therefore highly desirable to find an alternative which can effectively detect and treat prostate cancer while limiting the side effects associated with current strategies.

One promising, less harmful alternative to the traditional therapeutic strategies, is the use of aptamer based therapeutic conjugates. Aptamers, developed in 1990 and named from the Greek aptus meaning 'to fit', are small pieces of DNA or RNA that can fold into different 3D conformations

and bind to a desired target with extreme specificity. Aptamers have demonstrated the ability to bind with virtually any target and to trigger responses upon the occurrence of correct aptamer-target interactions^[3]. The intramolecular forces of an aptamer are unique to each and depend on the sequence of bases and chain length. These forces permit the aptamer to fold and twist into shapes that can bind to a variety molecular targets, including large proteins, cells, metal ions, and even viruses or parasites^[4]. Due to these applications, aptamers draw many comparisons with antibodies. However, aptamers can bind with much higher specificity, are more cost effective, and can be constructed in vitro, negating animal use.

Aptamers are created using the systematic evolution of ligands by exponential enrichment (SELEX) process, which works by exposing a library of randomly generated oligonucleotide sequences, typically 1014 to 1018 sequences, to a target and isolating the ones that interact with some degree of affinity. The sequences which do not bind are washed away and discarded. The aptamers that bind are repeatedly subjected to the target under different conditions to increase stringency in the selection process. Alternating elution solvents, changing temperature, or decreasing target concentrations are all employed until a few aptamer sequences are isolated that bind to the target with incredibly high affinity^[5].

Aptamer technology showing the greatest promise as a prostate cancer therapeutic involves a collaborative strategy in association with a chemotherapeutic drug, such as doxorubicin or docetaxel and a nanoparticle like a quantum dot (QD). The end product is called a bioconjugate, which is simply a compound made up of different molecules covalently bound together. Each element of the bioconjugate plays a significant and independent role. For example, an aptamer can act as a drug carrying vehicle and target individual cancerous cells by binding to the prostate specific membrane antigen (PSMA) protein. PSMA is a membrane protein which is over-expressed on the surface epithelial cells of prostate tumours[6]. Once the bioconjugate is bound, uptake into the cell is triggered via endocytosis. Depending on other components of the bioconjugate, it can serve several purposes once inside the cell including signalling, imaging and cytotoxicity. Moreover, the therapeutic

destroys the cell and the nanoparticle provides fluorescent light emission and allows the cytotoxic cargo to be transferred safely by encapsulating it, thus protecting it from nuclease degradation^[5]. The bioconjugate therefore not only delivers a targeted dose of chemotherapy but can also be used to image the tumour mass by utilizing its inherent fluorescent properties^[7]. Aptamer targeting mechanisms and the wide variety of multipurpose conjugates that can be constructed using aptamers is showing significant promise to be one of the safest and most effective future developments in medicine.

SYNTHESIS

The first step in producing a therapeutic aptamer for a bioconjugate involves the isolation of a desired target. For the example presented in this paper, the desired target was PSMA, as it is found in abundance almost exclusively on prostate tumour cells. Lupold et al. (2002) isolated PSMA by identifying and culturing the cancerous cell lines from prostate tumour (LNCaP cells), isolating PSMA DNA found within the cells and preparing recombinant xPSM-expressing Baculoviruses. The isolated target was subsequently used for in vitro selection of aptamers that would bind via the SELEX process for nine rounds. By the sixth round of selection, 95% of the aptamers were sequences xPSM-A9 and xPSM-A10. The xPSM-A9 aptamer bound non-competitively to PSMA, and altered the active site, while the xPSM-A10 aptamer bound competitively, directly to the PSMA active site, which made it a more useful option for bioconjugate delivery. Afterwards the aptamer was selected and further modified with the addition of 2'-fluoropyrimidines to increase its stability in biological fluids, through the prevention of nuclease degradation[6]. Because aptamers are made of naturally occurring molecules, they a have a limited half-life in vivo, due to nuclease degradation and natural excretion. Modifications such as oligonucleotide terminal caps. cholesterol, and non-deoxyribose sugars can be added in order to protect the aptamer and increase half-life exponentially within the blood stream^[9].

The second major part of the bioconjugate provided as an example is the quantum dot nanoparticle. QDs are semiconductor nano crystals that are often used in biological imaging, as they are fluorescent in nature and immune to chemical degradation. The QD and xPSM-A10 were then amalgamated creating a QD-aptamer conjugate with the aptamer acting as an escort for this system. The chemotherapeutic chemical, doxorubicin, which is also a fluorescent molecule, was then intercalated between the single 5'-CG-3' regions of the 57 base pair xPSM-A10 aptamer sequence. When the doxorubicin loaded aptamer interacts with the quantum dot, it becomes a chemical beacon to signify the delivery of the chemotherapeutic payload. The florescence of the QD is "turned off" from a quenching interaction between the gold of the QD and the doxorubicin molecule. After the doxorubicin is released, the quenching interaction no longer exists and the QD florescence "turns on" [2.5].

APPLICATION

Once administered into the body, the bioconjugate interacts with PSMA proteins on the cell membrane of cancerous cells and binds with affinity and specificity. Upon binding, the entire bioconjugate is absorbed into the cell via endocytosis. Once inside the cell, doxorubicin is released from the aptamer through physical dissociation from the conjugates or from biodegradation of the aptamer by the cell's lysosomal enzymes^[7]. After the doxorubicin is released from the intercalated position in the aptamer, it is now free to kill the cell by cytotoxic mechanisms. In addition, the QD's florescence is turned "on" as the fluorescence of the bioconjugate is no longer quenched by the doxorubicin. The light emitted from this nanoparticle can be captured by biological imaging devices to enable observation of the tumour with extreme precision. Tests have demonstrated that by using this targeted imaging method there is very little background noise, suggesting that this bioconjugate is accurate enough to detect cancerous cells at the single cell level [7].

In a study using a similar bioconjugate (docetaxel as opposed to doxorubicin), Farokhzad et al. (2006) measured the cytotoxic effectiveness of adding an aptamer targeting system to chemotherapeutic-nanoparticle bioconjugates. Using nude mice with a xenograft of cancerous human prostate cells, two approaches were compared to study aptamer effects in chemotherapy. One group of mice was administered a chemotherapeutic-nanoparticle including an aptamer to target specific cells. This procedure resulted in

complete survival of all the mice, while 71% exhibited complete tumour reduction. In contrast, a second group of mice were administered chemotherapeutic nanoparticles without a conjugated aptamer guide. In this case, the mice exhibited complete tumour reduction in only 29%, with a survival rate of just 57%^[2]. This experiment clearly demonstrated the potential benefits of using aptamers to specifically target diseased cells and the enhanced therapeutic efficacy of bioconjugate strategies. Not only is the aptamer included nanoparticle very effective, but it also appears to increase safety and decrease side effects. Regular chemotherapy is non-targeted and will affect all rapidly dividing cells in other organs and structures within the body. With a targeting system, only the desired tissues are subjected to chemotherapeutics. preventing unnecessary drug exposure[8].

BENEFITS OF USING APTAMERS

Aptamers are a promising new area of study and many of the patents involving SELEX have only recently expired. This has alleviated a major obstacle in aptamer utility for many innovative biomedical and environmental ventures. As a therapeutic, aptamers can easily replace antibodies as an inexpensive, customizable, and more effective option. Antibodies are time consuming to discover, difficult to generate, easily contaminated and have a relatively short half-life. Alternatively, aptamers are extremely inexpensive, easy to create quickly in large amounts, and are difficult to contaminate^[9].

Due to the many possible applications, low toxicity, and extensive modification strategies, it is likely that aptamers will greatly influence the future of medicine. Research is being done on using aptamer-based therapeutics to treat "incurable" diseases such as lupus, cancer, and HIV, and has shown some very promising results. Aptamer research may also yield medications that can manage allergies and prevent migraines[9]. In addition to the biomedical applications listed above, aptamer technology is also being explored in the fields of environmental biodetection and food inspection^[9].

CONCLUSION

With aptamers becoming a staple in biochemical research, the possible applications for this technology appear to be endless. However, one of

the most promising recent applications is their use as a component of bioconjugates for the treatment and imaging of prostate cancer. Prostate cancer, the most prevalent cancer among Canadian men, is being treated using strategies that result in numerous side effects. The method of using aptamers is more effective and may eliminate these undesired effects. Clinical trials are the next step for this treatment option, and if the trials yield results as positive as those in Farokhzad's mice experiment, the use of aptamer-nanoparticle bioconjugates could become the standard of prostate cancer treatment.

With the prevalence of aptamers in biochemical research increasing, patent restrictions being lifted and discovery costs decreasing, aptamers may become a very popular and profitable treatment option for many diseases while concurrently increasing the quality of patient experiences.

KEY WORDS Aptamer; Bioconjugate; Quantum Dots: Prostate Gland: Doxorubicin

ABBREVIATIONS

DNA Deoxyribonucleic acid

PSMA Prostate specific membrane antigen

SELEX Systematic evolution of ligands by

exponential enrichment

QD Quantum Dot

ACKNOWLEDGEMENTS

First and foremost. I'd like to thank Dr. Aaron Witham from EBPI for mentoring me for the past semester. He put a lot of time and effort teaching me about a topic he is extremely passionate about and helped me gain a passion for it too. For that and the countless hours he spent helping me revise and edit my paper, I will eternally be grateful. I am also very thankful towards Mrs. Cecelia Danesi, who was my teacher for this co-op experience. I learned a lot of valuable skills from her. which I know will steer me towards success for the rest of my life.

Thank you so much!

REFERENCES

- 1. Canadian Cancer Society. Canadian Cancer Statistics Publication, 2015, http://www.cancer. ca/en/cancer-information/cancer-101/canadiancancer-statistics-publication/?region=on.
- 2. Farokhzad, O.; Cheng, J.; Teply, B.; Sherifi, I.; Jon, S.; Kantoff, P.; Richie, J.; Langer, R. Targeted nanoparticle-aptamer bioconjugates for cancer chemotherapy in vivo. PNAS, 2006, 103, 6315-6320.
- 3. Gold, L.; Janjic, N.; Jarvis, T.; Schneider, D.; Walker, J.; Wilcox, S.; Zichi, D. Aptamers and the RNA World, Past and Present. CSHPB, 2012, 1-9.
- 4. Famulok, M.; Hartig, J.; Mayer, G. Functional Aptamers and Aptazymes in Biotechnology, Diagnostics, and Therapy. ACS, 2007, 107, 3715-3743
- 5. Özalp, V.; Schäfer, T. Aptamer-Nanoparticle Bioconjugates for Drug Delivery. The Delivery of Nanoparticles, 2012, 133-148.
- 6. Lupold, S.; Hicke, B.; Lin, Y.; Coffey, D. Bind Human Prostate Cancer Cells via the Prostatespecific Membrane Antigen, Cancer Res. 2002, 62. 4029-4033.
- 7. Bagalkot, V.; Zhang, L.; Levy-Nissenbaum, E.; Jon, S.; Kantoff, P.; Langer, R.; Farokhzad, O. Quantum Dot-Aptamer Conjugates for Synchronous Cancer Imaging, Therapy, and Sensing of Drug Delivery Based on Bi-Fluorescence Resonance Energy Transfer. ACS, 2007, 7, 3065-3070.
- 8. Kolishetti, N.; Dhar, S.; Valencia, P.; Lin, L.; Karnik, R.; Lippard, S.; Langer, R.; Farokhzad, O. Engineering of self-assembled nanoparticle platform for precisely controlled combination drug therapy. PNAS, 2010, 107, 17939-17944.
- 9. Keefe, A.; Pai, S.; Ellington, A. Aptamers as Therapeutics. Nature, 2010, Vol. 9, 537-550.
- 10. Witham, A. Structural Analysis of Detrimental Oxidative Products from Phenolic Carcinogens and Construction of Nucleotide Tools from Analogous Processes. Ph.D. Thesis. The University of Guelph, Guelph, ON, May 2014