Organ-on-a-chip: The Future of Drug Screening and Safety for Opioids

Andrew P. Howell ‘20

Feature Article, Hampden-Sydney College, Hampden-Sydney, VA 23943

The “Opioid Crisis” has swept across America leaving thousands in its wake addicted and dying. The Center of Disease Control data showed that in 2017, “70,237 drug overdose deaths occurred in the United States” with “Opioids—mainly synthetic opioids (other than methadone)—being the main driver of drug overdose deaths [1]. During the late 1990s, “pressure on medical practitioners to resort to opioids for managing chronic pain led to a nation awash with prescription opioids [2]. Advances in medicine have vastly improved the overall health of citizens and ensured that most afflictions could be treated or cured. Pain management has become a branch of responsibility for physicians that has led to the over-prescribing of opioids as a form of pain relief. Not all the responsibility falls on physicians for the creation of the “Opioid Crisis” [3].
Pharmaceutical companies have a responsibility to ensure the safety of their products prior to their release to the public. The safety measures, while strenuous, do not always ensure that patients, especially those who need long-term treatment, will be free from negative side effects with one of the most prevalent side effects that are faced by chronic opioid users is dependence. A proactive solution to this problem is to advance drug screening to help improve opioid efficiency before reaching the market. An “organ-on-a-chip” is a revolutionary way for pharmaceutical companies to have detailed *in vitro* testing on human organ systems prior to clinical testing. These testing methods could help reduce complications from opioid-based drug solutions and the possibility of drug dependence, as well as lead to a more personalized approach to medicine.

What is an Opioid?

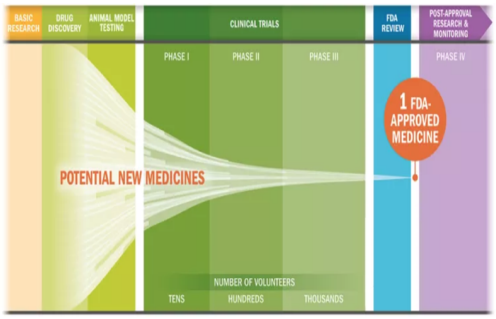
An opioid, in its most literal sense, is referred to as “opium”, an extract of the poppy plant. “Opioid” in today’s sense typically refers to a synthetic substance that mimics the effect of opium. According to the Mayo Clinic, “Opioids are a broad group of pain-relieving drugs that work by interacting with opioid receptors in your cells” [4]. Today, opioids can fall into one of four categories: Endogenous (opioid compounds produced in the body, such as endorphins), Opium alkaloid (Drugs made with opium, including codeine and morphine), Semi-synthetic (opioids synthesized from opium, such as heroin and oxycodone), or Synthetic (opiates created in a laboratory using chemical reactions, including fentanyl) [5]. When used correctly, opioids can be beneficial in providing pain relief, especially for those that suffer from chronic, debilitating pain.

However, opioids are not a perfect solution to pain management and can often become highly addictive or even negate the body’s ability to combat pain naturally. With the brain’s high degree of plasticity, the introduction of opioids can lead to alterations in the connections inside the brain. Harvard researcher J.W. Younger and his team analyzed the effects of extended administration of morphine on ten subjects with chronic low back pain. They found that “opioid exposure causes structural and functional changes in reward- and affect-processing circuitry” and that “morphologic changes occur rapidly in humans during new exposure to prescription opioid analgesics” [6]. The ability for pharmaceutical companies to design drugs that can lessen the potential for dependence, while mitigating pain, can save thousands of lives lost to opioid overdose.

The Drug Discovery Timeline and its Issues

Before a pharmaceutical company can bring a drug to market, it must first pass a battery of strenuous tests to ensure its safety [7]. Potentially tens of thousands of drugs are discovered that may be useful products to the market. *However, they must first pass multiple phases of testing such as, animal testing, three stages of clinical trials, and, finally, an FDA approval process [8] (Figure 1).

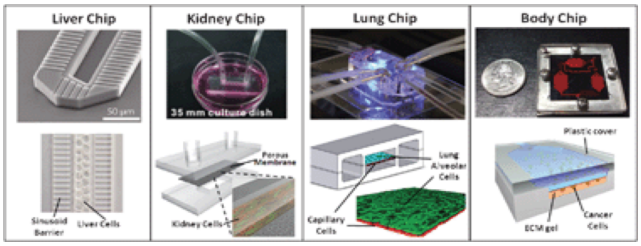
Figure 1



The main issue with these processes regarding opioid-type drugs is that they may not directly address addictive properties. Animal testing, for example, may prove a drug to be safe to progress to the clinical stages but does not determine that a drug is not addictive. These issues also apply to clinical trials, as many of the trials, while thorough, last, on average, a few months to a few years, depending on the stage of development. However, a few months of clinical testing is not enough time for patients to become thoroughly addicted to the potential drugs that will be brought to market. Another issue with clinical drug testing is that patients may not disclose any new-found dependence to researchers which can allow potentially highly addictive drugs to reach the market.

"Organs on a chip" can help to give pharmaceutical researchers time to analyze their potential drugs on specific organ systems. An organ-on-a-chip which is defined as "living cells cultured within microfluidic devices that have been micro-engineered to reconstitute tissue arrangements observed in living organs in order to study physiology in an organ-specific context and to develop specialized *in vitro* models" [9]. These chips can have various designs based on the tissues they aim to mimic (Figure 2).

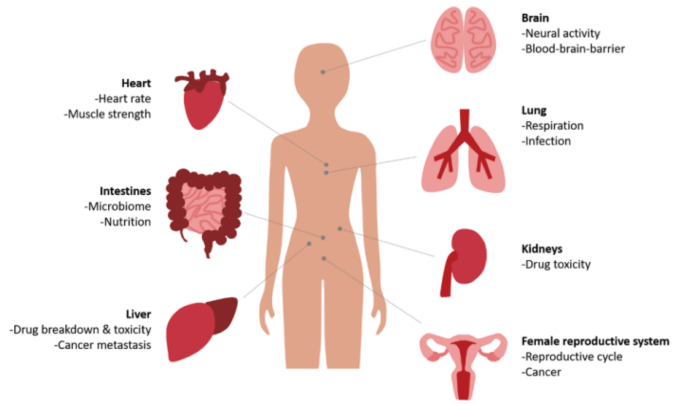
Figure 2



Improving the Drug Creation Process via Organ-On-a-Chip Testing

Improving the drug development process by mitigating potential adverse side effects can save pharmaceutical companies and consumers millions of dollars. Organs on a chip can be a vital tool for pharmaceutical companies to achieve a higher level of predictive power in preclinical trials regarding drug-tissue interactions [10]. While an organ-on-a-chip cannot fully replicate the internal environment of the body, it can give researchers insight into the potential interactions a drug can have with various organ systems (Figure 3).

Figure 3

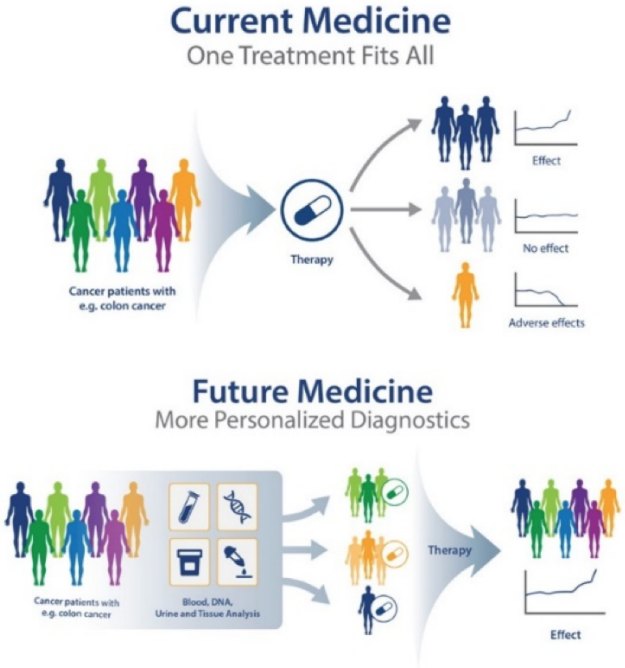


One area of research, neurological organs-on-a-chip development, can be especially helpful to pharmaceutical companies aiming to analyze the effect of a potential drug on the brain. An advantage to the organ-on-a-chip model is that researchers can test drug-tissue interactions for various types of cells in the brain (ganglia, vasculature, or support cells). For opioids, researchers could test the effects of a potential drug on the ganglion cells, specifically, to mimic the drug-tissue interaction in the brain of patients. This research could help to mitigate the over or under excitement of the neurological cells and reduce the adverse side effects of the drug, such as the potential for dependence.

Personalized Medicine

Presently, pharmaceutical companies create drugs that are compatible with the majority of patients. However, this model of drug design is not beneficial to all patients. While organs on a chip can improve the drug development timeline, they can be even more useful in personalized medicine. The Mayo Clinic defines personalized medicine as, "individualized, precision or personalized medicine providing a genomic blueprint to determine each person's unique disease susceptibility, define preventive measures and enable targeted therapies to promote wellness [11]." When used in conjunction with systems such as an organ-on-a-chip, medical care can become something that no longer targets a wide range of patients. Instead, a higher level of precision in drug creation will occur, aiding to reduce the risks that a new drug may entail for an individual and increasing the efficiency of the drug for the patient. The current system of "one drug for the masses" could be replaced with a system of target drug prescription with the use of organ-on-a-chip drug design using a patient's cells (Figure 4).

Figure 4



Conclusion:

The benefits of organ-on-a-chip and its use in drug development and design have made it an attractive solution for pharmaceutical companies. However, due to the novelty of these solutions, the wide scale implementation of these devices is still progressing. For opioid testing, organ-on-a-chip models can fundamentally change the way that pharmaceutical companies ensure the safety of their products. Millions of dollars and months of testing can be saved because these developmental drugs can be tested on organ systems before the clinical trials. These tests can better prepare medications for clinical trials and shorten the drug development and design process. Organ-on-a-chip models can also give researchers a better understanding of the types of interactions developmental drugs can have on various organ systems. The ability to test specific organ systems can pave the way to personalized medicine, as the patient's cells can be examined to detect any possible negative interaction to a particular drug. Personalized medicine has a good outlook in the medical community due to its ability to tailor medications and dosages to individual patients rather than to the majority of the population. The ability to adapt drugs to a patient can increase the efficacy of a drug, reduce the harmful side effects of a drug, and reduce the number of prescriptions an individual may have to try before one is found that is most effective for them. The organ-on-a-chip style of drug development will be a staple for pharmaceutical companies for many years to come. The benefits of organ-on-a-chip drug design such as reduced side effects such as dependency, lessening death from overdose, and enabling precise, personalized medicine, make this model an item of interest for future of drug design and development.

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