Department of Epidemiology Travel Award Application Winter 2022 – Ze Zhang

Total Amount Requested: $1,000
Destination: Cedars-Sinai Medical Center**,** Los Angeles, CA
Purpose of Travel: Poster presentation at Cell Symposium: Advances in Therapeutic Applications of Stem Cells (CSTE) 2022
Dates of Trip: December 7th, 2022 – December 11th, 2022

My abstract titled "DNA methylation traces human embryonic stem cell lineage revealing the landscape of fetal cell origin in aging, normal, and diseased tissues" was accepted for a poster presentation at CSTE 2022. This project led by Drs. Salas and Christensen at the Department of Epidemiology and Center for Molecular Epidemiology developed a novel DNA methylation biomarker to trace cells that are of fetal origin – the FCO signature[1]. I led projects that investigated the FCO signature in cancer tissues and kidney that resulted in two publications[2,3]. We also have an ongoing project to investigate FCO in Down syndrome patients. I am particularly excited to present and promote our work on FCO to the stem cell research community because our observations demonstrated potential applications of FCO in stem cell therapeutics research, developmental toxicology, and clinical trials. Attending CSTE 2022 will give me the opportunity to communicate our work of FCO with top researchers in the field of stem cell therapeutics and I will seek research collaboration opportunities between the Center for Molecular Epidemiology at Dartmouth and other stem cell research laboratories. Furthermore, I look forward to improving myself as an early stage researcher on research presentation, scientific communication, and scientific thinking by attending large conferences like CSTE.

References

1 Salas, L. A. *et al.* Tracing human stem cell lineage during development using DNA methylation. *Genome Res* **28**, 1285-1295, doi:10.1101/gr.233213.117 (2018).

2 Wiencke, J. K. *et al.* Identification of a foetal epigenetic compartment in adult human kidney. *Epigenetics*, 1-21, doi:10.1080/15592294.2021.1900027 (2021).

3 Zhang, Z. *et al.* Absence of an embryonic stem cell DNA methylation signature in human cancer. *BMC Cancer* **19**, 711, doi:10.1186/s12885-019-5932-6 (2019).

Ze Zhang 2022 CSTE in-person meeting December 7th-11th in Los Angeles, California estimated itemized budget

1. IKCS meeting registration fee: $520;

2. Round-trip flight tickets: $500;

3. Round-trip Dartmouth coach tickets to airport: $62;

4. Hotel room from December 7th-11th: $1392;

5. Estimated other expenses, e.g. Uber, Food $200

Total: $2674

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AT DARTMOUTH

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November 15th, 2022,

Margaret Karagas, Ph.D.
Chair
Department of Epidemiology

Dear Dr. Karagas,

I am pleased to nominate my Ph.D. student, Ze Zhang, to apply for the **Department of Epidemiology Travel Award in Winter 2022**. Ze is a Ph.D. candidate in the Quantitative Biomedical Science program at Geisel who works diligently on cancer epigenetics, epidemiology, and bioinformatics projects. His work on using DNA methylation to trace human embryonic stem cell lineage in aging, normal, and diseased tissues has been accepted for a poster presentation at the Cell Symposium: Advances in Therapeutic Applications of Stem Cells 2022 (CSTE) meeting in December in Los Angeles, CA.

Ze's poster entitled "DNA methylation traces human embryonic stem cell lineage revealing the landscape of fetal cell origin in aging, normal, and diseased tissues" has been scheduled for presentation in the Poster Session at the CSTE 2022 (See attachment below). Ze's work on the understanding of the fetal cell origin (FCO) DNA methylation signature in early aging, depletion in carcinogenesis, prognosis in kidney cancer, underdevelopment in children with Down's syndrome, and fibroblast to iPSC reprogramming promises future investigations and applications of FCO in stem cell therapeutics research, developmental toxicology, and clinical trials. Thus, I enthusiastically recommend Ze for this travel award opportunity. Please do not hesitate to contact me if additional information is required.

Sincerely,

Lucas A Salas, MD MPH PhD

GEISEL SCHOOL OF MEDICINE
AT DARTMOUTH

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Attachment.

Letter of acceptance (CSTE, 2022)

Dear Ze Zhang,

Your submission 75 titled 'DNA methylation traces human embryonic stem cell lineage revealing the landscape of fetal cell origin in aging, normal, and diseased tissues' is part of the **Poster programme** for **Cell Symposia: Advances in Therapeutic Applications of Stem Cells**. The programme is now completely finalised, and all presentations have been allocated a new reference number to enable a sequential system at the symposium.

Your new reference number is **P1.25.**
Note, this number will be used in the poster programme and in all documentation at the symposium.

Poster presentation
The timings of your poster presentation are as follows:
Day: Friday, 9th December 2022
Session: Poster session 1
Session time: 14:00 to 15:30
Pin up time: 08:30
Take down time: 16:30
Room : NTC

DNA methylation traces human embryonic stem cell lineage revealing the landscape of fetal cell origin in aging, normal, and diseased tissues

Ze Zhang, John K. Wiencke, Karl T. Kelsey, Devin C. Koestler, Brock C. Christensen, Lucas A. Salas

Background: DNA methylation is essential to lineage specification in human cell development and maturation. In early development, differentiated cells that arise from embryonic stem cells retain DNA methylation features that provide a memory trace of their fetal cell origin (FCO). We developed a DNA methylation signature that traces the embryonic stem cell lineage and allows one to estimate the proportion of cells of a fetal origin, in a mixture of cell types.

Methods: The FCO signature was developed based on differentially methylated CpGs between fetal and adult blood leukocytes across six lineages (granulocytes, monocytes, B lymphocytes, CD4+ T lymphocytes, CD8+ T lymphocytes, and natural killer lymphocytes). The FCO signal was profiled in multiple fetal and adult stem and progenitor cells and the association between FCO and age was investigated in multiple tissues. The FCO proportion was also estimated in normal and diseased tissues, including solid cancer and blood of Down syndrome. Finally, the FCO was projected through fibroblast to iPSC reprogramming.

Results: The cell fraction displaying the FCO signature depended upon the developmental stage (fetal versus adult) as it described a dynamic transition during the first 5 yr of life. Fetal and adult stem/progenitor cells demonstrated a significant difference in FCO. Across 19 normal tissue types, the kidney contained the highest FCO proportions. A consistent decrease in the FCO proportion was observed in cancerous tissues when compared to their corresponding normal tissues. Also, a higher level of FCO was significantly associated with better survival in kidney cancer patients. The blood FCO level was significantly lower in Down syndrome children compared to healthy children during the first 5 years of life. The FCO tracked with fibroblast to iPSC reprogramming (0 to 100%).

Conclusion: We developed a DNA methylation biomarker to trace cells of embryonic stem cell origin. The observations of FCO's association with early aging, depletion in carcinogenesis, prognosis in kidney cancer, underdevelopment in Down syndrome children, and fibroblast to iPSC reprogramming promise future investigations and applications of FCO in stem cell therapeutics research, developmental toxicology, and clinical trials.