## IMPLANTABLE MICROFLUIDIC DELIVERY PLATFORMS FOR CHRONIC ADMINISTRATION OF AGENTS FOR SCIENTIFIC DISCOVERY AND THERAPY

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We have developed the first implantable microfluidic delivery device for compounds in their unaltered format. In particular, these miniaturized delivery platforms enable fluid delivery directly to targeted sites in the eye, especially difficult-to-reach regions of the posterior segment. Multiple methods of controlled dosing and regulation enable custom administration in both bolus and continuous infusion modes with exquisite spatiotemporal control.

Genetic diseases are associated with localized manifestations in specific cell types or populations, typically resulting in degeneration and/or tissue reorganization. Investigation and intervention must address the spatial extent of genetic effects to maximize efficacy with minimal systemic risk. Thus, a new paradigm for studying and treating ocular diseases using microfluidic delivery devices was developed. Our delivery devices are refillable for chronic use and capable of controlled delivery of unaltered agents. Only a single surgical intervention is required to implant the device following which long term operation with potentially fewer side effects is possible.

Microfluidic delivery platforms contain a refillable fluid reservoir, flow regulation valve, and cannula to direct the dose. Devices are suitable for use in a variety of animal models including rat and rabbit. In the rabbit, the reservoir is implanted subconjunctivally, while the cannula is inserted through an incision into either the anterior or posterior segment. Placement of the tip of the cannula is determined by the desired site of therapy. A specific dose is dispensed either electronically or manually from the reservoir, directed into the eye via the cannula, and is released from the cannula tip. Once the reservoir is depleted, it is refilled by injection using a small gauge non-coring needle with the same or alternate agent. Repeated refillability is a key feature and enables chronic delivery for several months.