Syndrome is an autoimmune disorder that is associated with pregnancy complications, such as thrombosis, a medical term for an abnormal blood clot. Heparin, an effective blood thinner used to prevent thrombosis of the placental vessel (Figure 1), is used to increase chances of pregnancy. During pregnancy and the differences were not statistically significant, meaning larger trials are required. In the BCWC study, of the 14 women using UFH, 1 also did not conceive. 4 of the 13 (31%) given UFH had a successful pregnancy. Of the 14 women treated with LMWH, in collaboration with the University of Tennessee Health Sciences Center, which had consistent positive antiphospholipid antibodies were started on aspirin (LDA) for treatment of APS as compared to UFH plus LDA in patients with APS and women with APS. A case study evaluated the use of LMWH in combination with low dose aspirin (LDA) for treatment of APS as compared to UFH. Though, it was not until May 1935 that heparin was refined to a safe, nontoxic version that could be administered in a saline solution by Connaught Medical Research Laboratories in Sweden. Not only is heparin used to prevent thrombosis in pregnancy, but it is also used for a variety of procedures and saves lives every day. Currently, heparin is used to treat and prevent blood clots in the veins, arteries, or lung. Heparin is also used before surgery to reduce the risk of blood clots.

Objective

The objective of this research is to compare the outcomes of LMWH to UFH used in pregnant women with APS. This study evaluated the use of LMWH in combination with low dose aspirin (LDA) for treatment of APS as compared to UFH plus LDA in patients with APS and recurrent pregnancy loss (RPL). Of the 25 patients treated with LMWH, 21 (84%) delivered viable infants and 4 (16%) miscarried. Of the 25 patients treated with UFH, 20 (80%) delivered a viable infant and 5 (20%) miscarried. Limitations in this study include that women treated with LMWH had a tendency towards earlier delivery and the miscarriages occurred significantly later than the UFH group. No patients had any major complications during pregnancy and the differences were not statistically significant, meaning larger trials are required. In another study, an APS trial comparing LMWH to UFH proved LMWH an effective alternative to UFH for treatment of APS in pregnancy. Of the 14 women using LMWH, 1 did not conceive. 9 of the 13 (69%) given LMWH had a successful pregnancy. Of the 14 women using UFH, 1 also did not conceive. 4 of the 13 (31%) given UFH had a successful pregnancy. No preterm births or fetal demises in either group. Dapaparin group, LMWH, had a live birth rate of 69% whereas the UFH group had a live birth rate of 31%. This study demonstrated that LMWH may be an effective alternative to UFH.

Materials and Methods

Patients were eligible to participate in the following three studies if they had 3 or more recurrent pregnancy losses (RPL). However, the materials and methods differ in each study. In the study conducted about the safety of LMWH in pregnancy losses in the UK, patients were given aspirin (LDA), then LMWH, then UFH. In the study at the Health Sciences Center (HSC) in El Paso, Texas, which had extensive experience with the use of LMWH, in collaboration with the University of Tennessee Health Sciences Center, which had extensive experience with UFH. In this study, 1 patient had positive results at least twice for antiphospholipid antibodies, were screened for previous conditions, and were started on LDA and prenatal vitamins before conception. In the LMWH group, 25 women received enoxaparin once daily and in the UFH group, 25 women were given 5,000 U SC heparin twice daily. All patients were instructed to stop LDA 3 weeks before due date. UFH was continued until full term and discontinued only when the patient initiated spontaneous labor while LMWH was stopped 5 days before a scheduled induction or cesarean section. In the final study, the Reproductive Medicine Program at British Columbia's Women's Health Centre (BCWC), 31 women with consistently positive antiphospholipid antibodies were started on heparin in the luteal phase for a maximum of 5 cycles. Dapaparin, a LMWH, was prescribed at a dosage of 2500 units subcutaneously (SC) every 24 hours. The dosage was increased to 5000 units SC in the second trimester and 7500 units SC in the third trimester. UFH was prescribed at a dosage of 5000 units SC every 12 hours. The dosage was increased to 7500 units SC in the third trimester and 10000 units SC in the third trimester.

Results

In the HUHF study, incidence rates did not differ between groups (LMWH vs control): 1.56% vs 1.1% for thrombocytopenia; 8.7% vs 6.5% for preterm delivery; 0.7% vs 0.3% for still birth, 1.4% vs 1.0% for severe pre-eclampsia; 2.7% vs 2.2% for fetal growth restriction, and 10.7% vs 7.8% for antenatal bleeding. This shows no difference in use of LMWH is safe during pregnancy. Though, a limitation would be that the data was obtained from patient's electronic hospital records, meaning the researchers had no interaction with the patients. In the HSC study, the 25 patients treated with LMWH, 21 (84%) delivered viable infants and 4 (16%) miscarried. Of the 25 patients treated with UFH, 20 (80%) delivered a viable infant and 5 (20%) miscarried. There were no cases of deep vein thrombosis, thrombocytopenia, pre-eclampsia, gestational diabetes, or bone fractures noted in either group. There were 3 cases of preterm birth and 1 intratrophic growth restriction in both groups. The differences were not statistically significant, meaning larger trials are required. In the BCWC study, of the 14 women using LMWH, 1 did not conceive. 9 of the 13 (69%) given LMWH had a successful pregnancy. Of the 14 women using UFH, 1 also did not conceive. 4 of the 13 (31%) given UFH had a successful pregnancy. No preterm births or fetal demises in either group. Dapaparin group, LMWH, had a live birth rate of 69% whereas the UFH group had a live birth rate of 31%. This study demonstrated that LMWH may be an effective alternative to UFH.

Conclusions

Overall, many researchers have clashed over whether LMWH is more effective than UFH, and vice versa. LMWH and UFH both seem to be effective in lowering RPL. The recent rise in usage of LMWH over UFH in most cases is due to the ever increasing side effects of UFH, such as weight gain and the differences were not statistically significant, meaning larger trials are required. In the BCWC study, of the 14 women using UFH, 1 also did not conceive. 4 of the 13 (31%) given UFH had a successful pregnancy. No preterm births or fetal demises in either group. Dapaparin group, LMWH, had a live birth rate of 69% whereas the UFH group had a live birth rate of 31%. This study demonstrated that LMWH may be an effective alternative to UFH.

Relevant Application to Biotechnology

Women with APS considering fertility options would have been presented with far less options without the discovery of heparin in 1916 at Johns Hopkins University. Heparin was first discovered by Jay McLean and William Henry Howell. McLean was a second year medical student at Johns Hopkins University who was assisting Howell in the investigation for pro-coagulant preparations. McLean isolated a fat-soluble anticoagulant in canine liver tissue. Though, it was not until May 1935 that heparin was a safe, nontoxic version that could be administered in a saline solution by Connaught Medical Research Laboratories in Sweden. Not only is heparin used to prevent thrombosis in pregnancy, but it is also used for a variety of procedures and saves lives every day. Currently, heparin is used to treat and prevent blood clots in the veins, arteries, or lung. Heparin is also used before surgery to reduce the risk of blood clots.

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**Objective**

Preeclampsia is a condition that occurs during pregnancy and is characterized by hypertension and proteinuria. Preeclampsia poses a significant threat to both the mother and the fetus, sometimes leading to morbidity and mortality. Researchers have not yet been able to identify the exact causes of preeclampsia. The objective of this poster is to explore the relationship between polymorphisms in genes that encode complement proteins (complement genes), which can determine inflammatory response, and the development of preeclampsia during pregnancy.

**Methods and Materials**

A case-control study was conducted in Taiyuan, China, among 3166 pregnant women greater than 18 years of age who came to the hospital for delivery (gestational age ≥ 20 weeks). A questionnaire was used to collect data regarding demographics, reproductive and medical histories, behavioral factors, occupational history, physical activity, and diet of the participants. Additionally, information on birth outcomes and pregnancy complications (including birth-weight, whether the birth was a caesarean section, etc.) was extracted from medical records. Blood samples from the women were collected for genotyping. Among the study participants, 203 had been diagnosed with preeclampsia, based on high blood pressure levels (≥140/90 mmHg) and proteinuria (≥ 0.3 g/l in a 24 hr urine collection period or 2 random urine specimens showing at least 1+ protein by dipstick test). The 203 cases were matched with 233 randomly selected controls by age, residence, and time of conception. 51 single nucleotide polymorphisms (SNPs) in six different complement genes, C3, C5, C6, MASPI, MBL2, and CD55, were analyzed using the blood samples.

**Results**

The preeclampsia cases in the study were further divided into subtypes, including early-onset preeclampsia, late-onset preeclampsia, mild and severe preeclampsia (Figure 2). The demographics and other selected characteristics were compared between the cases and the controls, the cases were more likely to be less educated, overweight, and to have had a caesarean section. No significant differences were observed among the cases and controls regarding parity and smoking status. Statistical analysis of data using logistic regression demonstrated that SNPs in the C6 complement gene were significantly associated with the risk of preeclampsia (C6 rs7444800: OR=2.40; 95% CI=1.38-4.18; p-value=0.002; C6 rs4957381: OR=2.24; 95% CI=1.31-3.83; p-value=0.004). SNPs in C6 were also associated with early-onset preeclampsia (min P=0.001). An increased risk of late-onset preeclampsia was observed among participants with polymorphisms in the MASPI gene (MASPI rs1357134: OR=3.16; 95% CI=1.46-6.83; p-value=0.003; MASPI rs6908090: OR=2.22; 95% CI=1.47-7.07; p-value=0.001). MASPI polymorphisms was also associated with early-onset preeclampsia (min P=0.005) and severe (MASPI rs1357134 and MASPI rs6908090) preeclampsia (min P=0.021) (Figure 3).

**Conclusions**

Preeclampsia and related conditions affect about 5 to 8 percent of pregnancies in the United States, but in the developing world, the incidence of preeclampsia is estimated to be seven times higher. If left untreated, preeclampsia can lead to eclampsia and other life-threatening complications. The results of this study demonstrate that there is a relationship between SNPs in complement genes and preeclampsia risk and suggest that the immune response may have a role in the pathogenesis of preeclampsia. Another study examined the relationship between autoimmune diseases caused by complement-mediated injury and the risk of preeclampsia. It was found that patients with genetic mutations in complement genes were at risk of developing preeclampsia. These findings can facilitate better treatment and management of preeclampsia.
The Effect of Polycyclic Aromatic Hydrocarbons (PAH) and Heterocyclic Amines (HCA) Consumption on Breast Cancer for Women

Sophia Carpinelli
Guajome Park Academy

Objective

The focus of this research is to evaluate Heterocyclic amines (HCA) and Polycyclic aromatic hydrocarbons (PAH) that are commonly found in cooked red meats and demonstrate how a diet high in HCA and PAHs can increase a woman's risk for breast cancer. This research will also highlight how a diet such as a Mediterranean or Vegetarian diet that contains higher amounts of fruits and vegetables that contain carotenoids, vitamin C, fiber, and potassium can significantly decrease one's risk for breast cancer.

Abstract

Breast cancer is the second of the leading cause of death in women. The exact causes of breast cancer are still being researched today. There is evidence suggesting that certain foods are putting women at an increased risk for breast cancer. This research will demonstrate how a diet high in aromatic hydrocarbons can increase your risk for breast cancer as an adolescent by 12%

Method and Materials

In 1991, 97,813 nurses from ages 24-43 agreed to be a cohort study that would evaluate their usually food intake while monitoring their health. Each subject could complete a food frequency questionnaire that would help the researchers evaluate the nurse's daily food intake and health. Women that had implausible total energy intake during early adulthood were not significantly associated with a lower risk of breast cancer. An adult diet that contained high amounts of polyunsaturated fats which change the cooking process of poultry items over red meats. HCAs and PAHs being created while red meat is being cooked at high temperatures, such as wood fire cooking. These two naturally occurring chemicals have been seen to promote estrogen activity and cause breast tissue carcinogenic activity. HCA and PAH are both chemicals that affect the Aryl Hydrocarbon Receptor (AHR). AHR has been known to handle immunotoxicity in response to new chemicals and environmental contaminants that enter the body and as known to target Cytochrome P450 (CYP450) genes. However, AHR has been known to cause increases of cancer, autoimmune diseases and other diseases in response to this reaction. With diets such as a Western that is high in fats and red meats, the number of amounts of HCAs and PAHs are being products and are affecting the AHR which in return is causing more carcinogenic activity within the breast tissue, thus, increasing a woman's risk of breast cancer by 13%. Yet, a diet such as a Mediterranean or vegetarian diet that contains little to no red or processed meats are decreasing the amounts of HCAs and PAHs being consumed and are then replacing meats with fruits and vegetables that are highly enriched in substances such as carotenoids, vitamin C, fiber, and potassium. Thus, decreasing a woman's chance of breast cancer by 25%. With this evidence in mind, a diet that contains little to none red or processed meats, such as a Mediterranean or vegetarian diet, should be encouraged in adolescents and young adults to decrease their chances for premenstrual breast cancer. However, more research should be done to discover more relationships between carcinogens and risk for breast cancer, diet in early life and risk for breast cancer, as well as the impact of timing of dietary exposure and cancer risks.

Discussion

This research further the evidence that a great consumption of red meat that contains HCA and PAH is connected to a higher risk of breast cancer for premenstrual breast cancer, while an early adult diet that contains higher amounts of fruit and vegetables that contain carotenoids can greatly lower a woman's risk for cancer. Certain fruits such as apples, bananas, grapes and kale have been seen to provide a significantly lowered risk of breast cancer as they contain more materials, such as carotenoids, vitamin C, fiber, and potassium. This decreases the risk of breast cancer. While the red meat associated with a 13% increased risk of breast cancer for all women, poultry items were associated with a lower incident of breast cancer in postmenopausal women. Many poultry items are known to have higher amounts of polyunsaturated fats which change the cooking process of poultry items over red meats. HCAs and PAHs are created while red meat is being cooked at high temperatures, such as wood fire cooking. These two naturally occurring chemicals have been seen to promote estrogen activity and cause breast tissue carcinogenic activity. HCA and PAH are both chemicals that affect the Aryl Hydrocarbon Receptor (AHR). AHR has been known to handle immunotoxicity in response to new chemicals and environmental contaminants that enter the body and as known to target Cytochrome P450 (CYP450) genes. However, AHR has been known to cause increases of cancer, autoimmune diseases and other diseases in response to this reaction. With diets such as a Western that is high in fats and red meats, the number of amounts of HCAs and PAHs are being products and are affecting the AHR which in return is causing more carcinogenic activity within the breast tissue, thus, increasing a woman's risk of breast cancer by 13%. Yet, a diet such as a Mediterranean or vegetarian diet that contains little to no red or processed meats are decreasing the amounts of HCAs and PAHs being consumed and are then replacing meats with fruits and vegetables that are highly enriched in substances such as carotenoids, vitamin C, fiber, and potassium. Thus, decreasing a woman's chance of breast cancer by 25%. With this evidence in mind, a diet that contains little to none red or processed meats, such as a Mediterranean or vegetarian diet, should be encouraged in adolescents and young adults to decrease their chances for premenstrual breast cancer. However, more research should be done to discover more relationships between carcinogens and risk for breast cancer, diet in early life and risk for breast cancer, as well as the impact of timing of dietary exposure and cancer risks.

Relevant Application to Biotechnology

Biotechnology has been used greatly to study the Aryl Hydrocarbon Receptor (AHR) and its impact on mice and humans. Through Biotechnology, scientist were able to use mice to discover that the AhR was responsible for responding to new chemicals and environmental contaminants that enter the body, thus leading to cancer and may other diseases. However, Biotechnology could further studies on cooked meats and HCA and PAH effect on the AHR. Biotechnology could help further research to see how much red or processed meat is needed in order to activate the AHR receptor and start to cause carcinogenic activity within the breast tissue. This research could help educate society on how their diet could greatly increase or decrease one’s chances of breast cancer, and help create a decrease in the number of breast cancer incidents.

References


Results

NHSII's data trend established that a diet that contains 2.9 servings of certain fruits and vegetables such as tomatoes, carrots, and lettuce could complete a food frequency questionnaire that would help the researchers evaluate the nurse's daily food intake and health. Women that had implausible total energy intake during early adulthood were not significantly associated with a lower risk of breast cancer. An adult diet that contained high amounts of polyunsaturated fats which change the cooking process of poultry items over red meats. HCAs and PAHs being created while red meat is being cooked at high temperatures, such as wood fire cooking. These two naturally occurring chemicals have been seen to promote estrogen activity and cause breast tissue carcinogenic activity. HCA and PAH are both chemicals that affect the Aryl Hydrocarbon Receptor (AHR). AHR has been known to handle immunotoxicity in response to new chemicals and environmental contaminants that enter the body and as known to target Cytochrome P450 (CYP450) genes. However, AHR has been known to cause increases of cancer, autoimmune diseases and other diseases in response to this reaction. With diets such as a Western that is high in fats and red meats, the number of amounts of HCAs and PAHs are being products and are affecting the AHR which in return is causing more carcinogenic activity within the breast tissue, thus, increasing a woman's risk of breast cancer by 13%. Yet, a diet such as a Mediterranean or vegetarian diet that contains little to no red or processed meats are decreasing the amounts of HCAs and PAHs being consumed and are then replacing meats with fruits and vegetables that are highly enriched in substances such as carotenoids, vitamin C, fiber, and potassium. Thus, decreasing a woman's chance of breast cancer by 25%. With this evidence in mind, a diet that contains little to none red or processed meats, such as a Mediterranean or vegetarian diet, should be encouraged in adolescents and young adults to decrease their chances for premenstrual breast cancer. However, more research should be done to discover more relationships between carcinogens and risk for breast cancer, diet in early life and risk for breast cancer, as well as the impact of timing of dietary exposure and cancer risks.

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An Analysis of the Anticancer Potential of Malaysian Tualang Honey and its Efficacy as a Cancer Treatment

Hilltop High School
Sarah Esparza

Objective

The most common treatment for patients with cancer is chemotherapy in which multiple drugs are administered. Although treatments using such hormonal therapy has been efficient in reducing the mortality rates of cancer, undesirable side effects arise as a result of the drugs’ inability to specifically target cancer cells. Additionally, cancer cells have begun to develop resistance to such treatments. This poster will provide an analysis of the potential for Malaysian Tualang Honey to be used as a natural cancer treatment and alternative to traditional treatments.

Abstract

While many of the causes for cancer remain unidentified, researchers have found the following to assist in its development: accumulation of toxic free radicals, chronic infections, low immune status, chronic inflammation, and chronic non-healing ulcers. Malaysian Tualang Honey (TH) has shown potential of being an anticancer agent against cancer because it is high in antioxidants, is a scavenging agent for toxic free radicals, is a natural antimicrobial, is a natural immune booster, is a natural anti-inflammatory agent, and heals chronic ulcers and wounds. The purpose of this investigation is to research the level of efficacy of TH in the treatment of Breast and Cervical cancers. In order to assess the anticancer potential of TH, human breast (MCF-7 and MDA-MB-231) and cervical (HeLa) cancer cell lines, as well as normal breast epithelial cell line, were treated with increasing dosages of TH (1-10%) for up to 72 hours. The results showed that the TH was cytotoxic and induced significant cell death in all three cancer cell lines, with 93% cell death of MDA-MB-231 with 10% TH, 91% of MCF-7 with 5% TH, and 100% of HeLa with 5% TH. The treatment of the normal breast epithelial line did not show clear cytotoxic effects with 1-10% TH, however the maximum cell death was only 28% with 5% TH. In another study, the MCF-7 and MDA-MB-231 cell lines were treated with either 1% TH, 2.5, 5, 10, or 15 μM Tamarxifen (TAM) alone, or a combination of TH and TAM for 6-72 hours. This study showed that the combination of TH and TAM significantly increased the percentage of apoptotic cells compared to single treatments (31.2% with TH-TAM, 31.2% with TAM). In conclusion, my research has shown that Malaysian Tualang Honey is an effective anticancer agent. I propose that physicians work to combine chemotherapeutic treatment with TH.

Methods and Materials

In the first study, human breast (MCF-7 and MDA-MB-231) and cervical (HeLa) cancer cells and normal breast epithelial cells were treated with various concentrations of TH (1-10%) for up to 72 hours. Cells were collected at 6, 24, 48, and 72 hours after treatment. To determine the amount of apoptosis, cells were analyzed using the fluorescent activated cell sorter. The apoptotic analysis was then compared to that of Tamarxifen. Three independent experiments were performed. In the second study, human breast (MCF-7 and MDA-MB-231) cancer cells were treated with 1% Tualang Honey or in combination with various concentrations of Tamarxifen (2.5 μM-15 μM) or Tamarxifen alone. Cells were collected at 6, 24, 48, and 72 hours after treatment and incubated with JC-1 dye the accumulates within intact mitochondria and turns red, but changes to green with a reduction of mitochondrial membrane potential. Three independent experiments were performed.

Results

The results of the first study showed that the TH was cytotoxic and induced significant cell death in all three cancer cell lines, with 93% cell death of MDA-MB-231 with 10% TH, 91% of MCF-7 with 5% TH, and 100% of HeLa with 5% TH. The treatment of the normal breast epithelial line did not show clear cytotoxic effects with 1-10% TH, however the maximum cell death was only 28% with 5% TH. When the cells were stained with Annexin V Fluorescence antibody and Propidium Iodide (Fig. 4), it was found that the percentage of apoptotic cells was significantly higher in those treated with TH than untreated cells. The results of the second study showed that the combination of TH and TAM significantly increased the percentage of apoptotic cells compared to single treatments (43.8% with TH-TAM, 31.2% with TAM), and the difference between the percentage of TH and TH-TAM treated cells was not significant. Both studies found that there was a reduction in Mitochondrial Membrane Potential. After treatment with TH, it was found that caspase-3/7 and -9 were activated. The second study also identified activation of caspase -8 by TH and only caspase-7 by TAM.

Conclusions

Malaysian Tualang Honey has been found to be rich in flavonoids, phenolic acids, hydroxymethylfurural (HMF) contents, and main fatty acids, all of which either inhibit tumor cell growth or induce cell death. But tumor cell-independent effects are strong. Furthermore, Tualang Honey activated caspases that initiate and execute apoptosis. It proved to be effectively cytotoxic to cancerous cells, while not killing normal cells, making Tualang Honey potentially useful as an anticancer agent and more advantageous than current anticancer agents. It was also discovered that the combination of Tualang Honey and Tamarxifen has a higher efficacy in inhibiting tumor cell growth than Tamarxifen alone. This indicates that the required effective dose of Tamarxifen may be reduced, as well as the side effects of its use.

Applications to Biotechnology

The biotechnology that made this research possible includes the Annexin V Fluorescence antibody, Propidium Iodide JC-1 dye, and the Fluorescent Activated Cell Sorter that were used to differentiate between the apoptotic cells and the normal cells. The Annexin proteins and Propidium Iodide were used in the work by binding to and detecting the morphological changes of the cell membranes. The JC-1 dye accumulates in varying amounts depending on the membrane potential of the mitochondria of the cells. The Fluorescent Cell Sorter organizes the cells based on the marker that they express.

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References

The Correlation Between Higher Levels of Dioxin in the Atmosphere and Decreased Sertoli Cell Proliferation

Esin Gumustekin, Francis Parker School

Objective

The purpose of this poster is to examine the correlation between dioxin in the air and decreased Sertoli cell proliferation, which is causing men to have decreased sperm count as adults. Dioxin is an extremely toxic pollutant which is a by product of many industrial processes including chlorine bleaching of paper, the manufacturing of certain pesticides, incineration of medical waste and plastic, and smelting. Sertoli cells are somatic cells found in the testes that are essential for spermatogenesis. They enable the progression of germ cells to become spermatozoa. The number of Sertoli Cells entirely determine how many sperm cells adult males will be able to form.

Methods and Materials

From 1989-2005, Dr. Le Moal and fellow researchers studied the sperm count of men aged 18-70 in clinics around France. 26,609 men were the partners of women who were infertile due to blocked or missing fallopian tubes were part of the study. They came from over 126 clinics located in a diverse mixture of the major cities as they were not known to be infertile. The men provided fresh ejaculate and sperm concentration, motility and morphology were all analyzed as part of the study. The researchers calculated the mean sperm data for each year group and adjusted the results in order to represent a 15 year old man. The results from this study are very fascinating and can be applied to many other developed countries in the world. Evidence suggests that one cause of decreasing sperm count is because of increased dioxin in the air. This can be seen in the study Results where the sperm count decreases as the dioxin concentration increases.

Abstract

In a population of 7 billion, decreasing fertility rates may not be viewed as an urgent issue. However, it is estimated that in 2050 the world population will start to decrease, one main cause of this being decreased sperm count in men. In my poster, I will be analyzing the correlation between dioxin in the air and decreased Sertoli cell proliferation, which is causing men to have decreased sperm counts as adults. Decreasing sperm count throughout the world is an emerging issue. This became evident in Dr. Le Moal’s study in France in which over 26,000 men aged 18-70 were sampled at clinics around the country from 1989 to 2005. These men were the partners of women who were known to be infertile and were going through fertility treatments at clinics around the country. The men weren’t known to be infertile and thus were a representative sample of the population. The study found that during the 17 years, sperm count decreased by a third. Evidence suggests that one main cause of decreasing sperm count is perinatal exposure to dioxins. Dioxins interfere with the proliferation of Sertoli cells, which determine the number of sperm produced in adult life. Dioxin’s detrimental effect became evident in the 1976 industrial accident in Seveso, Italy in which a trichlorophenol plant explosion resulted in dioxin contamination in the surrounding area. Thirty nine men who were born near Seveso between 1977 and 1984 were followed through life and had semen samples drawn as an adult. When compared with the 58 men who were used as a control group who were not born in Seveso but in a different city during the explosion, the 39 men who were prenatally exposed to high levels of dioxin had significantly lower sperm count, thus demonstrating dioxin’s toxic effects.

Results

During Dr. Le Moal’s 17 year study, the mean sperm count of French men decreased by 32.2%, 1.9% each year. The sperm concentration of an average 35 year old man fell from 73.8 million/ml to 49.9 million/ml. This drastic trend of declining sperm count is not only noted in France but in many other industrialized nations as well including India, Japan and Germany. Evidence suggests that one main cause of decreased sperm count is perinatal exposure to dioxins. Dioxins interfere with the proliferation of Sertoli cells, which determine the number of sperm produced in adult life. The results of this study show that exposure to low concentrations of dioxin perinatally results in permanent impairment of a male’s reproductive system (50% reduction in sperm count and 20% decreased sperm motility as seen in Figure 2). For example, the 21 breast-fed sons whose exposed mothers had a median serum dioxin concentration of 19 ppt at conception had lower sperm concentration (36.3 vs. 86.3 million/ml), total count (116.9 vs. 231.1), progressive motility (55.8 vs. 44.2%), and total motile count (38.7 vs. 98 million) than did the 36 breast-fed comparisons. The breast-fed exposed group even had significantly decreased sperm count when compared to the formula-fed exposed group as they were exposed to dioxin for a longer period of time, in which Sertoli Cell proliferation was continuous. Once the receptor binds to the aryl hydrocarbon receptor (AhR), AhR forms a nuclear translocator complex which then binds to the dioxin-responsive element (DRE) on target DNA. Then, the expressed AhR/ARNT, when ligand activated, interacts with many transcription factors that ultimately influence tissue development. AhR/ARNT then directly intervenes in male reproductive system development. Dioxin response in the body can be seen in Figure 3.

Conclusion

In conclusion, there is a strong correlation between dioxin in the atmosphere and decreased Sertoli cell proliferation which is causing decreasing sperm count in adult life. Increasing amounts of dioxin in the air due to industrialization are a cause of declining sperm count. Sperm count decreases with increasing dioxin exposure, for instance, creates 40% of the world’s dioxin production and has a radically declining birth rate, one of the lowest in the world. Japan contains 1,800 household-waste incinerators while the U.S. has about 250. The excessive amounts of dioxin in the air and decreasing birth rates are not coincidences. Other research has shown that there are other adverse health effects associated with exposure to dioxins.

Application to Biotechnology

Through improved technology, researchers have been able to conduct better studies that are more detailed and accurate. Through advancements in microscopy, scientists have been better able to count and determine the morphology of sperm. In the future as technology continues to advance, we will be better able to find the factors that are leading to decreased sperm count throughout the world and understand all of the mechanisms contributing to it.

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References

Da Vinci System: Improving Hysterectomy Surgery for Endometrial Cancer Patients

Jennifer Harrison • Castle Park High School

Objective

The Premier Perspective database provided statistics of robot-assisted hysterectomies for benign indications, from nine centers, and abdominal, vaginal, and laparoscopic hysterectomy data from 405 hospitals from 2011 to 2013. The study included 6,088 patients, of which 9,745 were abdominal, 8,121 were vaginal, and 11,952 were laparoscopic, and 2,308 were robot-assisted. Although this study did not measure surgeries done for malignancy, it clearly demonstrates the effectiveness of the da Vinci system over other surgical methods. The surgeons who contributed to this study were largely experienced in open surgery, although the da Vinci surgeons had variable levels of experience, with some being relatively inexperienced. The results show that the da Vinci system was superior in comparison to other surgical procedures, with a lower risk of complications and better outcomes for patients.

Methods and Materials

The da Vinci System needs many improvements before it is the perfect universal surgical method. It definitely has potential to improve tremendously since it has only been readily available for hospital utilization for around 11 years, and new technologies and surgical advancements are awaiting refinement and improvement. Over the years, the da Vinci System has undergone many innovations, such as having the docking improved, the robotic arms manipulated to prevent clashing, and adding an autofocus universal endoscope. Yet, there are still many improvements that could be made to it, to lower the mortality, blood loss, pain, surgery complications, operation time, and hospital stay even more. Also, to get the overall cost of the robot-assisted hysterectomy procedure lower than the traditional laparoscopic surgery. Someday, hysterectomies may even be performed without incisions. Robot-assisted laparoscopic surgery should be universally utilized for endometrial cancer treatments, thus many postmenopausal women diagnosed with endometrial cancer can receive optimal care.

Conclusion

In 2014 there was an estimated 52,638 new cases of endometrial cancer and 8,590 deaths from it, making it the most common cancer of the female reproductive organs. Generally, postmenopausal women treat their endometrial cancer with a hysterectomy, regardless of what stage it is at. For laparoscopic surgery, the chance of recurrence was 11.9%, for traditional laparoscopy it was 7.2% chance, and for the robot-assisted laparoscopy the chance was 6.9%. Robotic surgery has only been FDA approved since 2005, therefore these amazing statistics are proof of the potential for a cure to cancer, as the machinist becomes more and more precise and the recurrence levels get lower and lower from upgrades and innovations.

Relevant Applications to Biotechnology

First of all, I would like to especially thank Dr. Erick Sensager-Mitchell for being such an amazing mentor by pushing me beyond my limits, challenging me to better myself as a person, and for believing that I was capable of going through both this class and school. Thanks to Ms. Patricia Winters and Kathleen Pulver for keeping me on my toes and for being such sweet and kind people throughout the program, and to all the speakers/presenters/hotels for dedicating their time and effort to sharing valuable knowledge and advice. Special thanks to my amazing teacher and friend Mrs. Dari Kibimba for introducing me to the Oncology Science Academy and for everything else she does to lead me in the right direction and prepare me for college and a career. My last thanks go to my family. I would not have worked on this with such amazing, talented, and intelligent OSA sisters who taught me true friendship and support. Once an OSA sister, always an OSA sister!
The Zika Virus and microcephaly have a correlation that will guide science along its way towards preventing for Zika or preventing increased incidents of microcephaly but scientists are trying to determine whether or not Zika is a causality of microcephaly. Zika has been proven to have a surface level connection with microcephaly, however, more microbiological research to support the hypothesis that Zika causes microcephaly is needed to draw conclusions on this topic. The current Zika outbreak and its teratogenic effects, if not treated properly, might cause irreversible damage to the brain of the fetus. Scientists are very close to finding out why certain viruses travel the blood stream into the brain of the fetus. Scientific possibilities about how Zika infects the fetus are currently being contemplated such as the direct transfer hypothesis, as shown in Figure 3, which suggests that the Zika virus enters through the trans-placental and intrauterine transmission. From my research, the data has shown that there is a connection between Zika and microcephaly, possibly a causality. The results found in the first study suggest the strong neurotropism of Zika, as viral damage is only present in the brain, no other fetal organs. The localization of immunofluorescence signals and the morphological appearance of the calcification resembled destroyed neuronal structures. This indicates the probable presence of the virus in the neurons of the fetus which would indicate the likely pathway that this virus takes from the mosquito to the brain of the fetus.

**Objective**

The Zika Virus is a current mosquito-borne pandemic, attacking millions, but especially dangerous when infecting pregnant women. It is correlated with microcephaly, a neurodevelopmental birth defect, as illustrated in Figure 1. As a public health emergency, the scientific community is working hard to research on this virus and its relation to microcephaly would benefit those who are infected with Zika and are at risk of passing the virus to their future children in the form of microcephaly. The intent of this study is to determine how Zika is correlated with microcephaly and to support the hypothesis that Zika causes the brain to develop microcephaly, which is the reason why microcephaly is often referred to as ‘Zika brain’. The hypothesis of Zika causing microcephaly is supported by the growing evidence that the virus can enter the neural tissue of the brain. This is why we are observing an increased number of newborns with microcephaly in Zika infected regions.

**Results and Interpretations**

From my research, the data has shown that there is a connection between Zika and microcephaly, possibly causality. The tests found in the first study suggest the strong neurotropism of Zika in pregnant women. The hypothesis of Zika causing microcephaly is supported by the growing evidence that the virus can enter the neural tissue of the brain. This is why we are observing an increased number of newborns with microcephaly in Zika infected regions.

**Discussion**

The Zika Virus and microcephaly have a correlation that will guide science along its way towards preventing for Zika or preventing increased incidents of microcephaly but scientists are trying to determine whether or not Zika is a causality of microcephaly. Zika has been proven to have a surface level connection with microcephaly, however, more microbiological research to support the hypothesis that Zika causes microcephaly is needed to draw conclusions on this topic. The current Zika outbreak and its teratogenic effects, if not treated properly, might cause irreversible damage to the brain of the fetus. Scientists are very close to finding out why certain viruses travel the blood stream into the brain of the fetus. Scientific possibilities about how Zika infects the fetus are currently being contemplated such as the direct transfer hypothesis, as shown in Figure 3, which suggests that the Zika virus enters through the trans-placental and intrauterine transmission. From my research, the data has shown that there is a connection between Zika and microcephaly, possibly a causality. The results found in the first study suggest the strong neurotropism of Zika, as viral damage is only present in the brain, no other fetal organs. The localization of immunofluorescence signals and the morphological appearance of the calcification resembled destroyed neuronal structures. This indicates the probable presence of the virus in the neurons of the fetus which would indicate the likely pathway that this virus takes from the mosquito to the brain of the fetus.
Objective
The purpose of this poster is to define select Neural Tube Defects, to highlight insufficient results concluding any teratogenic properties of caffeine, and to show how ingesting excessive amounts of caffeine during pregnancy could possibly harm fetuses by possibly developing select birth malformations.

Abstract
Ever since the popularity of caffeinated drinks arose, 90% of American women that consumed caffeine before pregnancy continued ingesting caffeine through beverages, bringing concern to the risk of developing Anencephaly, Spina Bifida, Encephalocoele, and other select Neural Tube Defects (NTDs). Since the amount of research on caffeine containing teratogenic properties is restricted to very few studies, excessive amounts of caffeine may become a threat for developing fetuses. A 2010 research study conducted an evaluation of 133 case mothers with children with NTDs and 273 control mothers with children for possible effects of substances consumed before and during pregnancy, including caffeine, and found mothers ingesting caffeine before and during pregnancy did have an increased risk for developing spina bifida, a common NTDs. A daily average of caffeine consumption was recorded a year prior and during pregnancy for mothers who gave birth to children between 2000 through 2008. After collecting all data, the study conducted more extensive research should be completed to find whether consuming caffeine could increase the risk of NTDs. A similar study observed caffeine to not hold any effect to the risks of developing any select NTDs, from a lack of any convincing changes. Overall, the evaluations did not find a convincing connection between excessive maternal caffeine consumption during pregnancy and NTDs, due to caffeine lacking teratogenic properties that may trigger select birth malformations. Due to few research studies resulting in similar conclusions, the connection between caffeine and NTDs is not available. More financial support, willing clients, and awareness to caffeine’s effect to fetuses may bring possible correlation between caffeine and birth malformations.

Methods and Materials
A 2010 research study conducted an evaluation of 133 case mothers with children with NTDs and 273 control mothers with children for possible effects of substances consumed before and during pregnancy. Out of 850 initial case mothers, 133 who participated were Caucasian Italians, gave information within 24 months after the delivery of the index pregnancy, and their child gave birth to a child that was having symmetrically open or closed spinal dysraphism. While 332 control mothers were invited to participate in the study, only 273 mothers agreed to participate. Eligible control mothers were Caucasian, and gave birth to healthy children, reviewed by checking birth registration forms prior to the evaluations. Before any were conducted, interviewers obtained all mother’s history prior to pregnancy, including lifestyle habits and exposure information 3 months before until 3 months after conception. Information solicited about all mother’s history included: mother’s birth date, date of delivery, country of birth, educational level, annual family income, marital status, reproductive history, pregnancy history. Lifestyle and exposure information included: Caffeine, alcohol, fruit, and vegetable consumption, smoking and stress levels, medication use, multi-vitamins and iron therapies, radiation, toxins, and pollutant exposure, and residency to waste cities. All NTD cases were questioned 20 months in total, while all case mothers were questioned for 18 months in total.

Results
Overall, the evaluation did find some types of lifestyles that increases the risk of select Neural Tube Defects (spina bifida), and concluded that excessive amounts of caffeine lead to increased risks of developing select NTDs. Alongside caffeine consumption, a low calorie diet and occasional consumption of fruit and vegetables was observed to have the strongest association to the development of NTDs. Caffeine consumption was recorded by the amount of coffee consumed daily, excluding any other caffeinated beverages. Measurement was more than 3 cups of coffee to less than 3 cups of coffee, possibly leaving a gap to the connections of other caffeinated beverage consumption, and the development of other select NTDs.

Conclusions
Due to few research studies resulting in similar conclusions, the connection between caffeine and NTDs is not available. Since this study was one of the first of it’s kind conducted in Italy, a feasible conclusion whether specific exposure to some elements and consumption habits, including caffeine could raise the risk of developing select NTDs. Similar studies conducted with the same findings, that caffeine may possibly hold a connection to the development of select NTDs, but with the lack of research following the effects of caffeine, convincing data is still yet to be found. More financial support may bring more willing clients, and awareness to caffeine’s effect to fetuses. Due to the lack of a confident conclusion connecting NTDs and caffeine consumption, the potential danger of consuming caffeinated products could bring risk to developing infants before and during pregnancy. Because of the lack of data collection for other caffeinated beverages (caffeinated drinks, sodas), the connection to NTDs is only researched through the consumption of coffee. More awareness to excessive caffeine consumption, daily lifestyle habits, and exposure to some materials may cause more studies to be conducted, in order to possibly find a connection to NTD development.

Relevance to Biotechnology
Within the past few decades, methods to finding any potential effect from substances consumed was restricted due to the technological status at that time. Because of the advancement of biotechnology, more clinical trials may be conducted due to the methods of collecting such data. For example, most clinical trials were recorded from communication based data, through interviews that may not be accurate. Now, data can be more accurate from the means of collecting data with their respective instruments.

Acknowledgements
I would like to thank Dr. Ericka Senegar-Mitchell, Ms. Patricia Winter, and my OSA sisters for their support, patience, and energy to allow the Oncofertility Science Academy to become an enjoyable and unique experience. I would also like to thank my family, Mr. Nick, and Mrs. Sara for supporting my endeavors that will propel me to new places.

References

Claudia Monarrez
High Tech High Chula Vista
Effects of Ooplasmic Transfer to Revitalize Oocytes in Middle-Aged Women
Vanessa Nyawabila
Mt. Carmel High School

Abstract
Ooplasmic transfer, also known as cytoplasmic transfer, is an emerging treatment procedure in IVF, In Vitro Fertilization, that was first conducted by embryologist Jacques Cohen. Transfer of mitochondria from good quality oocytes to poor amplifies the sanctioned amount mitochondrial material, which then, enables the receiving oocyte to create sufficient, metabolic products for normal development. This research poster will focus on the use of cytoplasmic transfer to assist older women, significantly after the age of 35, who are probable to suffer from infertility due to deficient or damaged mitochondria. The methods used to conduct ooplasmic transplantation is performed by transferring 5-15% of donor ooplasm to recipient oocytes either by cytoplast construction of the donor oocyte or by electrofusion of the cytoplasm to the patient oocyte, followed then by ICSI, Intracytoplasmic Sperm Injection. The results from these studies revolve around the different techniques were broken down into two categories. These methods were conducted 30 times on 27 couples. The injection technique culminated in 10 single births, 1 set of twins, 1 quadruplet birth, 1 miscarriage, and 1 ongoing pregnancy. The electrofusion technique, only tested on 3 patients, resulted in no improvement in embryo development or pregnancy. The occurrence of chromosomal abnormalities was 1/17, or 5.9%, which is slightly higher than the populations congenital abnormalities. The increasing factor of maternal age and uspurga in sex chromosome aneuploidy after ICSI is a possible correlation to the high statistics of indiscernible chromosomal abnormalities in patients aged 35-37 years old after transplantation of ooplasm resulted in singletons pregnancies (5%), similarly equal to the amount of pregnancies from women <35 after the same ooplasm procedure. From older women who suffered from damaged mitochondria, implantation rates decreased which correlated to high amounts of damaged mitochondria. The data suggests that high levels of impaired components of cytoplasm results in increase embryonic implantation failures that correlates to maternal age, aneuploidy, and embryonic implantations. Thus, inter-cytoplasmic transfer in conjunction with ICSI can be presumed to have a positive effect in the improvement of oocyte development.

Results
The results from these studies revolve around the different techniques were broken down into two categories. These methods were conducted 30 times on 27 couples. The injection technique culminated in 10 single births, 1 set of twins, 1 quadruplet birth, 1 miscarriage, and 1 ongoing pregnancy. The electrofusion technique, only tested on 3 patients, resulted in no improvement in embryo development or pregnancy. The occurrence of chromosomal abnormalities was 1/17, or 5.9%, which is slightly higher than the populations congenital abnormalities. The increasing factor of maternal age and uspurga in sex chromosome aneuploidy after ICSI is a possible correlation to the high statistics of indiscernible chromosomal abnormalities in patients aged 35-37 years old after transplantation of ooplasm resulted in singletons pregnancies (5%), similarly equal to the amount of pregnancies from women <35 after the same ooplasm procedure. From older women who suffered from damaged mitochondria, implantation rates decreased which correlated to high amounts of damaged mitochondria. The data suggests that high levels of impaired components of cytoplasm results in increase embryonic implantation failures that correlates to maternal age, aneuploidy, and embryonic implantations.

Discussion
I would like to thank my high school, Mt. Carmel High School for giving me an academic foundation where I have been able to apply my learnings outside of the classroom. I would also like to thank all the professionals involved in this program that have given not only myself, but the rest of my OSA sisters an eye opening experience with quality support and knowledge. In addition, I would like to thank Dr. Ericka especially for all her help and guidance through this academic process. I would like to say thanks to Ms. Winter for coordinating this exceptional academy process. I would like to say thanks to Ms. Winter for coordinating this exceptional academy process. I would like to say thanks to Ms. Winter for coordinating this exceptional academy process. I would like to say thanks to Ms. Winter for coordinating this exceptional academy process. My incredible family who has supported me in everything I have ever strived to pursue, and giving me the encouragement and push I needed to move forward. My brilliant OSA sisters, who I have grown close to in just a few weeks and will forever cherish to have been welcomed into my life. Above all, I need to thank God for opening doors for me and giving myself the strength and courage to be the best person I had planned to be.

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Methods and Carmel High School

Objective
The aim of the present study is to augment the development and viability of embryos by improving the quality of unfertilized eggs suspected of having deficiencies by supplying them with ooplasm from normal donor oocytes. Demonstrated will be how the transfer of cytoplasm from young and healthy oocytes helps rejuvenate old oocytes in older women, with the expectation of improving the ability to impregnate. The performance of ooplasmic transfer is to replace damaged mitochondria located in the cytoplasm that have withered away with time or subjected to genetic defects, thus leading to a variety of disorders. New techniques towards this area of IVF will increase the ability of obtaining mature oocytes to be used in various IVF procedures.

Application to Biotechnology
The direct injection approach was relatively simple and entailed minimal disturbance of the usual ICSI routine with even more encouraging clinical electrofusion is technically more complex and radical of the two; although it is by far the more versatile. For the future of biotechnology, however, it may become the method of choice in future attempts to redress ooplasmic imbalance and deficiencies. Exploration involving the two techniques for medicine can increase the chances of having full terms of pregnancies as the advancement in data of how to eradicate the right amount of cytoplasm to input into oocytes to obtain the maximum amount of full term pregnancies.

References
The Increase of Lifespan Using siRNA Assisted Chemotherapy Treatment

Shelby Richards
West Valley High School
2016 Oncofertility Science Academy

Objective
To see which method is most effective, the research poster will compare Monochemotherapy and siRNA assisted treatment. Additionally, the data will show the percentages of tumor decline with the given treatment and look at the benefits and side effects of the treatment.

Abstract
Combining chemotherapeutics with siRNA using Nano Carrier Platforms is much more effective than Monochemotherapy. siRNA (small interfering RNA) attaches to the miRNA (micro RNA) and the Argonaut will slice the miRNA resulting in the piece being recognized as abnormal and destroyed. Scientists have discovered a way to take a Nano Particle core containing a chemotherapeutic drug and cover it with the siRNA endosomal escape mechanism for the drug to exit later. The last stage is to cover the siRNA with a molecular tumor targeting mechanism for the Nano Particle to reach its final destination. The drug will be diagnosed in multiple doses depending on the patient. Half of the drug will be released within the first couple of days and then the rest will be dispersed over a period of 2-4 months. The purpose is to stop the tumor from growing so the clinician can do further therapy for the patient. Dr. Paula Hammond and her team of researchers at MIT (Massachusetts Institute of Technology) have successfully tested the process. The team tested the procedure on a mouse with DOX that had triple negative breast cancer. When injected with dox + mrp1 siRNA the tumor decreased in size by ~20% within a 15-day period. Many scientists are testing different siRNA assists to find the best one with the best dosage. With 160 companies and 65 universities testing ~250 cancer based drugs, RNA therapeutics have grown to 12% CAGR (Compound Annual Growth Rate) and is expected to reach $1.2 billion by 2020. In Conclusion, the results from the studies have shown this poster are laying out a large poster and what it will look like in print. If you are using half-scale dimensions, be sure to preview your graphics at 200% to ensure that the output from PowerPoint® longer than anyone in the industry; data output is high quality, and the output from Powerpoint® is longer than anyone in the industry.

Methods and Materials
There has been many different procedures and trials being tested to find the best formulas and methods on how to undergo the procedure. Some of the procedures have been done on rats and then on humans. Three rats were injected with dox + mrp1 siRNA and the tumor decreased in size by ~20% within a 15-day period (figure 1) which shows that the siRNA assisted chemotherapy can be successful in humans. Up until 2010, no RNAi trial has moved past stage three trial until siRNA was introduced into the therapy because the injection of chemotherapy is ~70% silencing. The siRNA bonds to each of the RISC and unwound the ATP-dependent manner as well as mediating the sequence of miRNA and catalyzes the cleavage and slices the miRNA for the antisense agent to sequence. The first half of the 121 mg/kg dose of the drug is rapidly released for the first 1-2 weeks, then the rest is slowly delivered within a four month period. This procedure is the framework for a lot of scientific testing where the results show in favor of siRNA assists. Twelve patients took 1 mg of siRNA and there was no tumor growth within a 8-12 week span after all the siRNA was released. Another trial was given where the scientists were trying to figure out what dose of medication is most effective. The experiment lasted 26 months with 50 doses total. The first dose was 1 mg but the serum knocked down by 40% with infusion treatments. The dose then exacerbated where 32 patients and 17 healthy volunteers were given a dose of .15-3 mg per kg and there was a 85% serum knockdown. The remaining amount of serum reduced to 60% after four weeks. During the next phase the patients took a .3 mg per kg dose every three weeks for six months. There was a 80% sustained knockdown of serum. Only 15% of the patients had a mild to moderate TTR (transl砌hydrin) but they stabilized and the patients returned to normal. There is another phase that was initiated in 2013 and should be completed in 2017.

Results and Interpretations
Based on the diagnosis of the 15 patients in the first trial, each patient was only supposed to live from 8-10 months. As a result of the siRNA induced drug, the patients lived for about half a year longer. When the scientists tried figuring out the correct quantity of medication to give to the patients, each time there was a larger percentage of sustained knockdown of the serum. Sustained knockdown is important because the gathered information shows an indication that the method is working. There are 21 siRNA therapeutics that have been made for a variety of different diseases, ranging from cancer, viruses and genetic disorders.

Methods and Materials
Combining chemotherapeutics with siRNA carrier platforms have been shown to have a positive correlation with tumor size. Using innovative procedures on a molecular scale allows scientist to understand cells and target the root of the problem. RNA therapeutics are becoming more prominent now that clinical trials are collecting positive information. The function of siRNA and the benefits of the process in science is not only being studied on Cancer Biology but is being tested on all types of diseases and infections such as different forms of STD’s. If scientists can interact and do more experiments with siRNA and other molecular science then the root (cells) of the problem can be addressed and understood better.

Biotechnology Attributes
Being able to understand the cell is critical to all molecular sciences. For this particular therapeutic, understanding the Central Dogma will allow scientists to understand how to use the process to target specific malfunctions that occur. In this study, the cell become abnormal because an error occurs as the cells divides and the DNA within the cell is damaged. siRNA treatment targets the root cause of DNA mutations by stopping the production of protein so the cells cannot continue to multiply. Using biotechnology to manipulate the process to fight against cancer is a crucial part of the procedure. Biotechnology is essential to all sections of science and the more advanced the biotechnology becomes, the more scientists are able to discover.

Acknowledgements
I would like to thank Dr. Ericka for constantly supporting everything I do in the program and going above and beyond to teach me, Ms. Winter for always answering every question I have and working with me throughout the entire program., Kathleen Pulvers for always answering every question I ask and helping me a lot with my project, all the presenters and speakers that have taught me more than I could ever think about knowing at this age and my OSA sisters for being wonderful and growing a bond that we will last forever.

References
The Effects of Intravenous Chemotherapy on the Prefrontal Cortex in the Development of Major Depressive Disorder in Adolescent Patients

Leila Saloo
Mira Mesa High School

Objective

The objective of this investigation is to determine how decreased brain activity in the prefrontal cortex may lead to adverse psychological changes in adolescents and young adult cancer patients. This poster will demonstrate that decreased activity of the prefrontal cortex causes major depressive disorder (MDD), that is most common in adolescent and young adults due to lack of maturation in that part of the brain. Evidence will show that symptoms recorded in adolescents and young adults undergoing intravenous chemotherapy mirror those of MDD and occur due to disturbances of the prefrontal cortex functionality. MDD, which causes pervasive depressed mood and disinterest in social interaction, often devastates effects cancer patients because they are torn away from family and friends and placed in a hospital where they must fight to survive every day, and in addition, battle overwhelming negativity they feel inside. Forms of therapeutic stimulation of brain activity to encourage positive emotions in preparation for intravenous chemotherapy will be discussed. A possible solution to hinder the development of MDD in adolescent and young adult cancer patients.

Methods and Materials

The Istanbul Institute of Oncology in Turkey studied the adverse neural changes of 154 lung cancer patients undergoing intravenous chemotherapy. 10 of whom were between the ages of 20-29. The Quality of Life Index-Cancer Version was used to calculate based on the experience of sadness, anxiety, and restlessness in patients, all symptoms of MDD. Patients were divided into two groups: the control group, 7 days after chemotherapy treatment; the experimental group, 1 hour after chemotherapy treatment. The study utilized descriptive statistics, means, median, frequencies, and percentiles to assess personal characteristics and cortisol levels. In a separate study, at Case Western University in Cleveland, Ohio, 11 cancer patients ranging in ages 20-47 were compared for symptom distress in regards to their intravenous chemotherapy treatment. The study utilized the Symptom Distress Scale (SDS) to measure distress caused by symptoms in chronically ill patients. The instrument is a 13-item Likert-type scale that measures a variety of physical and psychological symptoms, one of the most prevalent symptoms tested being anxiety, an indicator of MDD. The scale takes 5-10 minutes to administer with a higher score representing greater symptom distress. The participants of the study were in their first diagnosis of cancer and within the first four months of their initial chemotherapy treatment, and required at least three additional phases of intravenous chemotherapy. They were administered a questionnaire modeling SDS and State- Trait Anxiety Index for Children (STAIC)-1 criterion before each cycle to determine any pre-chemotherapy symptoms. Immediately following intravenous chemotherapy treatment and 48 hours after chemotherapy treatment the SDS instrument scale was used again to determine the impact of the patient’s chemotherapeutic emotional distress.

Abstract

Cancer is identified as being among the leading causes of death in adolescence and young adults and chemotherapy has become a routine part of treatment. Intravenous chemotherapy results in many known physical symptoms but also presents risks to mental health, especially in adolescent and young adult patients. The prefrontal cortex is the site of the most prolonged and dramatic brain development until adulthood, and lesions or disturbances to its activity can affect its ability to properly regulate emotional and behavioral expression and can result in psychological disorders. The objective of this investigation is to determine how decreased brain activity in the prefrontal cortex may lead to adverse psychological changes in adolescent and young adult cancer patients. Ten lung cancer patients among 154, ranging from age 20-29, undergoing intravenous chemotherapy were evaluated using the Quality of Life Index-Cancer Version that numerically analyzes different aspects that affect a patient’s satisfaction with life. In a separate study, 11 adolescent cancer patients aged 10-17 were measured for symptom distress using the Symptom Distress Scale (SDS) before, during, and after intravenous chemotherapy treatment to determine the impact of the symptoms of chronic illness on emotional distress. In the first study, the average Quality of Life Index-Cancer Version received a score of 23.5, indicating a high activity of the psychological and spiritual subscale score was 24.7±3.4. In the second study, SDS was the highest just prior to chemotherapy and 48 hours after chemotherapy treatment. The first chemo treatment mean score was 24.0 out of 25 before treatment and 23.8 after; round two was 19.0 before and 18.0 after, and round three was 19.5 before and 20.0 after. In a third study, 10 adolescent cancer patients, seven undergoing chemotherapy treatment and three in remission, were evaluated and all exhibited symptoms of MDD, some of whom had already received treatment. The data from the first study displays low average QoL scores, and correlated low psychological subscale scores that were calculated based on the experience of sadness, anxiety, and restlessness in patients, all symptoms of MDD. The second study presents that the stress that adolescent patients felt from their symptoms was the highest before and after their intravenous chemotherapy treatments, and that negative psychological changes evaluated in the patient’s SDS were indicators of MDD. This proves that intravenous chemotherapy for adolescent and young adult cancer patients can result in the psychological symptoms of major depressive disorder and also suggests, based on brain anatomy and pathology, that these symptoms are attributed to decreased activity of the prefrontal cortex.

Results

In the first study, as represented by figure two, the quality of life of lung cancer patients (n=154) received a mean score of 23.5 (±3.4) on the psychological subscale (p<0.05). The data displays low average QoL scores, and correlated low psychological subscale scores that were calculated based on the experience of sadness, anxiety, and restlessness in patients, all symptoms of MDD. Patients with higher scores than one, presented a higher level of distress, whereas participants with lower scores displayed low average QoL scores, and correlated low psychological subscale scores (p<0.03). This indicates that patients who were evaluated as having high distress levels and low psychological well-being in cancer patients. Psychology, Health & Medicine, 12(4), 421-432. doi: 10.1080/13548500601084271

Figure 3. Results from study two present higher SDS scores pre-intravenous chemotherapy treatment. Though VR was administered to patients experiencing SDS in disease and after 48 hours experienced by patients treated with VR 48 hours after chemotherapy treatment. Though VR was administered to patients during chemotherapy treatment, which presented a decrease in symptom distress immediately following VR administration.

Applications to Biotechnology

From analysis of the study results, intravenous chemotherapy for adolescent and young adult cancer patients can result in the psychological symptoms of major depressive disorder and also suggests, based on brain anatomy and pathology, that these symptoms are attributed to decreased activity of the prefrontal cortex. The prefrontal cortex of an adolescent is most vulnerable to damage and lesions due to its delayed stage in brain development and data from the studies suggests that intravenous chemotherapy interferes with neural activity and delays part of the brain from regulating emotion. MDD has been linked to decreased activity of the prefrontal cortex. The prefrontal cortex displays low average QoL scores, and correlated low psychological subscale scores that were calculated based on the experience of sadness, anxiety, and restlessness in patients, all symptoms of MDD. Patients with an ECOG score of 2 or higher also suffered from worse psychological subscale scores (p<0.05). This indicates that patients who were evaluated as having high distress levels and low psychological well-being in cancer patients.

Discussion

I would like to thank my parents, whose endless love and support have pushed me to maximize my potential and provided me with the platform I used to become successful. I would also like to express my sincere appreciation to Dr. Ericka Smegar-Mitchell, Patricia Winters, and Kathleen Pulvers for guiding me in my exploration of oncology and being inspiring examples of strength and motivation that they have impacted in the scientific world. Without their enthusiasm, this research would not be possible. Last but certainly not least, I would like to express how grateful I am for my OSA sisters, who have grown to think of not as classmates, but as great friends. Thank you for being my support unit and making the experience all the more memorable.

Acknowledgements

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References

The Correlation Between Use of Hormonal Contraception and the Impairment of the Ovarian Reserve

Background
Hormonal contraception (HC) works by increasing the levels of estrogen and progesterone through artificial products, estradiol and progestin as commonly used in most contraceptives. The use of hormonal contraception thereby disrupts the natural biochemistry of the woman’s body and feedback cycle of hormone synthesis and essentially tricks the body into believing it’s pregnant. Once pregnant, levels of estrogen and progesterone remain high in the normal ovulating woman. The hormones FSH (follicle stimulating hormone) and LH (luteinizing hormone) are prevented from being released by the pituitary which prevents ovulation and therefore pregnancy. On a separate note, the ovarian reserve is evaluated based on two distinct characters: levels of AMH (Anti-Müllerian Hormone) and AFC (Antral Follicle Count). AMH is produced by the granulosa cells mostly during the early antral stage. The progesterone through artificial products, estradiol and progesterone as commonly used in oral contraception and this limits the ability of researchers to draw conclusions.

Methods and Materials

In a case controlled study by the University of Nottingham, 34 healthy women who had been taking combined oral contraceptive pills (COCP) within the last year and 36 normo—ovulatory, age matched women who had not taken hormonal birth control within the last year underwent several areas of testing, including a series of 3D ultrasounds to evaluate antral follicle counts. These tests were done in the first few days of the early follicular phase (days 2-5 of menstrual cycle).

In a similar study by the VU University Medical Center, 25 women between the ages of 18 and 40 and had been taking hormonal contraception regimens for at least 3 months volunteered for vaginal ultrasounds to analyze both ovary size and number of antral follicles. Testing for these patients were done in the hormone free interval and measured for comparison during the two subsequent natural menstrual cycles. In all cases, participants also submitted to blood testing to monitor levels of the AMH, FSH, LH, and Estradiol.

Furthermore, a study by the National Institute of Health compared 126 cancer survivors with at least one functional ovary and a uterus and one year of cancer therapy with a control group of 123 similarly aged women with normal cycles. Data was collected over a course of approximately 2 years and the control group was frequently exposed to several forms of hormonal contraception, including the pill.

Results

The study by the National Institute of Health found AMH levels were 55% lower than the normal for the control and HC control groups for the cancer survivors. The AFC for the control was 20% lower as was the AFC for survivors. Based on the individual, the control group during their use of HC had a 17-35% decreased AMH level and a 11% lower AFC.

The University of Nottingham found that there was a significant difference in the size of ovaries (P<0.001) and also significantly decreased amounts of follicles greater than 6mm (P<0.001). There was no significant change in the levels of AMH according to this particular study.

VU University Medical Center produced the following results: significant increases in AMH (P<0.001) and AFC values (P=0.004).

Discussion

Based on the data it is reasonable to assume there is a connection between the use of hormonal contraception and an impairment in the ovarian reserve. In each study, there was a significant difference in levels of AMH, FSH, LH, and quality of antral follicles. Based on the three studies, it can be concluded that while using HC, the follicle size and count is decreased compared to woman at that same moment in their cycle. Because the pituitary is inhibited by the levels of estrogen and progesterone in the body, while this change appears to be reversible, the availability of data and research available for long term use of hormonal contraception is limited. The purpose of this poster is to avoid the possibility of an unmet medical need that may result due to prolonged use of synthetic hormones. In addition there is a limited facton of the population that truly understands how hormonal contraception works and that in itself is a problem.

Connections to Biotechnology:

HC is a great example of the innovation and advancements to science that biotech allows for. The ability to accurately mimic natural hormones by isolating similar ones from plants. The future possibilities for advancements in the field of biotechnology for contraceptives is vast. There are so many different paths to travel down from the mechanical device currently being developed for men which consists of a temporary vasectomy, to more effective long term hormonal birth control that could potentially increase the reproductive lifespan for women.

Acknowledgements:
Special thank you to Dr. Chang for being an ongoing inspiration to my scientific career, Dr. Ericka for encouraging my perseverance and showing me how to not only be a scientist but also how to fail and keep going. Thank you also to Ms. Winter for her passion and ability to organize effectively.

Abstract

Historically, birth control pills have opened up unprecedented opportunities for women on a global scale. However, in recent studies, data being collected can potentially link oral contraception to decreased ovarian reserves in users. Participants in three studies were placed in categories based on either usage of hormonal contraception or no usage of hormonal contraception. The participants underwent transvaginal ultrasound, blood testing, and were evaluated on full medical history to determine data and demographic for each patient. Studies showed when comparing the ovarian reserve based on AMH levels AFC, and the ovarian volume, women with prolonged uses compared to non-users had significantly decreased counts for each (50% lower volume, 13% lower AMH, and 18% lower AFC). Similar studies found the ovarian reserve to be affected in women taking oral hormonal contraceptives, but when compared to those same women’s measurements after cessation, levels were more typical. The studies showed synthetic compounds, estradiol and progestin, components in oral contraceptives could effect the ovarian reserve due to the role these hormones have in inhibiting the pituitary gland from releasing LH and FSH which are essential to the development of oocytes. Limited research is available for the long term use of oral contraception and this limits the ability of researchers to draw conclusions as to the reversibility of the effects. The importance of quantification is to avoid the medical need for future. A 2011 study by the CDC shows approximately half of all pregnancies in the U.S. were unplanned, meaning there is an immense need, however there is always room for the improvement of such drugs.
Pregnanate plays a vital role in preparing the endometrial lining for pregnancy by stimulating a rapid increase in hormones in response to human chronic gonadotropin (hcG) that is produced by the corpus luteum in the luteal phase of the menstrual cycle. Embryonic implantation occurs in the luteal phase and is dependent on the efficacy of the corpus luteum. In Luteal Phase Defect, progesterone is produced in low amounts, or the endometrium is not responding the progesterone being produced. Therefore, ART, such as IUI, supply women with progesterone in order to improve implantation of the egg and pregnancy rates. The objective of this poster is in order to determine the impact of luteal phase support with vaginal progesterone on pregnancy rates in ovulation stimulation and intrauterine insemination (IUI) in couples with unexplained infertility.

A prospective randomized trial was done at the Department of Obstetrics and Gynecology, Gazi University School of Medicine, Ankara, Turkey that included couples with unexplained infertility that were treated with ovarian stimulation and IUI using recombinant FSH from November 2004 to 2006. The duration of infertility was at least 1 year for each subject who had regular menstrual cycles with midluteal P levels ≤10 ng/mL. Bilateral fertility potential was confirmed with a hysterosalpingography, and normal semen analysis. Once a patient was randomized in the first cycle, she remained in the same treatment group during the entire study; a placebo was not used. Patients in the study group received vaginal P gel (Cinnohe 8% vaginal gel) for luteal phase support beginning 2 days after ovulation. Semen samples were taken by masturbation. For the procedure, sperm concentration, sperm motility, and total motile sperm number were evaluated and the semen was stored in an incubator at 37°C until the time of insemination. The IUI was performed 36 hours after hCG administration in the experimental group. Luteal phase was supported with vaginal progesterone gel once a day beginning 2 days after insemination until pregnancy testing, and then continuing onto the 12th week of pregnancy if the patient conceived. Patients in the control group did not receive any luteal phase support. All patients underwent baseline transvaginal ultrasonography (TVU) on day 3 of the menstrual cycle and then were treated with a starting dose of 75 IU recombinant FSH. Cycles were triggered with 10,000 IU hCG when at least one dominant follicle had reached 18 mm in diameter. Pregnancy testing was determined by performing the quantitative serum hCG level at 14 days after hCG administration, and intrauterine pregnancy was confirmed by using TVU 2 weeks after a positive pregnancy test. A clinical pregnancy was defined as the presence of a gestational sac on TVU or by demonstration of fetal cardiac activity. The rate per cycle in conception in patients who were aborted. Live birth was defined as having a child who was living at 1 week after birth.

In conclusion, outcomes would suggest that luteal phase P support can significantly improve the likelihood of clinical pregnancy and live birth in IUI cycles where ovulation induction was achieved with gonadotropins. The study also indicated that luteal support is required in ovulation induction cycles with gonadotropins where a multifactorial response has been achieved.

**References**


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**Abstract**

Progestrone plays a vital role in preparing the endometrial lining for pregnancy by stimulating a rapid increase in hormones in response to human chronic gonadotropin (hcG) that is produced by the corpus luteum in the luteal phase of the menstrual cycle. Embryonic implantation occurs in the luteal phase and is dependent on the efficacy of the corpus luteum. In Luteal Phase Defect, progesterone is produced in low amounts, or the endometrium is not responding the progesterone being produced. Therefore, ART, such as IUI, supply women with progesterone in order to improve implantation of the egg and pregnancy rates. The objective of this poster is to determine the impact of luteal phase support with vaginal progesterone on pregnancy rates in ovulation stimulation and intrauterine insemination (IUI) in couples with unexplained infertility. A prospective randomized trial was done included 214 couples with unexplained infertility that were treated with ovarian stimulation and IUI using recombinant FSH. Semen samples were taken by masturbation and after the procedure, sperm concentration, sperm motility, and total motile sperm number were evaluated and the semen was stored in an incubator at 37°C until the time of insemination. The IUI was performed 36 hours after hCG administration in the experimental group. Luteal phase was supported with vaginal progesterone gel once a day beginning 2 days after insemination until pregnancy testing, and then continuing onto the 12th week of pregnancy if the patient conceived. Patients in the control group did not receive any luteal phase support. All patients underwent baseline transvaginal ultrasonography (TVU) on day 3 of the menstrual cycle and then were treated with a starting dose of 75 IU recombinant FSH. Cycles were triggered with 10,000 IU hCG when at least one dominant follicle had reached 18 mm in diameter. Pregnancy testing was performed by determining the quantitative serum hCG level at 14 days after hCG administration, and intrauterine pregnancy was confirmed by using TVU 2 weeks after a positive pregnancy test. A clinical pregnancy was defined as the presence of a gestational sac on TVU or by demonstration of fetal cardiac activity. The rate per cycle in conception in patients who were aborted. Live birth was defined as having a child who was living at 1 week after birth.

**Methods and Materials**

- **General Information:**
  - **Participants:** 427 cycles, 84 pregnancies occurred; 58 pregnancies were in the study group and 35 were in the control group, therefore, the difference was not significant.
  - **Patient Population:** Eighty-six patients had only one cycle; 46 patients had two cycles, and 82 patients had 3 cycles.
  - **Duration of Study:** The duration of infertility was at least 1 year for each subject who had regular menstrual cycles with midluteal P levels ≤10 ng/mL. Bilateral fertility potential was confirmed with a hysterosalpingography, and normal semen analysis. Once a patient was randomized in the first cycle, she remained in the same treatment group during the entire study; a placebo was not used.
  - **Cycles:** The study group received vaginal P gel (Cinnohe 8% vaginal gel) for luteal phase support beginning 2 days after ovulation.
  - **Control Group:** Patients in the control group did not receive any luteal phase support.

**Results**

- **Pregnancy Tests:**
  - The application of luteal phase support with vaginal P gel was associated with significantly higher clinical as well as live birth rates compared with patients without luteal phase support. In conclusion, outcomes would suggest that luteal phase P support can significantly improve the likelihood of clinical pregnancy and live birth in IUI cycles where ovulation induction was achieved with gonadotropins. The study also indicated that luteal support is required in ovulation induction cycles with gonadotropins where a multifactorial response has been achieved.

**Conclusions**

In conclusion, outcomes would suggest that luteal phase P support can significantly improve the likelihood of clinical pregnancy and live birth in IUI cycles where ovulation induction was achieved with gonadotropins. The study also indicated that luteal supports should be encouraged in ovulation induction cycles with gonadotropins where a multifactorial response has been achieved. Hormonal changes after ovarian stimulation for multifactorial response in ovulation stimulation and IUI cycles might reveal abnormal endometrial changes. It has long been known that in cycles with multifactorial growth, an advanced endometrium in the early luteal phase was observed in approximately 50% of women undergoing IVF treatment. It is suggested that multifactorial response in ovulation stimulation and luteal phases seems similar to superovulation in IFF cycles, and that high steroid environment in the luteal phase is responsible for the luteal insufficiency. It is suggested that luteal support is mandatory in ovulation induction cycles with gonadotropins where a multifactorial response has been achieved.

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The Effects of Anti-CD19 CAR-T Cell Therapy on Relapsed and Refractory B-cell Acute Lymphoblastic Leukemia (B-ALL)

Background
This poster intends to investigate an emerging immunotherapy, chimeric antigen receptor (CAR) T-cell therapy, as a therapeutic approach for relapsed and refractory B-cell acute lymphoblastic leukemia (r/r B-ALL). It focuses on two of a growing number of clinical trials evaluating the efficacy of CAR-T cell therapy to induce durable remission with minimal toxicity. With current salvage therapies unable to rescue most patients, novel modalities are greatly needed.

Methods and Materials
The cohorts comprised patients of different age groups and genders with varying treatment history and status. Baseline characteristics were unfavorable even in the context of an already poor prognosis population (Figure 3). In this trial, patients were transplanted with apheresis blood products from their matched donors, and CAR-T cells were administered at 1.1x10^9 to 9.7x10^9 cells/kg. Patients were monitored by flow cytometry and quantification (first month). Responses were classified as no response (NR), CR (<5% blasts in BM), and CR with residual disease detected by assay, or CRm (CR with MRD-).

Results
Outcomes demonstrated therapeutic potential for r/r B-ALL treatment with anti-CD19 CAR-T cell therapy. In the CHOP/Penn cohort, 27 of 30 patients achieved CR. 19 remained in remission, with 15 receiving no further treatment and 4 withdrawing to other treatment. 3 patients transitioned to allo-SCT and have since sustained remission while 1 with MRD+ underwent additional therapy, achieving and sustaining CRm. Median follow-up was 7 months (range 1-24). In the MSKCC cohort, 14 of 16 patients achieved CR. 7 transitioned to allo-SCT, with no incidence of relapse. In an updated report almost a year later, 8 additional patients have been treated. In 22 patients evaluable for response, 20 (91%) have achieved CR, 18 (82%) with MRD-. With median follow-up of 7.4 months (range 1-36), 6 patients have sustained CR beyond a year (range 12-36.4), and the median OS is 9 months. In vivo activity in both trials saw high levels of expansion but differed in persistence. Median duration of 19-28z CAR-T cells was 30 days (range 9-120) whereas CTL191 probability of persistence at 6 months was 68% with duration so far lasting up to 2 years. Scientists noted a correlation amongst CAR-T cell persistence, B-cell aplasia (for IgG replacement was administered to maintain levels >500 mg per dL), and sustained remission (in the context of post-LC therapy treatment). Sustained remission was also seen with subsequent allo-SCT. A substantial byproduct of "large-scale, synchronous T-cell activation" and concomitantly elevated cytokine levels (Figure 5) was a systemic inflammatory response, cytokine-release syndrome (CRS), symptomized by fever, myalgia, hypotension, respiratory insufficiency, ecchymosis, and/or cytophenia. CRS was treated with either steroid therapy (glucocorticoid-based) or tocilizumab, an interleukin-6 (IL-6) receptor antagonist, and toxicities were fully reversible within 3-5 days. Correlation was drawn between initial disease burden and severity of CRS (Figure 5). For the 7 (CHOP/Penn) and 3 (MSKCC) patients who relapsed, recurrence was tied to lack of CAR-T cell persistence (early loss or steroid interference; Figure 3) or CD19- relapse. Although data is limited to the Phase I cohorts and follow-up, progressive clinical phases will help to expand upon these preliminary findings.1,2

Discussion
Despite improved survival for de novo B-ALL, r/r B-ALL remains an immense challenge to induce and sustain remission in salvage chemotherapy drugs deliver <25% CR and short persistence.5 However both trials highlight potency and durability of CAR-T cells, clinical outcomes are remarkable for such a fatal disease compounded by high-risk populations. Mature follow-up and investigation is necessary to identify factors to maximize efficacy and minimize toxicities. Clinical trials for CAR-T cell therapy should conduct studies to investigate its effects on relapse, CRS prevention and management, CD19-relapse mechanisms, and post-treatment action.

Relevant Applications to Biotechnology
From agriculture during the Neolithic Revolution to modern day and beyond, biotechnology has and will continue to open new doors, and exponentially progress fields in science that provide useful, and sometimes controversial, services and solutions. In the discipline of medicine, biotechnology has allowed better understanding of diseases, providing the infrastructure for vast improvements in the medical field, and most notably, CAR-T cell therapy. From the conceptualization and construction of the cells themselves to the morphologic, molecular, and cyogenetic assays used to analyze, CAR-T cell therapy is a direct product of biotechnology and will continue to revolutionize r/r B-ALL and other diseases to follow.

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References

Poster:
This poster intends to investigate an emerging immunotherapy, chimeric antigen receptor (CAR) T-cell therapy, as a therapeutic approach for relapsed and refractory B-cell acute lymphoblastic leukemia (r/r B-ALL). It focuses on two of a growing number of clinical trials evaluating the efficacy of CAR-T cell therapy to induce durable remission with minimal toxicity. With current salvage therapies unable to rescue most patients, novel modalities are greatly needed.

Abstract
B-ALL is an aggressive disease as the leading cause of cancer-induced pediatric death with a dismal prognosis in adults. It is distinguished by uncontrolled growth and accumulation of immature B-lineage lymphoblasts in the bone marrow (BM). The leukemic cells prove rapidly fatal, invading the body and impeding production of healthy blood cells. Decades of advances in upfront therapy have escalated initial complete remission (CR) up to 90% in children and 80% in adults and overall survival (OS) rates around 80% and 40%, respectively. However, contemporary first-line treatment is confined to prolonged intensive chemotherapeutic regimens that bring significant short and long-term toxicities. Moreover, patients are highly susceptible to relapse (20% of children and 50% of adults), which uses a cycle of greater resistance (refractoriness) and lower efficacy (fewer incidences of resistance) to the use of rescue drugs OS rates to <30% and <10%, respectively, with median OS 6 months. Although allogeneic stem cell transplant (allo-SCT) is presently viewed as the greatest prospect for long-term survival with r/r B-ALL, only 5% of patients transition to allo-SCT with many ineligible for the risky procedure.2 Recently, scientists have approached the challenge of r/r B-ALL through harnessing the body’s inherent power. By reprogramming T-cells, lymphocytes that secrete cytokines to direct, regulate, and attack cancerous cells in immune responses, to overcome tolerance through antigen-specific activation, scientists have conducted clinical research to study CAR-T cell therapy. Phase 1 trials from Children’s Hospital of Philadelphia and University of Pennsylvania (CHOP/Penn) and Memorial Sloan Kettering Cancer Center (MSKCC) have resulted in 90% and 88% CR, respectively, and strong evidence of sustainment.2 Responses encouraged continued follow-up to comprehensively explore long-term efficacy and toxicity, while further research is needed to better understand CAR-T cell therapy.