Theme 2-2: Drug Delivery, Microfluidics and Lab on a Chip - 2023

Title	Name of the PI	List the Names of the Co-Is	Department	Abstract	Starting Date	Ending Date	Funding	Amount of Funding
Folate-targeted Metal-Organic Frameworks (MOFs) as Drug Delivery Carriers using Ultrasound	Rana Sabouni	Ghaleb Husseini	CHBE	Cancer is the uncontrolled growth of cells in the body and is considered as one of the significant causes of death globally. There are several cytotoxic chemotherapeutic agents used to treat cancer including methotrexate, 5-fluorouracil, cisplatin, tamoxifen, doxorubicin and others. Although billions of dollars have been spent on cancer research to develop these chemotherapies, it still remains a significant illness for mankind, partly due to the shortcomings of these therapies. These shortcomings include low targeting specificity, severe side effects (due to high doses) and poor pharmacokinetics. To avoid these drawbacks, anti-cancer drug delivery systems have been developed recently using nanocarriers including liposomes, micelles, polyelectrolyte capsules and others. One of the recent classes of nanoparticles investigated for chemotherapeutic use are metal-organic frameworks (MOFs) which are hybrid polymers that consist of metal ions or clusters and organic ligands. MOFs are used in many applications including gas/vapor separation, gas storage, catalysis, luminescent materials, and biomedical imaging. These structures have additional features that promote their use as drug carriers in the biomedical field. First, they are nontoxic, biodegradable and are capable of carrying high loadings of the anti-neoplastic agent due to their porous nature. Also, they have well-defined crystalline structures that can be characterized by different analytical techniques, and their sizes are suitable to control their in vivo drug release. Accordingly, the primary objective of the current research proposal is to synthesize functional metal-organic frameworks (MOFs) (e.g. amine functional group) using microwave assisted synthesis technique. In addition, several parameters on the efficiency of drug loading and release will be investigated such as pH, amount of drug, type of drug, US power density and wave frequency, respectively. Two types of encapsulated molecules will be tested including doxorubicin and the model drug calcein. Spectrofluorimeter will be used to measure and quantify the drug loading and release percentages. Moreover, in vivo drug release study will be performed against breast cancer cell (cell lines are MCF7 and MDA_MB 231).	02/06/2018	02/01/2020	FRG	139949
Liposome-Coated Metal Organic Framework (MOF) for Combination Therapy and Controlled Release of Anticancer Drugs under Ultrasound Stimulus	Rana Sabouni	Hassan Gomaa	CHBE	Cancer has emerged to become one of the predominate diseases ever known to mankind, with chemotherapeutic agents as leading methods for treating it. However, this blind sighted treatment method that targets all cells healthy and cancerous has led to a broad spectrum of side effect include fatigue, hair loss, nausea and even heart problems. Although potential drug nano-carriers currently used in the market, e.g., liposomes, yet, their drug loading capacity is still a challenging aspect limiting their usage. One of the recent classes of nanoparticles investigated for chemotherapeutic use are metal-organic frameworks (MOFs). They are nontoxic, biodegradable and are capable of carrying high loadings of the anti-neoplastic agent due to their porous nature. Although several studies had proven the capability of both liposome and MOFs as promising chemotherapeutic noncarriers in terms of high loading capacity, yet one of the main problems for effective treatment of cancer is resistance, which often requires combination therapy for effective treatment. Accordingly, the primary objective of the current research proposal is to propose and develop a new type of drug carrier: liposome- coated metal organic framework (MOF) for effective combination therapy (cockatiel of drugs). In addition, several parameters on the efficiency of drug loading and release will be investigated such as pH, amount of drug, drug ratio, ultrasound power (US) density and wave frequency. Three types of encapsulated molecules will be tested including doxorubicin, 5-fluorouracil and the model drug calcein. Spectrofluorimeter will be used to measure and quantify the drug loading and release percentages. Moreover, in vivo drug release study will be performed against breast cancer cell (cell lines are MCF7 and MDA_MB 231). Animal study will be conducted on nude mice to investigate the toxicity of the new hybrid developed nanocarrier and its effectiveness against breast cancer. Preliminary results have shown promising results as follows: 1) successful liposome coating of Fe-BTC MOFs sample, which was confirmed by an increase in MOFs diameter by 17.4 nm using DLS and TEM images; 2) drastically increase in the release profiles of model drug (calcein) from MOFs under ultrasound irradiation of up to 65% within 70 mins compare to without external stimuli. Finally, this new hybrid liposome-coated MOFs could be considered as a promising new generation of nonocarriers which can advance the field of anticancer drug delivery systems.	02/06/2020	02/06/2022	FRG	120000
Novel Microwave and Light Stimuli-Responsive Anticancer Drug Delivery System (DDS) Based on Metal-Organic Framework (MOF) Nanocarriers	Rana Sabouni	Hassan Gomaa	CHBE	Cancer has emerged to become the second leading cause of death worldwide after cardiovascular diseases. Cancer and its treatments can often affect person's lifestyle in many ways from health, wellness, diet and eating habits. There are several types of cancer treatments which depend on the type of cancer and how advanced it is. Among these treatments, chemotherapy is the most common one. However, this blind sighted treatment method that targets all cells healthy and cancerous has led to a broad spectrum of side effect include fatigue, hair loss, nausea and even heart problems. Although potential drug nanocarriers currently used in the market, e.g., liposomes, yet, their drug loading capacity is still a challenging aspect limiting their usage. One of the recent classes of nanoparticles investigated for chemotherapeutic use are metal-organic frameworks (MOFs). They are nontoxic, biodegradable and are capable of carrying high loadings of anti-neoplastic agent due to their porous nature. Several studies have proven the capability of MOFs as promising chemotherapeutic nanocarriers in terms of high loading capacity, yet one of the main challenges for effective treatment of cancer is targeting. Recent advances in this field, have directed researches toward exploring new external stimuli responsive drug delivery systems (DDS) including: ultrasound (US), magnetic field, near infrared light (NIR) and microwave irradiations (MW). Accordingly, the primary objective of the current research proposal is to develop new stimuli-responsive nanocarriers based on Metal Organic Frameworks (MOFs) for effective targeted therapy. The current course of studies will focus on employing external stimuli, in particular US, NIR and MW irradiations and study their effects on the in-vitro and in-vivo release profiles. In addition, several parameters on the efficiency of drug loading and release will be investigated such as pH, amount of drug, drug ratio, and power density and wave frequency. Three types of encapsulated molecules will be tested including doxorubicin, 5-fluorouracil and the model drug calcein. Spectrofluorometer will be used to measure and quantify the drug loading and release percentages. Moreover, in-vivo drug release study will be performed against breast cancer cell (cell lines are MCF7 and MDA_MB 231). Animal study will be conducted on nude mice to. Preliminary results from our previously funded research studies have shown promising results when using ultrasound as an external stimulus. A dramatic increase in the release profile of doxorubicin from MOFs under ultrasound irradiation was observed and reaching up to 80% within 245 min as compare to without external stimuli (6% release only). This encourages our group to expand on research ideas and include microwave irradiation as a new	02/06/2021	02/06/2024	FRG	149900
A microfluidic platform for preparation and evaluation of estrone liposomes for drug delivery in breast cancer therapy.	Mohamed Abdelgawad	N/A	MCE	Encapsulating cytotoxic drugs into nano-carriers (e.g. liposomes) with surface-conjugated moieties to lead the drug to the tumor is now proven to reduce the unwanted side effects of conventional chemotherapy. However, preparation of the liposomes with the required surface moieties is usually an arduous process that involve long protocols with multiple sequential steps that stand as an obstacle in the path of spreading the use of such drug delivery vehicle. Moreover, the resulting liposomes are usually of varying sizes and large batch-to-batch variations. Furthermore, screening and evaluation of the prepared liposomes is usually done by testing their effects on cells cultured inside well plates or petri dishes under static conditions that differ significantly from the dynamic flow conditions within the body. This discrepancy led to variations in the therapeutic effect of these drug delivery carriers, when administered to patients, from the effects measured inside laboratories. In this project, we propose to use microfluidics as a platform for preparation and evaluation of Estrone conjugated liposomes as a drug delivery vehicle for breast cancer therapy. Microfluidics, which involves control of fluid flow inside microchannels, was recently proved as an effective platform for preparation of nanoparticles and liposomes in a continuous flow technique that results in liposomes with smaller sizes and better homogeneity. Additionally, by evaluating the therapeutic effect of these nanocarriers on cells cultured inside microchannels under flow conditions that are closer to the in-vivo environment, more accurate results can be obtained.	01/06/2022	31/05/2024	FRG	483000
Characterization of the response of sperm cells to changes in the physical environment inside the female reproductive tracts and its relation to male infertility	Mohamed Abdelgawad	N/A	MCE	Rheotaxis, which is tendency of spermatozoa to adjust their swimming direction according to the surrounding flow conditions, was recently proposed as a potential mechanism for sperm guidance to the ovum in the female reproductive tracts. According to this theory, spermatozoa swim against outflow of fluids, which are secreted in the oviducts after coitus, to reach the ovum in the Fallopian tube. In rheotaxis, sperm navigation is entirely based on the ability of sperm cells to sense the surrounding physical environment inside the female reproductive tracts and to respond to any hydrodynamic changes in this environment. Therefore, studying sperm response to changes in the surrounding fluid flow conditions is of utmost importance to understand this new navigation mechanism and, consequently, to discover new possible causes for infertility. Moreover, understanding normal response of spermatozoa to fluidic stimuli during their journey to the ovum can lead to establishing new standards for sperm selection in assisted reproduction techniques. In this proposal we plan to develop a microfluidic setup to characterize changes in swimming behavior of spermatozoa in response to changes in the hydrodynamics of the surrounding flow. Spermatozoa with heads immobilized inside microchannels will be subjected to different conditions of flow velocity, shear rate, and static pressure and their dynamic response in terms of amplitude, frequency and symmetry of the beating pattern of the flagellum will be measured. Such experiments will be carried out separately on sperm cells exhibiting positive or negative rheotaxis.	01/06/2020	01/12/2023	FRG	510000
Counting white blood cells using smartphone microscopy	Mohamed Abdelgawad	Michel Pasquir	MCE	In many parts of the developing world, access to good quality healthcare could be a struggle. Blood cells diagnosis is becoming an essential step to ensure a proper treatment to blood related diseases. Examinations such as the white and red blood cell count is considered invaluable as they provide us with information that can help diagnose medical illnesses like infections, anemia, and leukemia. Since the procedure to obtain the RBC and WBC require a lot of funding to provide adequate hospital equipment, this may not be an option in poor or third world countries. After research we concluded that a mobile application with an attachable microscope lens will be the most effective solution. The patient will provide a tiny blood sample and using the microscope lens and sophisticated computer algorithms we can get a count of the RBCs and WBCs present. In addition to that, the count of RBCs and WBCs can immediately give us an idea if the patient is within the normal range and in severe cases a physician will be contacted.	01/01/2020	31/05/2020	URG	5000
Development of a Multilayer paper- based Digital Microfluidics Device	Mohamed Abdelgawad	N/A	MCE	This is a project proposal for the development of a low-cost multilayer paper-based digital microfluidic device. Digital microfluidic (DMF) devices are used to manipulate and control the motion of small droplets electrically over substrate of several electrodes. DMF devices are currently used in many biomedical applications including diagnostics, DNA analysis, and laboratory automation. This project aims to create a paper-based device with inkjet-printed electrodes and circuit that is used for different biomedical applications. Since the device is paper based, the cost of the device is low compared to conventional devices that serve the same function. In addition, the fact that the device can be easily fabricated using mainly a printer allows the benefit of conducting certain biomedical applications in resource-poor settings. The project starts by optimizing and creating the device design using numerical modeling. The device design includes choosing electrodes shape, establishing ground connections, and creating a connections circuit. After that, a low-cost high voltage supply circuit is to be constructed. The high voltage circuit provides a signal with sufficient voltage and frequency to generate strong actuation forces for droplet motion. Later, the multilayer device is to be fabricated. The fabrication process starts with using an Inkjet printer with compatible conductive ink to print the electrodes and the connections circuit each on a separate paper (layer). Afterwards, the printed electrodes pattern is coated with an insulating material and water -repellent material. Then, a conductive connection between the electrodes layer and the connections layer are to be established. Finally, actuation forces and droplet speed data are acquired and compared with reference data obtained from a conventional digital microfluidic device. All in all , a low-cost multilayer digital microfluidic device is produced using mainly an Inkjet printer which is the main outcome of this project.	01/05/2020	31/12/2020	URG	4700
Design of an alternating pressure flow controller for mixing on the microscale	Mohamed Abdelgawad	N/A	MCE	The main objective of this project is to develop an alternating pressure flow controller to experimentally investigate improvement of mixing inside microchannels using sequential segmentation. In sequential segmentation, streams of the two liquids to be mixed are cut into short segments along the channel axis to allow for fast mixing due to Taylor-Aris dispersion. To achieve this goal, several objectives are to be achieved as listed below: 1. Build an experimental setup that will enable us to generate segmented flow inside microchannels. 2. Design and build a microfluidic channel that will be used as a sample microflow reactor 3. Study the effect of various parameters such as the magnitude, frequency, and duty cycle ofthe applied pressure on the mixing efficiency.	01/12/2021	31/12/2022	URG	8260
Characterization of the electrical properties of epoxy resins as low-cost dielectric coatings in Inkjet-printed Digital microfluidic devices	Mohamed Abdelgawad	N/A	MCE	Digital microfluidics (DMF) is a method of manipulating liquid droplets using electric fields over an array of microelectrodes. DMF can allow for the manipulation of droplets with volumes ranging from picoliters to milliliters [2]. This technology allows for the dispensing, mixing, and splitting of liquid droplets, as seen in figure 1a, which are used in automating sample processing for chemical and biological assays [1]. DMF devices are composed of an array of microelectrodes coated with a dielectric layer to generate the electric fields required for droplet manipulation as seen in figure 1b. This project aims at testing alternative low-cost, and accessible dielectric materials to fabricate chips that are viable for experimental use. We will fabricate the required DMF devices using inkjet printing of conductive ink (silver nanoparticles) on paper substrates. By finding cheaper dielectric materials, we can cut down the costs drastically, which will allow for the usage of DMF in resource-poor institutions. We hypothesize that cheaper alternatives for creating dielectrics exist commercially but have not yet been tested for this purpose.	01/03/2023	20/12/2023	URG	4000
A portable thermal cycler for PCR applications	Mohamed Abdelgawad	N/A	MCE	The goal of the pocket PCR project is to develop a polymerase chain reaction (PCR) instrument that is small, portable, and reasonably priced that can be used for the quick and accurate detection of a variety of biological targets, such as viruses, bacteria, or genetic changes. In order to benefit from its capacity to amplify and detect minute amounts of DNA, PCR technology must be made available to a wide range of users, including researchers and medical professionals. Creating a small size PCR device will allow for the use of this technology in a wide range of environments including resource poor environments and will provide a way to sustainably detect life-threatening pathogens. The key elements of a PCR machine, such as heat cyclers, detectors, and power sources, have been miniaturized as part of a pocket PCR effort to create a portable, battery-powered device that can be utilized in a variety of scenarios. This may make running PCR assays less expensive and time-consuming while also making it easier and simpler to utilize this potent diagnostic tool.	25/04/2023	20/12/2023	URG	5000
"Prediction of Drug Release Using Machine Learning Techniques"	Nabil Abdel Jabbar	None	CHBE	Over the last decade, increasing interest in the area of drug delivery systems (DDS) has explored the application of machine learning (ML), a sub-field of artificial intelligence (AI) for analyzing and interpreting biological information, and predicting drug release. In this study, several machine learning techniques (supervised and unsupervised) and their applications in drug delivery systems will be examined, including the strategies adopted to develop these algorithms and datasets fed into these frameworks. The performance of these models will be evaluated using three regression evaluation metrics, i.e., mean absolute error (MAE), mean squared error (MSE), and the coefficient of determination (R2). The results from the evaluation metrics will reveal the predictive performance of the chosen machine learning technique. Further study will entail using other algorithms (Ensemble methods and Support vector machine) to predict drug release and compare all three algorithms with the highest predictive performance.	01/06/2023	31/05/2024	FRG	10000