Title: Micro-Nanofluidics for Medicine on-Earth and in Space

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Unprecedented development in controlled delivery systems have allowed for mimicking of endocrine glands responsive to biological cues for the treatment of hormonal and metabolic disorders. In this context, micro and nanofluidic systems represent unique platforms that can be exploited to recapitulate organ functions or enable superior control of drug administration.[1] By implementing cutting-edge microfabrication techniques, we created nanofluidic membranes (Fig. 1) with dense arrays of monodisperse nanochannels as small as 2.5 nm with accuracy of ± 2 Å.[2] Two implantable platform technologies were developed based on these membranes, which leverage new fluid physics at the nanoscale: a nanochannel drug delivery system and a surface-modified 3D-printed polymer system for cell transplantation. Implantable drug delivery devices were created by incorporating these nanochannel membranes within bioinert metallic or polymeric capsules serving as drug reservoirs. The drug delivery system utilizes adaptable nanochannel sizes to constrain molecular transport and achieve constant and linear (zero-order) release of drugs and biomolecules.[3] Depending on therapeutic indication, minimally invasive device implantation could occur subcutaneously or intratumorally. Notably, our subcutaneous implants allow for transcutaneous drug refilling to extend treatment duration, as demonstrated in non-human primates whereby clinically-relevant dosage of TAF for HIV pre-exposure prophylaxis were achieved over 83 days. Using the same drug delivery platform for GC-1 delivery in pre-diabetic obese non-human primate, normalization of glycaemia, insulin and cholesterol levels and complete clearance of fatty liver were observed in conjunction with substantial adipose tissue loss.[4,5] Additionally, intratumoral immunotherapy[6] delivery via the nanochannel platform resulted in immune activation and tumor growth inhibition in a murine model of triple negative breast cancer. Ongoing innovations include active, on-board control systems to permit remote manipulation or activation, enabling telemedicine or chronotherapy regimens.[7,8] The 3D-printed polymeric cell transplantation system was developed for encapsulation of endocrine cells.[9-11] The system provides an immune protective environment for bioactive allografts by releasing drugs for local immunosuppression while permitting graft vascularization. This presentation will provide an overview of our platform technologies for medical applications on-Earth and in Space on the International Space Station.

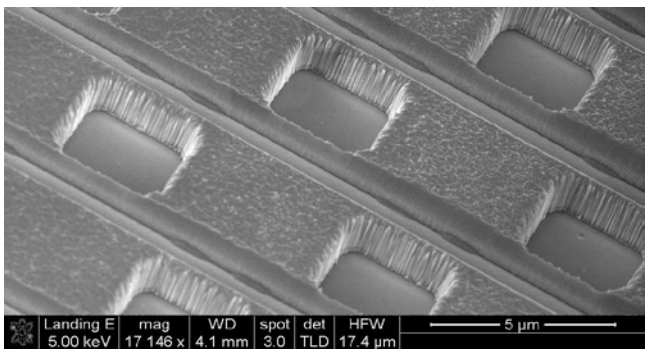


Figure 1. *SEM micrograph of the surface of the micro-nanofluidic membrane designed in our laboratory for controlled drug delivery*

References:

1. Farina M*, Alexander Jf*, Et Al. *Advanced Drug Delivery Review*. 2018 April. Doi.Org/10.1016/J.Addr.2018.04.018
2. Bruno G, Et Al. *Nature Communications.* 2018 Apr 27;9(1):1682. Doi: 10.1038/S41467-018-04133-8.
3. Ferrati S, et al. *The Journal of Sexual Medicine.* 2015 Jun;12(6):1375-1380. doi: 10.1111/jsm.12897.
4. Filgueira CS, et al. *Nature, International Journal of Obesity*. 2016 Nov; 40(11):1776-1783. doi: 10.1038/ijo.2016.129.
5. Filgueira CS et al. *Nanomedicine.* 2017 Jul; 13(5):1739-1744. doi: 10.1016/j.nano.2017.02.012.
6. Hood RL et al. *Journal of Biomedical Nanotechnology*. 2016 Oct;12(10):1907-1915. doi: n/a.
7. Bruno G, et al. *Nanoscale.* 2016 Nov;8(44):18718-18725. doi: 10.1039/c6nr06235k.
8. Geninatti T, et al. *Nanoscale.* 2015 Mar; 7(12):5240-5248. doi: 10.1039/c4nr06209d.
9. Adamo F*, Farina M*, Et Al. *Journal Of The Mechanical Behavior Of Biomedical Materials*. 2018 Mar; 21(82)133-144. Doi: 10.1016/J.Jmbbm.2018.03.023.
10. Farina M, et al. *Biotechnology Journal.* 2017 Sept; 12(9):1700169. doi: 10.1002/biot.201700169.
11. Sabek OM et al. *Journal of Tissue Engineering* 2106 Apr; 21(7):2041731416638198. doi: 10.1177/2041731416638198. 2041731416638198.

Biography: Alessandro Grattoni, Ph.D. *Chairman, The Department of Nanomedicine, The Houston Methodist Research Institute (HMRI).* His research activities are dedicated to the development and clinical translation of implantable nanofluidic platforms for controlled, long-term drug delivery and cell transplantation. He has also engaged in the analysis of electrokinetic transport in nanochannels for modulating the release of therapeutics from reservoirs. The objective is to achieve a remotely controlled drug delivery implant, which will enable telemedicine approaches and personalized treatment. Additionally, his team has created a 3D printed encapsulation device, the NICHE, for cell transplantation. Dr. Grattoni established the Center for Space Nanomedicine at HMRI, focusing on leveraging microgravity on the International Space Station for the investigation of nanomedicine for applications on-Earth and in-space. Dr. Grattoni's research has received support from, NIH, CASIS, NASA, numerous foundations and the industry.

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