Let There Be Light Activated Drug Release

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Abstract
In some instances systemic drug delivery, either orally or intravenously, may not be the ideal dosing strategy. Repeated intravenous injections are unpleasant and sometimes a more localized delivery is needed such as in treatment of a tumor. A method that would allow a reservoir of drug to be implanted in a patient and be released in a controlled manner on demand would allow repeated dosing in a localized area and could prove extremely beneficial in the clinic by limiting the total dose needed and therefore the related side effects. The present article highlights a new approach utilizing reservoir capped by a light-responsive membrane that can be made permeable using an external near-infrared light source that was recently published by Timko et al.

Keywords: dosing, drug, gold, implant, laser, light, near infrared

Introduction

There is an ever present need to improve the specificity and delivery of the drugs available for the treatment of patients. While the discovery of new drugs is one way for this improvement to occur, changes in the delivery of current drugs can yield the same benefits. Traditionally, drugs must be introduced into the body in separate doses. While some therapeutics use a "time release" system such as special coatings, they more or less provide a steady rate of delivery into the system. There is currently no commonly used method in which multiple doses of a drug can be delivered into the body and then released at set times or even upon an external trigger. The closest current method is perhaps an insulin pump that introduces insulin into the patient's system through a catheter attached to a reservoir worn around the patient's waist. Oftentimes, repeated dosing is painful or difficult for a patient, resulting in low compliance. In a recent issue of PNAS, Timko *et al.* described a device that can be loaded with multiple doses of a drug, implanted into a patient, and then that drug can later be released by a physician using near-infrared (NIR) light [1]. This device has the potential to change the way many diseases are currently treated including diabetes, cancer, and chronic pain, among others.recent issue of PNAS, Timko *et al.* described a device that can be loaded with multiple doses of a drug, implanted into a patient, and then that drug can later be released by a physician using near-infrared (NIR) light [1]. This device has the potential to change the way many diseases are currently treated including diabetes, cancer, and chronic pain, among others.

Authors' Results

The Kohane laboratory at the Boston Children's Hospital and Harvard Medical School previously described a system in which a reservoir is triggered for release using oscillating magnetic fields [2]. Here, their objective was to develop a device that could be triggered to release drug using NIR light [1]. NIR has multiple advantages over other triggers such as magnetic fields including ease of manufacturing a point-of-care device (it can be similar to a laser pointer) and that it is much more precise, shooting a narrow beam rather than creating a wide field.

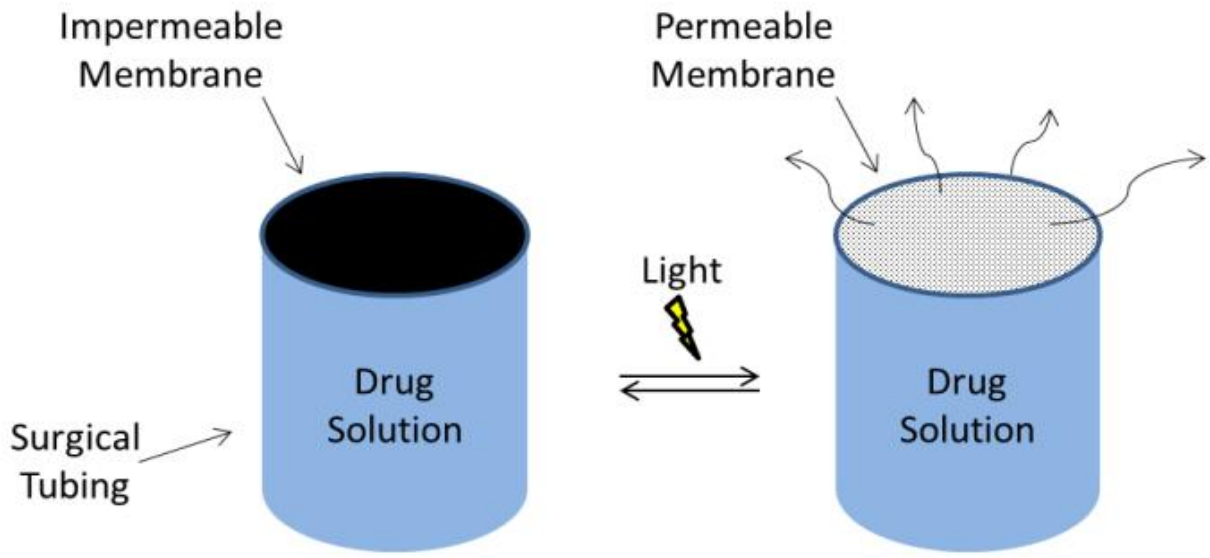

Figure 1. Drug repurposing through the use of currently available bioinformatics data. Gene signatures from cells treated with FDA approved drugs are compared to those of the target disease. Ability of each drug to oppose this malignancy is computed to yield an activity score. Low scoring drugs are eliminated while high scoring drugs and further investigated experimentally.

NIR light is not absorbed by tissues, but is converted into heat by gold particles. The authors utilized this property by creating a surgical tubing reservoir that is capped on one end by an acrylamide-based polymer that is impermeable at body temperature but becomes permeable when heated by the interaction of NIR and gold particles that are interspersed in the membrane. Temperature, and therefore permeability, can be controlled by the intensity of the NIR shone onto the device. To test the system *in vivo*, the authors loaded the device with an insulin analog and implanted it into diabetic ras. In order to deliver between 0.5 and 1.5 units in a 30-minute dose, the authors used a 13 mm diameter device that contained 200 µL of solution and delivered it at a rate of 1.5 U/hour. This design allowed them to deliver twice daily 30-minute doses for five days. This strategy successfully decreased blood glucose levels in these rats. Importantly, inflammation due to the implant was similar to other current biological implants [1 and 3] and the wavelength of light needed did not cause any noticeable effects.

It is not difficult to imagine many uses for a device such as this. For instance, this could prove useful in the cancer treatment arena as researchers are currently searching for ways to target cytotoxic chemotherapy to the tumor, limiting the damage to normal tissue. A surgeon could implant one of these devices during surgical removal of a tumor, allowing localized adjuvant treatment to prevent relapse. A similar approach is currently available through Gliadel wafers [4], however these wafers provide a time-release dose of carmustine, whereas a pulsing dose is generally used with chemotherapy to allow recovery of normal tissue. The development of the NIR activated system could allow this pulsatile regimen to be replicated in this scenario. As with Gliadel, it would also allow the use of therapeutics to treat brain cancers that traditionally are unable to cross the blood/brain barrier.

Timko et al. also suggest placing one loaded with analgesic near a nerve, allowing the patient to

give a dose precisely where it is needed and at the level needed to reduce pain and providing a convenient method of controlling chronic or long-term pain. Similarly, it could prove useful in the treatment of psychoactive disorders including seizures, allowing a dose of drug to remain very near its site of action and providing a convenient and extremely rapid dosing strategy. It will be interesting to see which of these ideas come to fruition along with the myriad other possibilities.

Acknowledgements

I thank the reviewers for their helpful critiques.

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