BIOGRAPHICAL SKETCH

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NAME: James A Ankrum

eRA COMMONS USER NAME (credential, e.g., agency login): JANKRUM

POSITION TITLE: Assistant Professor of Biomedical Engineering

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Iowa, Iowa City, IA	BSE	05/2007	Biomedical Engineering
Cambridge University, Cambridge, England	MPhil	11/2008	Engineering Design
Massachusetts Institute of Technology, Cambridge, MA	PhD	09/2013	Medical Engineering & Medical Physics
University of Minnesota, Minneapolis, MN	Post-doc	08/2014	Medical Innovation

A. Personal Statement

I am an Assistant Professor in Biomedical Engineering and lead a lab housed in the Diabetes Research Center and Pappajohn Biomedical Institute. My lab utilizes biomaterials and drug delivery strategies to influence the fate and function of cells both in vitro and in vivo. My long-term goal is to engineer enhanced cell-based and -inspired therapeutics to restore function to diseased and damaged tissues. I have a broad background in biomedical engineering and specific expertise in engineered mesenchymal stem cell-based therapies, drug delivery, and nanoparticle and microparticle design. In vivo tracking and development of novel contrast agents have been a long time interest in of mine, and the area in which my group interacts most with colleagues in imaging. While my lab is just 3 years old, I am firmly committed to mentoring and student training. My lab is composed entirely of trainees ranging from undergraduate to PhD candidates. My lab has already graduated 3 Masters students. Finally, three PhD candidates in Biomedical Engineering form the core of my group. I currently recruit students from the Biomedical Engineering Graduate Training Program and the Medical Scientist Training Program.

B. Positions and Honors

Positions

Jan. 2005 – Sept. 2007	Research Assistant, University of Iowa, Iowa City, IA
May 2006 – Aug. 2006	Corporate Intern, Caterpillar Inc., Peoria, IL
Oct. 2007 – July 2008	Research Assistant, Cambridge University, Cambridge, UK
Feb. 2009 – Aug. 2013	Research Assistant, Harvard Medical School (Brigham & Women's Hospital), Cambridge, MA
Aug. 2013 – Aug. 2014	Senior Innovation Fellow, Medical Devices Center, University of Minnesota, Minneapolis, MN
Aug. 2014 – Present	Assistant Professor, Diabetes Research Center, University of Iowa, Iowa City, IA

Other Experience

2016, NIDDK DiaComp Pilot and Feasibility Grant Reviewer
2016, NIDDK SBIR Review Panel: Development of New Technologies and Bioengineering Solutions for the Advancement of Cell Replacement Therapies for Type 1 Diabetes (R43/R44)

Professional Memberships
American Society of Gene and Cell Therapy
Society for Biomaterials, member of membership committee and *ad hoc* public relations committee
Biomedical Engineering Society
AABB
TERMIS

Honors & Awards
Excellence in Engineering Scholarship, University of Iowa 2003-2007
President's List, University of Iowa, 2003-2007
Dean's List, University of Iowa, 2003-2007
Paul D. Scholz Memorial Scholarship, University of Iowa, 2005
Barry Goldwater Scholarship, 2005
Rhodes Dunlap Collegiate Scholarship, University of Iowa, 2006
Distinguished Poster Award, Spring Undergraduate Research Forum, 2006
Collegiate Scholar Award, University of Iowa, 2007
Hancher-Finkbine Medallion, University of Iowa, 2007
Winston Churchill Scholarship, Cambridge University, 2007
Honorary Cambridge Overseas Trust Scholar, Cambridge University, 2007
National Science Foundation Graduate Research Fellowship, 2008-2011
Presidential Fellowship, MIT, 2008
Health Sciences & Technology Medical Engineering Fellowship, MIT, 2008
Lindau Nobel Laureate Participant, 2011
MIT 100K Elevator Pitch Semifinalist, 2011
Hugh Hampton Young Memorial Fellowship, MIT, 2011 & 2012
3 Articles highlighted for special significance to the field in F1000 Prime 2012, 2012, 2014
NIH Single Cell Analysis Program 'Follow that Cell' Phase I finalist, 2015
University of Iowa Research Foundation 'Inventor Award', 2015
Old Gold Faculty Development Fellowship, 2017
Plenary Speaker, International Meeting of the Portuguese Society for Stem Cells and Cell Therapies, 2017
National Blood Foundation Scholar, 2017

C. Contribution to Science

1. **Elucidating the impact of cryopreservation on MSC's in vivo function in the setting of Ischemia/Reperfusion injury.**
   In my lab at the University of Iowa my group has focused on identifying and overcoming challenges that currently limit the translation of MSC-based therapies. The impact of cryopreservation on MSC function has been a controversial topic in recent years with some groups claiming cryopreserved MSCs lose function. However, these claims were based largely on *in vitro* functional assays alone. We sought to address the question of whether cryopreservation negatively impacts MSC function in the context of a specific disease setting, ischemia/reperfusion injury to the eye. We found that cryopreserved MSC's displayed an insignificant decline in immunosuppressive function and growth factor secretion in *in vitro* assays, but performed equally as well as fresh MSC when transplanted into the eyes of mice hours after a pressure induced ischemia/reperfusion injury had been initiated[a]. We subsequently found that an attractive strategy to boost MSC function in culture via cytokine conditioning, did not translate *in vivo*, as xenogenic cytokine licensed MSCs lost over 50% of their ability to rescue retinal damage compared to naïve MSCs likely due to an increase in immunogenicity[b]. These two pieces of work both highlight the need to develop MSC therapy in the context of specific disease indications as well as the need to account for immunogenicity in non-autologous MSC therapies.
   a. Gramlich OW, Burand AJ, Brown AJ, Deutsch RJ, Kuehn MH, **Ankrum JA**. Cryopreserved Mesenchymal Stromal Cells Maintain Potency in a Retinal Ischemia/Reperfusion Injury Model: Toward an off-the-shelf Therapy. **Sci Rep**. 2016 May 23;6:26463. doi: 10.1038/srep26463.

b. Burand AJ, Gramlich OW, Brown AJ, **Ankrum JA**. Function of Cryopreserved Mesenchymal Stromal Cells With and Without Interferon-γ Prelicensing is Context Dependent. ***Stem Cell.*** 2016 Oct 19. doi:10.1002/stem.2528

2. Developed a platform technology to control and track MSC fate and function.
I have developed a platform technology to influence the phenotype of transplanted cells through intracellular agent loaded biodegradable microparticles. The biodegradable particles can be customized to release a broad range of agents, ranging from small molecule drugs to contrast agents. Cells modified with the particles show no difference in viability, differentiation potential, proliferation, or *in vivo* homing or survival. MSCs are able to carry the intracellular particles, and thus the drug delivery to the cell continues no matter where the cell goes *in vitro* or *in vivo*. Using this platform we can target delivery of phenotype altering drugs on the single cell level and have used the platform to induce differentiation of MSCs[a], enhance MSC immunosuppressive potential[b], and track the location of MSCs by MRI[c]. By delivering agents intracellularly, off-target systemic side effects are minimized. Recently, we demonstrated the technology can also be used to engineer pancreatic beta cells and immune cells[d].

a. *Sarkar D, ***Ankrum JA**, Teo GS, Carman CV, Karp JM. *Cellular and extracellular programming of cell fate through engineered intracrine-, paracrine-, and endocrine-like mechanisms*. Biomaterials. 2011 Apr;32(11):3053-61. doi: 10.1016/j.biomaterials.2010.12.036. PMID: 21262537, PMCID: PMC3043463 *Co-first authors
b. **Ankrum JA**, Dastidar RG, Ong JF, Levy O, Karp JM. *Performance-enhanced mesenchymal stem cells via intracellular delivery of steroids*. Sci Rep. 2014 Apr 10;4:4645. doi: 10.1038/srep04645. PubMed PMID: 24717973; PubMed Central PMCID: PMC3982175.
c. Xu C, Miranda-Nieves D, **Ankrum JA**, Matthiesen ME, Phillips JA, Roes I, Wojtkiewicz GR, Juneja V, Kultima JR, Zhao W, Vemula PK, Lin CP, Nahrendorf M, Karp JM. *Tracking mesenchymal stem cells with iron oxide nanoparticle loaded poly(lactide-co-glycolide) microparticles*. Nano Lett. 2012 Aug 8;12(8):4131-9. doi: 10.1021/nl301658q. PMID: 22769232
d. **Ankrum JA**, Miranda OR, Ng KS, Sarkar D, Xu C, Karp JM. *Engineering cells with intracellular agent-loaded microparticles to control cell phenotype*. Nat Protoc. 2014 Feb;9(2):233-45. doi: 10.1038/nprot.2014.002. Epub 2014 Jan 9. PubMed PMID: 24407352.

3. **Invented a single cell analysis tool to enable serial identification of unique single cells**.
My team at the University of Iowa is developing an intracellular fluorescent barcode that enables the serial identification of unique single cells within multi-cellular environments. The technology builds on our expertise delivering bioactive agents to the cytoplasm of cells through biodegradable particles and was inspired by the NIH Follow that Cell challenge. The technology was awarded a Phase 1 prize by the NIH Single Cell Analysis Program and is continuing to be refined to allow for rapid, reliable, and high throughput identification of single cells. This technology is transformative, as it allows for unique individual cells to be studied and monitored through time and space, enabling prospective studies at the single cell level. We have a full patent application currently under review[a] for the technology and are currently in talks for a licensing agreement to commercialize the technology in a kit.

a. **Ankrum J**, Burand AJ. *Cellular Barcode* US Patent App. 15/068,106, published March 11, 2016. Patent Pending

4. **Highlighted challenges to MSC translation and elucidated novel mechanisms of MSC engraftment**. MSC therapy has tremendous potential as a therapeutic due to both the cells differentiation potential and secretion of factors that are angiogenic, anti-apoptotic, and anti-inflammatory. However, many questions remain regarding the mechanism of action of MSCs for specific conditions, the ideal route of administration, and even the source and identity of the cells. I have authored several perspective pieces on the current state of MSC therapy and outstanding challenges that remain that have helped shape the direction and conversation around MSC therapy. In my first perspectives, I helped shift the focus of MSC therapy's mechanism from MSC differentiation and integration to a focus on MSC's trophic effects. MSCs short in vivo survival, yet profound impacts, highlight the fact that MSC function is not mediated via replacement of damaged tissue, but through MSCs instructing the host tissue to regenerate and suppress

inflammation[a]. My second perspective I co-authored focused on using non-invasive imaging modalities and nanoparticles to track the location and function of MSCs post-transplantation[b]. In my third perspective, I challenged the long-standing dogma in the field, that MSCs are immune privileged, and through a meta-analysis showed MSCs are not innately immune privileged, but their immunosuppressive phenotype makes them immune evasive[c]. Thus, any breakdown in their immunosuppressive phenotype or increase in immunogenicity allows allogeneic MSCs to be detected as foreign and cleared. These reports have been well received by leaders in the community and highly cited, noticeably changing the way MSCs are discussed. Finally, I have also helped elucidate the mechanism of MSCs extravasation from the vasculature after intravenous infusion[d]. Similar to leukocytes, MSCs can migrate between as well as directly through endothelial cells, however the mechanism is distinct from that used by leukocytes. Through this investigation we found the efficiency of MSCs to cross endothelial barriers was relatively poor compared to leukocytes, and MSCs predominately pass through inflamed endothelium, helping to explain MSCs' tropism for sites of inflammation.

a. **Ankrum JA**, Karp JM. *Mesenchymal stem cell therapy: Two steps forward, one step back*. Trends Mol Med. 2010 May;16(5):203-9. doi: 10.1016/j.molmed.2010.02.005. PMID: 20335067, PMCID: PMC2881950
b. Xu C, Mu L, Roes I, Miranda-Nieves D, Nahrendorf M, **Ankrum JA**, Zhao W, Karp JM. *Nanoparticle-based monitoring of cell therapy*. Nanotechnology. 2011 Dec 9;22(49):494001. doi: 10.1088/0957-4484/22/49/494001. PMID: 22101191, PMCID: PMC3334527
c. **Ankrum JA**, Ong JF, Karp JM. *Mesenchymal stem cells: immune evasive, not immune privileged*. Nat Biotechnol. 2014 Mar;32(3):252-60. doi: 10.1038/nbt.2816. Epub 2014 Feb 23. PubMed PMID: 24561556.
d. Teo GS, **Ankrum JA**, Martinelli R, Boetto SE, Simms K, Sciuto TE, Dvorak AM, Karp JM, Carman CV. *Mesenchymal stem cells transmigrate between and directly through tumor necrosis factor-α-activated endothelial cells via both leukocyte-like and novel mechanisms*. Stem Cells. 2012 Nov;30(11):2472-86. doi: 10.1002/stem.1198. PMID: 22887987, PMCID: PMC3479371

5. Improved therapies for wounds.

Wound closure has long relied on crude mechanical devices, such as sutures and staples, and chemical adhesives, such as Dermabond, both of which cause significant collateral damage to healthy tissue where they are applied. Thus, we sought to create a biomimetic solution to wound closure that could securely attach to tissue with minimal damage. To this end, we investigated and replicated the microtopography of the North American Porcupine Quill. We found that microscopic barbs on the tip of each quill enabled quills to penetrate tissue with 4-5X less force compared to barbless quills. In addition, penetration of just 2-4mm deep into tissue was able to generate significant adhesion due to tissue fibers hooking onto the barbs. These properties were reproduced in a synthetic bio-inspired system and prototype devices for hernia mesh fixation were produced[a]. This work was featured on the cover of PNAS and in media stories on Science Now, Nature, Nature Medicine, NPR, Discovery, Popular Mechanics, The Smithsonian, BBC, and the MIT homepage. A pending patent[b] arising from this work has been licensed by the French start-up, Gecko Biomedical, which has raised over 30 million Euro to develop bioinspired medical adhesives.

b. Cho W, **Ankrum J**, Guo D, Chester S, Kashyap A, Campbell G, Rijal R, Wood R, Karnik R, Langer R, Karp J. *Microstructured Barbs on the North American Porcupine Quill Enable Easy Tissue Penetration and Difficult Removal*. Proceedings of the National Academy of Sciences (2012), 109(52), 21289-21294.
c. Karp J, Cho W, Laulicht, B, **Ankrum J**, Karnik R, Langer R. *Deployable Barbed Microneedle Array and Uses Thereof*. International Publication Number WO 2012/100002, filed 18 January 2012. Patent Pending.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/james.ankrum.1/bibliography/43172139/public/

D. Research Support

Ongoing Research Support

Title: *Generation of a Novel Pharmacological Approach to Increase Adipose Tissue Thermogenesis*
Pappajohn Biomedical Institute Convergence Grant Role: Co-PI Nov 2016-Nov 2018
Objective: To target delivery of mitochondrial uncoupling agents directly to adipose tissue to combat obesity.

Title: *The functional role of microenvironmental cross-talk in mesenchymal stromal cell mediated diabetic wound healing.*
Diabetes Action Research and Education Foundation Role: PI Jan 2017-Jan 2018
Objective: To determine if secreted products harvested from MSCs are sufficient to promote diabetic wound healing or if in vivo activation of MSC's is required to initiate production of therapeutic factors.

Title: *Elucidating disease specific mechanisms of mesenchymal stem cell mediated polarization of macrophages from diabetic and healthy donors to an anti-inflammatory M2 phenotype*
BD Biosciences Immunology Grant Role: PI March 2015-June 2018
Supplemental resource grant that provides antibodies and ELISA assays from BD biosciences. Preliminary data was gathered using resources obtained from this grant.

Faculty Start-up Grant
University of Iowa Fraternal Order of Eagles Diabetes Research Center Aug 2014-Present
Unrestricted funds to set-up laboratory and hire staff.

Completed Research Support
Title: *Development of a Human White Fat Biomimetic*
UI OVPRED Internal Funding Initiative Role: Co-I March 2016-June 2017
Objective: To develop and characterize an in vitro model of obesity using 3D culture of primary adipocytes.

Title: *Development of a self-destructing cellular barcode for single-cell analysis*
UIVentures Gap Funding Role: PI Oct 2015 - Dec 2016
Objective: Development of an intracellular fluorescent barcode to uniquely identify individual cells in a multi-cellular environment.

Title: *Development of an off-the-shelf injectable MSC Microcarrier for Diabetic Wound Healing*
NIDDK DiaComp Pilot and Feasibility Grant Role: PI Sept 2015 – Dec 2016
Objective: Evaluation of the ability to maintain MSC potency through cryopreservation and enhance cell retention at the site of the wound through cell encapsulation on injectable microcarriers.

Title: *Elucidating the role of FOXO3 in restoring the potency of in vitro expanded Mesenchymal Stem Cells*
National Blood Foundation Grant Role: PI June 2015 – Dec 2016
Objective: Determine the role of FOXO3 in controlling the expression of IDO in MSCs to correct donor variability and enhance MSC's anti-inflammatory potency.