Dynamically Programmable Magnetic Fields for Controlled Movement of Cells Loaded with Iron Oxide Nanoparticles

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Cite This: https://dx.doi.org/10.1021/acsabm.0c00226

ABSTRACT: Cell-based therapies are becoming increasingly prominent in numerous medical contexts, particularly in regenerative medicine and the treatment of cancer. However, since the efficacy of the therapy is largely dependent on the concentration of therapeutic cells at the treatment area, a major challenge associated with cell-based therapies is the ability to move and localize therapeutic cells within the body. In this article, a technique based on dynamically programmable magnetic fields is successfully demonstrated to noninvasively aggregate therapeutic cells at a desired location. Various types of therapeutically relevant cells (neural stem cells, monocytes/macrophages, and chimeric antigen receptor T cells) are loaded with iron oxide nanoparticles and then focused at a particular site using externally controlled electromagnets. These experimental results serve as a readily scalable prototype for designing an apparatus that patients can wear to focus therapeutic cells at the anatomical sites needed for treatment.

KEYWORDS: CAR T cell, dynamically programmable magnetic field, immunotherapy, iron oxide nanoparticles, macrophage, magnetic transport, neural stem cell

INTRODUCTION

In recent years, there has been an increased interest in cell-based therapies. From regenerative medicine to cancer therapy, cell-based therapies are an expanding part of the therapeutic approach to a number of diseases.1−9 A common theme among this diverse repertoire of cell therapies is the importance of localization. Whether trying to heal an infarct site or treat a brain tumor, the efficacy of the therapy is largely dependent on the ability of the cell product to reach and be retained at a specific anatomical site. Currently, this site-specific localization is generally achieved by a local injection or by relying on cell-intrinsic homing mechanisms.6,10,11 However, these localization strategies are inefficient, and only a portion of the injected cell product is typically retained at the desired tissue site.10,11 Therefore, strategies that exert additional external control over cell localization could improve the efficacy of cell-based therapies.

Magnetic targeting is an emerging strategy for controlling cell localization. This general approach has been used in a number of applications and has been shown to alter cell localization both in vitro and in vivo without affecting cell viability.12−21 For nearly all magnetic targeting studies, cells are loaded ex vivo with superparamagnetic iron oxide nanoparticles (IONPs) to make them responsive to magnetic fields. A number of different IONP formulations have been used for magnetic targeting studies, with no clear consensus on what types of particles are best and few head-to-head comparisons between different formulations.16 Despite this variability in the types of IONPs used, these formulations are typically internalized inside the cells to achieve effective magnetic targeting.

The vast majority of previous studies, including our previous work on IONP-loaded immune cells,17 have employed permanent magnets to direct cell accumulation.13 This approach has clear drawbacks for focusing the accumulation of cells at a position within the body. A primary challenge is that no energetic minima can exist in a volume containing no magnetic elements—this is known as Earnshaw’s theorem.22 Therefore, magnetic material cannot be localized to a fixed position in the body using static external magnets. On the other hand, implanted magnets create minimum-energy wells at the target site but are invasive.

Earnshaw’s theorem, however, only applies to static magnetic fields. Using dynamically changing magnetic fields, energetic minima can be obtained. Thus, work in this area has focused on using electromagnets that can easily create adjustable fields, but these fields are typically weaker due to...
power and cooling requirements. Programmable magnetic resonance imaging (MRI) using open-loop control for fine movement is one approach that has shown proof of principle, although this solution requires a customized MRI instrument and would likely be prohibitively expensive for the multiday timescale expected to be necessary for cell localization in humans. Rapidly pulsing strong electromagnets have also shown promise for targeting nanoparticle accumulation to a focal point in their center. While this work illustrated the potential of this approach, it is uncertain if it could be extended to IONP-loaded cells as rapid magnetic field pulsing is known to cause IONPs to heat their local environment. Indeed, this strategy is being actively pursued for cancer therapy where IONPs are localized to tumors and then a rapidly alternating magnetic field is applied. In addition, given the size of the magnets used in this work, it is difficult to envision how this system could be utilized in a multiday application for human treatment.

Ideally, patients could be equipped with a wearable device that allows for programmable magnetic control over the course of days, and the fields applied would be nontoxic to the loaded cells. Here, we demonstrate an initial prototype of the key component of such a system: a miniaturized, flexible chip that allows for fine control of IONP-loaded cells using dynamically programmable magnetic fields (DPMFs). This prototype has an active area of 16 mm², consisting of a flexible polymer with eight individually controllable wires in both the horizontal and vertical directions overlapping in an electronic mesh grid. Because each wire is individually addressable, this system allows for millions of unique settings from which to generate unique fields and forces. Here, we demonstrate in vitro that this system can control 2D accumulation at resolutions below 300 μm with no toxicity to the cells. The location of accumulation can be switched multiple times. This was demonstrated using three different cell types currently used in cell therapies: neural stem cells (NSCs), monocytes (THP-1), and chimeric antigen receptor (CAR) T cells. To optimally load these cells with IONPs, two different coatings were used: PEGylation (DSPE-IONPs) and silica (Si-IONPs). NSCs and THP-1 cells were loaded with DSPE-IONPs via endocytosis. CAR T cells, however, did not endocytose DSPE-IONPs and were instead loaded with Si-IONPs, which stuck to the cell membrane. While the DPMF prototype is quite small, the device is passively cooled and the design can be directly scaled to larger areas. To the best of our knowledge, this work is the first to demonstrate a miniaturized device capable of rapidly programmable magnetic control of human cell movement.

## RESULTS AND DISCUSSION

We previously developed an apparatus that allows for live cell imaging while a magnetic field is applied and used it to show that when immune cells are loaded with immunostimulatory IONPs, the cells can be accumulated by applying a fixed permanent magnet. Here, we used this system to evaluate our DPMF chip. The cell box apparatus consists of a disposable, 3D printable chassis that fits in a 100 mm Petri dish (Figure 1a). A coverslip is affixed to the central region of the chassis, and the DPMF chip is inserted to be flush against the backside of the coverslip. The assembled apparatus is then placed in a Petri dish containing IONP-loaded cells and cell media. The chassis contains atmosphere distribution channels that allow for atmospheric regulation of the cell media and risers that keep the coverslip suspended just above the bottom of the Petri dish.

The DPMF system is capable of over 1 million unique magnetic profiles within a 16 mm² active area. Controller circuitry that electrically connects to the active area is housed separately. The active area is passively cooled via a copper heat sink behind the active area. The active area is thermally connected to the copper attachment using thermal paste. As a demonstration of the aggregating ability of the system, magnetic particles are moved to two different locations (Figure 1c). The particles (Bangs Laboratories, Indiana, USA) are magnetic microspheres large enough for visibility under microscopy (3 μm). The full video can be seen in Video S1.

Here, two types of surface modification chemistries (PEGylation by intercalation and silica coating) were used to convert hydrophobic oleic acid-coated IONPs to hydrophilic, biocompatible IONPs prior to loading onto cells (Figure 2a). Following purification by centrifugation and washing, successful surface functionalization was confirmed by TEM, DLS, and zeta potential as well as by the particles being readily dispersible in water (Figure 2b,c). The PEGylated particles (DSPE-IONP) showed an increase in hydrodynamic diameter from 30 to 98 nm and a relatively neutral zeta potential of −3.67, both of which are common for PEGylated particles. The Si-IONPs had a hydrodynamic diameter of 160 nm, a zeta potential of −16.56, and a coating visible in TEM images.

To determine what IONP concentrations could be tolerated by cells, each IONP formulation was screened for cell toxicity (Figure 2b). Because this is a proof of principle study focused on the development of DPMF, we were primarily concerned with ensuring that the cells remained intact (e.g., minimal necrosis and cell debris) during the course of the in vitro experiments. Thus, the cells were evaluated for acute toxicity.

Figure 1. (a) Design of cell box apparatus for imaging during DPMF. (b) Sample field profile for aggregating cells to a single point (left) and schema of the active area of the DPMF chip (right). (c) Positive control experiment. Magnetic particles (3 μm in diameter) are used to verify the magnetic aggregation capabilities of the system.
after 1 h of incubation with the IONPs. In general, it was found that doses at or above 45 μg were toxic to cells.

To confirm internalization of the IONPs, cells were incubated with 10 μg of particles and loading was evaluated by TEM imaging (Figure 3a and Figure S1). The Si-IONPs are readily identified by their distinctive fish-egg-like structure with the dark iron core and lighter silica coating (Figure S1A–E). However, the DSPE-IONPs are more challenging to identify as they only possess a dark iron core and transparent polymer coating, so they are most readily identified as dark aggregates of unusual shape (Figure S1F–J). It was found that the NSCs and THP-1 cells readily endocytosed both IONPs (especially DSPE-IONPs), but the CAR T cells did not show any IONP internalization. Surprisingly, despite this lack of IONP internalization, it was found in preliminary experiments that the Si-IONP-loaded CAR T cells were in fact magnetized, demonstrating that the Si-IONPs were associated with the CAR T cells in some way (Video S4). A closer examination of the TEM images consistently showed that Si-IONPs aggregated in close proximity to the cell surface of CAR T cells even after washing steps to remove free particles, possibly suggesting some sort of nonspecific association with the cell surface similar to the observations of Sanz-Ortega et al.9 However, the precise mechanism of Si-IONP association with CAR T cells is not known and will need to be thoroughly investigated before any therapeutic application. For the purposes of this proof of principle study of DPMF, though, we were satisfied with simply obtaining magnetized cells.

Having identified the preferred IONP for loading each cell type, we proceeded to evaluate the ability of our DPMF chip to control the accumulation of the cells. For each cell type, the DPMF chip was initially programmed to target cells at one point (represented by the red dot in the box over the first set of arrows in Figure 4), and then after cells had accumulated at that position, the chip was reprogrammed to target a second location (represented by the red dot in the box over the second set of arrows in Figure 4). Note that video was recorded for the entire duration of movement for each experiment (Videos S2–S4); only an illustrative sample of individual frames is presented in Figure 4. In these videos, it can be seen that the cells immediately change their trajectory when the target location is switched. It is evident from these observations as well as the positive control experiment involving the beads alone that the movement of the loaded cells is due to the magnetic field. To control for other nonmagnetic causes of cell movement, cells alone (no IONP loading) were exposed to the same DPMF focusing conditions. These negative controls showed no coordinated cell movement (data not collected). To serve as further validation, another negative control experiment showing no movement of loaded cells in the absence of a magnetic field is provided for reference (Video S5).

An image processing algorithm was used to track cellular speeds during the DPMF experiments (Figure 5). Due to random variations in spatial distributions of cells, there is a large variation in the number of cells tracked for speed calculations. A total of 120 CAR T cells, 390 THP-1 monocytes, and 230 NSCs were tracked. In general, cellular speed decreases as the cell moves closer to the aggregation point since the magnetic force’s in-plane (i.e., aggregating) component becomes weaker while its normal component becomes stronger. Reduction of speed also occurs because of cellular crowding. Note that there is more speed variability at farther radial distances due to the fact that the cells start from rest. Speeds of up to around 4.7 μm/s were recorded at distances less than a millimeter away. On average, CAR T cells tended to be the fastest, whereas THP-1 cells exhibited the slowest movement. A two-sample unequal variances t-test was employed to establish the statistical significance of the observed differences between the average speeds of different cell types.27,28 Specifically, at a 5% significance level (i.e., p ≤ 0.05), both CAR T cells and NSCs aggregate toward the center at least twice as fast as THP-1 cells do. On the other hand, CAR T cells and NSCs themselves exhibited no statistically significant difference between their average speeds over the entire range of distances for which data was recorded. At or beyond radial distances of 200 μm, however, the fastest CAR T cells were always at least 15% faster than the fastest NSCs (see
Figure 5e, for example). Note that differences in movement speeds among cells of the same type could be related to their hydrodynamic or adherent properties and/or variation in magnetic bead uptake. Overall, it was found that the movement of all three cell types loaded with two different IONP formulations could be readily controlled using the DPMF chip.

**CONCLUSIONS**

We have demonstrated a prototype for DPMF-controlled cell movement. The current system is a miniature programmable electronic grid that can be rapidly reprogrammed in real time. We identified surface coatings for IONPs that facilitated loading of three different cell types used in cell therapies: stem cells (NSCs), macrophages (THP-1), and CAR T cells. All of the loaded cells were readily controlled using the DPMF system, and this was visualized using our custom-designed apparatus. While the current prototype is quite small and would not be used for human applications, the design can be directly scaled to larger formats to cover a sufficient therapeutic area. In addition, we recognize that the forces exerted by the prototype are much too small to be effective in humans. However, the strength of the system could be dramatically boosted in future iterations by incorporating magnetizable materials that amplify the power of the programmable elements. The ability of DPMF to direct cell accumulation to a single focal point combined with its ability to rapidly change focal points make DPMF a good candidate for targeting cell therapies to specific disease locations inside patients. In addition to creating a true aggregation point, DPMF may allow for control of delivery paths throughout the body by adjusting fields to route particles along a desired trajectory.

**MATERIALS AND METHODS**

**Instrumentation.** Dynamic light scattering (DLS) and zeta potential (ZP) measurements were performed on a Brookhaven 90Plus/Bi-MAS instrument (Brookhaven Instruments, New York). DLS measurements were obtained by performing five runs at 30 s per run, and the ZP values were obtained by measuring 10 runs involving 20 cycles per run. All nanoparticle solutions were filtered through a 0.45 μm cellulose filter prior to performing DLS and ZP measurements.

Transmission electron microscopy (TEM) images were obtained with an FEI Tecnai T12 transmission electron microscope at an
accelerating voltage of 120 keV, and images were taken with a Gatan UltraScan 2K CCD camera. NPs dispersed in water at an optimal concentration were drop cast onto glow-discharged, 300 mesh carbon/formvar-coated grids and allowed to dry before imaging.

Materials. All organic and inorganic compounds (except PEG compounds) were purchased from Sigma-Aldrich. 1,2-Distearoyl-sn-glycero-3-phosphoethanolamine-N-[methoxy(polyethylene glycol)-2000] (ammonium salt) (DSPE-PEG2000) was purchased from Avanti Polar Lipids, Inc. (catalog #880120P). Superparamagnetic iron oxide nanoparticles suspended in chloroform (d = 30 nm, catalog #SOR-30-50) were purchased from Ocean Nanotech, Springdale, AR, USA.

Cell Culture. All cells were cultured and maintained at 37 °C in a humidified incubator (Thermo Electron Corporation, CA, USA) containing 5% CO₂. Neural stem cells were cultured in Dulbecco’s modified Eagle’s medium (DMEM; Invitrogen, CA, USA) supplemented with 10% fetal bovine serum (Gemini Bio, CA, USA), 1% L-glutamine (Invitrogen), and 1% penicillin–streptomycin (Invitrogen). When the cells reached 80% confluency, they were passaged using a 0.25% trypsin/ethylenediaminetetraacetic acid solution (Invitrogen); media were changed every 2–3 days. THP-1 cells were cultured in RPMI 1640 medium (ATCC, USA) supplemented with 50 μM β-mercaptoethanol, 10% fetal bovine serum (Gemini Bio, CA, USA), 1% L-glutamine (Invitrogen), and 1% penicillin–streptomycin (Invitrogen). THP-1 cell cultures were maintained at 2 × 10⁵ to 8 × 10⁶ viable cells/mL density by the addition of fresh medium or replacement of medium. CAR T cells were obtained from Christine Brown (City of Hope, CA). Briefly, central memory subsets of CD3 T cells were enriched and then transduced by lentivirus with an interleukin-13 (E13Y-mutated) ligand-based CAR, containing a 4-1BB costimulatory domain (IL13BBζ) and truncated CD19 (CD19t) as a marker for transduction efficiency. CAR T cells were cultured in X-VIVO 15 medium supplemented with 10% fetal bovine serum (Gemini Bio, CA, USA). Cytokines IL2 and IL15 were added into the cell culture three times a week.

Figure 4. Magnetic movement of fluorescent cells controlled by DPMF. Each cell type is localized to an initial position and then traversed to a secondary position. The localization positions are roughly indicated by the red dots. The final position of aggregation was deliberately changed during each experiment to showcase aggregation flexibility. (a) Magnetic movement of NSCs loaded with 0.5 μg of DSPE-IONPs. (b) Magnetic movement of THP-1 cells loaded with 0.5 μg of DSPE-IONPs. (c) Magnetic movement of CAR T cells loaded with 30 μg of Si-IONPs. The cells are made fluorescent in the green channel by staining with CellTrace CFSE dye. The numbers in the top left corner of each image are the time stamp for that frame (mm:ss). To view the full original videos, see Videos S2–S4, respectively.
Synthesis of DSPE-PEG-Coated Iron Oxide Nanoparticles (IONPs). In a 20 mL scintillation vial, 1 mg of IONPs (40 μL, 25 mg/mL Fe) suspended in chloroform was added into 200 μL of chloroform followed by the addition of an excess of DSPE-PEG2000 (DSPE/IONP = 30:1 by weight) in 800 μL of chloroform. While the mixture was being stirred at room temperature, DMSO (4 mL) was added into the chloroform slowly, and subsequently, the mixture was shaken on a nutator for another 30 min. After the chloroform was removed by reduced pressure, Milli-Q water (16 mL) was added to the DMSO mixture dropwise to disperse the DSPE-PEG-coated IONPs. The DSPE-IONPs were washed with Milli-Q water three times by centrifugation using a spin filter with a molecular weight cutoff of 100 kDa (3000 rpm, 1 min) and stored in Milli-Q water at 4°C.

Synthesis of Silica-Coated Iron Oxide Nanoparticles (Si-IONPs). The preparation of silica-coated IONPs was adapted from the method reported previously by Lu et al.29 In a 25 mL round-bottom flask, 1 mg of IONPs (40 μL, 25 mg/mL Fe) suspended in chloroform was added into a mixture containing 7.7 mL of cyclohexane, 2 mL of Triton X-100, 1.6 mL of hexanol, and 0.34 mL of Milli-Q water. The reaction mixture was stirred vigorously at room temperature for 5 min, and subsequently, tetraethyl orthosilicate (TEOS, 40 μL) was added. The microemulsion system was further stirred at room temperature for 5 h before ammonium hydroxide (100 μL) was added to initiate the TEOS hydrolysis reaction. After stirring the reaction at room temperature for 24 h, the entire mixture was transferred to a 50 mL conical tube before being quenched with absolute ethanol (40 mL). The Si-IONPs were collected by centrifugation (4000 rpm, 20 min) and washed three times with absolute ethanol with vortexing and sonication in between washes to help the NPs disperse back into solution.

Sample Preparation for Transmission Electron Microscopy (TEM). Transmission electron microscopy (TEM) was performed on an FEI Tecnai 12 transmission electron microscope equipped with a Gatan UltraScan 2K CCD camera. Cells labeled with DSPE-IONPs or Si-IONPs (as described above) were collected by centrifugation and washed once with PBS (500 g, 4 min). Cell pellets were then resuspended in fixative (2% glutaraldehyde in 0.1 M cacodylate buffer (Na(CH3)2AsO2·3H2O), pH 7.2, at 4°C) overnight. The following day, the cell pellets were washed three times with 0.1 M cacodylate buffer for 30 min, and washed three times with 0.1 M cacodylate buffer. The samples were then dehydrated stepwise via solvent exchange with 60, 70, 80, and 95% ethanol, 100% absolute ethanol (twice), and propylene oxide (twice); they were then left in propylene oxide/Eponate (1:1) overnight at room temperature in a sealed environment. The following day, the vials were left opened at room temperature (~2 to 3 h) to allow the propylene oxide to evaporate. The samples were then embedded in 100% Eponate with polymerization at ~64°C for 48 h. Ultrathin cell-containing sections (~70 nm thick) were cut using a Leica Ultracut UCT ultramicrotome with a diamond knife and picked up on 200 mesh copper EM grids.

Figure 5. Cell tracking during DPMF. (a–c) Cell trajectory contours (yellow lines) overlaid on a snapshot of the videos for (a) NSCs loaded with 0.5 μg of DSPE-IONPs, (b) THP-1 cells loaded with 0.5 μg of DSPE-IONPs, and (c) CAR T cells loaded with 30 μg of Si-IONPs. The cells identified by the tracking algorithm are circled, where brighter colored circles indicate more clearly identified cells. To ensure a low false positive rate for the tracking algorithm, not all cells in the video were successfully identified by the algorithm. (d) Average speeds of the tracked cells within a set of radial distance intervals (~±10 μm of the axis labels). The error bars represent 95% confidence intervals for the average speeds. (The error bars for the THP-1 cells are barely noticeable.) (e) Distribution of speeds at a radial distance of 450 μm. Note that the speed-axis labels represent the upper limits of the bins.
The cell box assembly was previously described by White et al. Briefly, a large coverslip was attached onto the opening of a sterilized cell box using a noncytotoxic silicone-based adhesive (Sibione Med Adhesive 4100 RTV, Factor II, catalog #A-4100). The adhesive was allowed to cure for 48 h at room temperature in a sterile environment (BS Level II hood). On the day of the cell box-induced cell movement experiments, cells (1 × 10⁶ cells) were cultured as described above and labeled with DSPE-IONPs (0.5 μg of Fe per 1 × 10⁶ NSCs or THP-1 cells) or Si-IONPs (30 μg per 1 × 10⁶ CAR T cells) for 1 h at 37 °C. The cells were also fluorescently labeled with CellTrace CFSE (per the manufacturer’s instructions). After exposure to the IONPs, the cells were washed once with PBS to remove unbound NPs before they were resuspended in full RPMI 1640 medium (10 mL) and transferred to a Petri dish with a diameter of 100 mm. The box-coverslip assembly was inverted and submerged into the Petri dish containing IONP-labeled cells in media. The experimental setup was enclosed in a glass chamber with a regulated CO₂ level (5%). Live cell imaging was performed on a Zeiss Axio Observer Z1 inverted microscope with the Pecon/Zeiss incubation system. The camera and microscope were controlled by the ZEN Blue software. A bright-field picture was taken to indicate the initial location of the cells in solution under the view of the microscope after the cell box was set up on the microscope. The electric current in the wires in the magnetic grid was switched on to generate a magnetic field. Simultaneously, a video in the bright-field channel was started to record the movement of the IONP-labeled cells in media under the cell box.

Dynamically Programmable Magnetic Field (DPMF) Device. The DPMF apparatus (Figure 6) comprises three components: a controller, inverted microscope, and cell box. The controller is interfaced through a computer. The first system is a controller used to generate a particular magnetic field profile. The controller consists of a computer interface to a custom printed circuit board (PCB) constructed using a standard FR4 two-layer board. The PCB simultaneously controls eight electromagnetic channels, each with a 16-bit current resolution and reversible polarity. A DAQ digital-to-analog converter (National Instruments, USA) is used to program voltage biases to the controller. Using a custom-developed software package, commands are input through the computer interface to dynamically program between various magnetic field profiles. The current setting is first regulated using a digital-to-analog converter. The analog signal is then buffered to a current source with a maximum swing of ±2 A, implemented using an integrated circuit operational amplifier connected in a feedback configuration via a p-type metal oxide semiconductor transistor to a resistive load. The DPMF array features 300 μm traces at a pitch of 300 μm.

Next, the controller system interfaces with the second system, a cell box. The cell box design was previously described. The disposable cell box was printed using a Replicator 2 3D printer (Makerbot, USA) and is meant to interface the DPMF device with the microscope to enable live cell imaging of cell movement. To promote cell viability, it features an inlet port and distribution channels that interface with the microscope’s incubation system to evenly distribute humidified CO₂ atmosphere in the Petri dish. A pressure relief port prevents the accumulation of pressure and ensures a continuous flow of atmosphere. To reduce heating of the active area, a copper heat sink was placed on the current grid. A thin (25.4 mm × 25.4 mm × 0.1 mm) diamond sliver, along with thermal paste, was placed between the heat sink and the current grid to help distribute heat to the heat sink.

Cell Speed Tracking. To track the cells and analyze their trajectories quantitatively, the videos demonstrating cell aggregation were analyzed using the TrackMate plug-in for the image processing program ImageJ (Figure 5a–c). The speeds of the cells were then calculated for each cell type (Figure 5d,e). A number of cells started from rest, as indicated by some of the slower speed data points far away from the aggregation center. Due to crowding near the aggregation center, many cells stopped moving near 50 μm and were no longer successfully tracked at distances less than 50 μm.
The authors declare no competing financial interest.

**AUTHOR INFORMATION**

**Supporting Information**
The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acsabm.0c00226.

- **Figure S1** Additional TEM images of loaded cells (PDF)
- **Video S1** Video showing the positive control for movement of magnetic particles (MOV)
- **Video S2** Video showing aggregation of neuronal stem cells (AVI)
- **Video S3** Video showing aggregation of THP-1 monocytes (AVI)
- **Video S4** Video showing aggregation of CAR T cells (AVI)
- **Video S5** Video showing the negative control for nonmagnetic movement of cells related to the experimental setup using loaded CAR T cells (AVI)

**ASSOCIATED CONTENT**

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**Notes**

The authors declare no competing financial interest.

**ACKNOWLEDGMENTS**

We gratefully acknowledge Marcia Miller, Zhuo Li, and Ricardo Zerda for electron microscopy performed in the EM core facility and Brian Armstrong, Loren Quintanar, and Tina Patel for their assistance with fluorescence imaging performed in the Light Microscopy and Digital Imaging Core. Research reported in this publication included work performed in the Electron Microscopy and the Light Microscopy and Digital Imaging Cores supported by the National Cancer Institute of the National Institutes of Health under award number P30CA033572. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health. The authors would like to thank R01CA155769, R21CA189223, R21 NS081594, NIH grant S1013.914960.6692, The Kenneth T. and Eileen L. Norris Foundation, and STOP Cancer for research funding.

**REFERENCES**


https://doi.org/10.1021/acsabm.0c00226


Welch, B. L. The Generalization of 'Student’s’ Problem When Several Different Population Variances Are Involved. *Biometrika* 1947, 34, 28−35.


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**NOTE ADDED AFTER ASAP PUBLICATION**

This paper was published ASAP on July 7, 2020, with an incorrect term in the Abstract. The corrected version was posted on July 8, 2020.