The Role of Aladdin Syringe Pumps in Organ-on-Chip Applications

A Comparative Study on HUVEC Confluency

World Precision Instruments' Aladdin 12-channel syringe pump with Firmware upgrade 1.0 (WPI #**AL-1200FW1**) was used by Synvivo™ to evaluate whether the system could serve as an effective, low-cost alternative solution to achieve healthy cell growth and maintenance of cultures in an on-chip based platform.

Among the vast landscape of cell lines explored in pre-clinical organ-on-a-chip (OOC) spaces, there are many high, medium, and entry-level pumping solutions available. While various high-end solutions offering utmost flow accuracy (within 1%) over an extended observation period may be attractive, this level of precision may not be critical to achieve confluency across all cell lines—opening doors for promising results to many end-users seeking simplicity in their workflows.

To establish whether the Aladdin pump could effectively maintain conditions required for healthy cell cultures under flow, an initial experiment was carried out examining expected vs actual volume dispensed, with a target flow rate of 1µL/min for 90 minutes, and at 0.1µL/min for 16 hours using the AL-1200FW1. Final weights of each syringe across all 12-rack positions were assessed over 3 trials.

The study was advanced to the next phase to test whether confluency and normal morphological properties of cell cultures could be maintained with the AL-1200FW1. Cultures were placed under a media exchange program and introduced to an extended step-flow program using Human Umbilical Vein Endothelial Cells (HUVECs) in Synvivo™ biochips.

HUVECs were seeded in fibronectin-coated channels on-chip for 4 hours, and then placed under the media exchange program for a total of 6 hours (Fig. 1A) and imaged after 20 hours (Fig. 1B). The step-flow program was initiated thereafter, where flow was ramped from a baseline of 0.02µL/min, increasing in a stepwise fashion by 0.03µL for 3 2-hour increments (Fig. 2A). When a rate of 0.1µL/min was achieved, cultures were maintained at this rate for a period of 72-hours. HUVECs were again imaged at the conclusion of the 72-hour period (Fig. 2B).

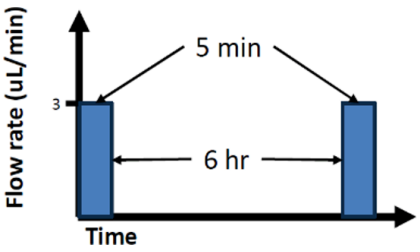

Fig. 1A–HUVECs maintained under a media exchange program that cycles between fluid flow (3µL/min for 15 min) and no fluid flow (6 hrs).

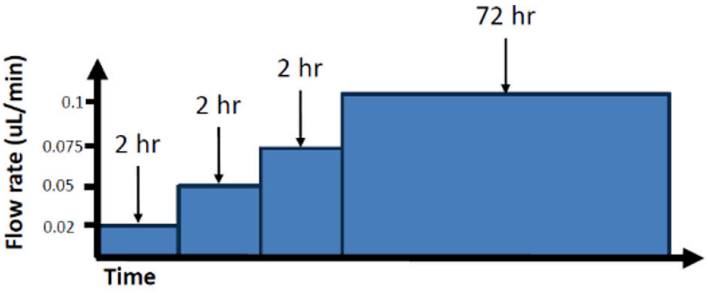

Fig. 2A–HUVECs maintained under a step-flow program, reaching a final constant flow rate of 0.1µl/min that was maintained for 72 hrs.

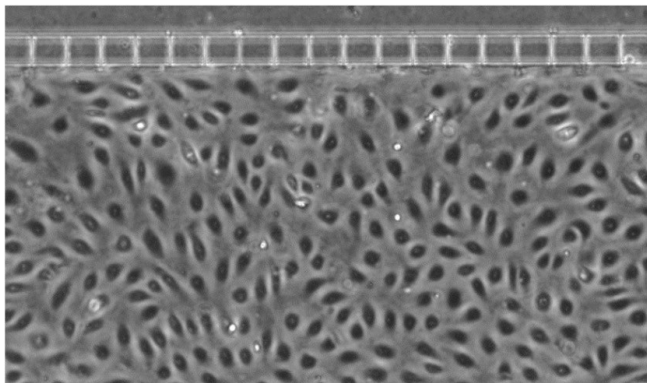

Fig. 1B–HUVEC morphology imaged after 20 hours under a media exchange program.

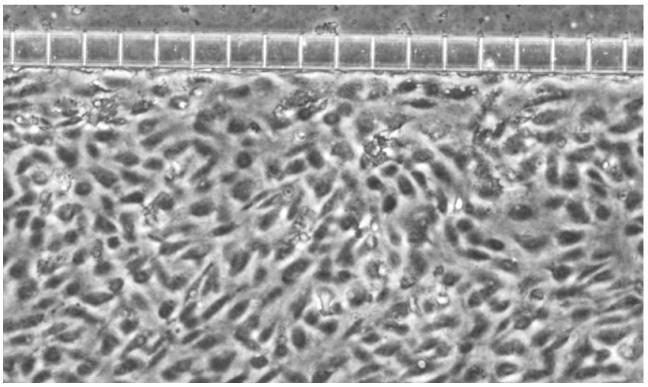

Fig. 2B–HUVEC morphology imaged after 72 hours under constant flow at 0.1µl/min.

Results

Initial AL-1200FW1 testing revealed that the actual volume dispensed at a 1µL/min flow rate was maintained within 5% of the expected value over three 90-minute trials, and within 10% of the expected value at 0.1µL/min over three 16-hour trials across all 12-syringe rack positions (n= 36). Performance was compared to two Harvard Apparatus PhD Ultra-10 systems (n= 40).

NOTE: Each syringe position per pump rack was counted per trial to form n's.

Once stability of flow was confirmed in the preliminary study, the AL-1200FW1 was used for both a media exchange and step-flow programs using HUVECs. Under each program, HUVECs remained healthy— depicting normal morphology and sustained confluency:

- At 3µL/min, HUVECs displayed a typical cobblestone morphology under static conditions (Fig. 1B)
- At 0.1µL/min, HUVECs displayed a typical elongated morphology under step flow (Fig. 2B)

Conclusions

Overall, the preliminary results suggest that the AL-1200FW1 serves as an effective alternative for extended endothelial on-chip applications under both constant, and varied flow protocols. When compared against the Harvard Apparatus PhD Ultra-10 system, there was no significant difference in flow rate or dispensing accuracy. Further, these results elude that the AL-1200FW1 may be implemented into models beyond endothelial subtypes.

Publications

Coupling fluid flow to hydrogel fluidic devices with reversible "pop-it" connections

Abbasi, R., LeFevre, T. B., Benjamin, A. D., Thornton, I. J., & Wilking, J. N. (2021). Coupling fluid flow to hydrogel fluidic devices with reversible "pop-it" connections. *Lab on a chip, 21*(10), 2050–2058. https://doi.org/10.1039/d1lc00135c

Versatile hybrid acoustic micromixer with demonstration of circulating cell-free DNA extraction from sub-ml plasma samples

Conde, A. J., Keraite, I., Ongaro, A. E., & Kersaudy-Kerhoas, M. (2020). Versatile hybrid acoustic micromixer with demonstration of circulating cell-free DNA extraction from sub-ml plasma samples. *Lab on a chip*, *20*(4), 741–748. https://doi.org/10.1039/c9lc01130g

Thermoplastic Elastomer (TPE)-Poly(Methyl Methacrylate) (PMMA) Hybrid Devices for Active Pumping PDMS-Free Organ-on-a-Chip Systems

Busek, M., Nøvik, S., Aizenshtadt, A., Amirola-Martinez, M., Combriat, T., Grünzner, S., & Krauss, S. (2021). Thermoplastic Elastomer (TPE)-Poly(Methyl Methacrylate) (PMMA) Hybrid Devices for Active Pumping PDMS-Free Organ-on-a-Chip Systems. *Biosensors*, *11*(5), 162. https://doi.org/10.3390/bios11050162

Revealing Antibiotic Tolerance of the Mycobacterium smegmatis xanthine/uracil permease mutant using microfluidics and single-cell analysis

Elitas, M., Dhar, N., & McKinney, J. D. (2021). Revealing Antibiotic Tolerance of the Mycobacterium smegmatis xanthine/uracil permease mutant using microfluidics and single-cell analysis. *Antibiotics (Basel), 10*(7), 794. https://doi.org/10.3390/antibiotics10070794

Thyroid-on-a-Chip: An Organoid Platform for In Vitro Assessment of Endocrine Disruption

Carvalho, D. J., Kip, A. M., Romitti, M., Nazzari, M., Tegel, A., Stich, M., Krause, C., Caiment, F., Costagliola, S., Moroni, L., & Giselbrecht, S. (2023). Thyroid-on-a-Chip: An Organoid Platform for In Vitro Assessment of Endocrine Disruption. *Advanced healthcare materials*, *12*(8), e2201555. https://doi.org/10.1002/adhm.202201555

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