

**BIOGRAPHICAL SKETCH**

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NAME: Salas Diaz, Lucas A

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

ORCID iD: <http://orcid.org/0000-0002-2279-4097>

POSITION TITLE: Assistant Professor

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<br>(if applicable) | END<br>DATE<br>MM/YYYY | FIELD OF STUDY                                   |
|--|---------------------------|------------------------|--|
| Universidad Nacional de Colombia, Bogota, Distrito Capital             | MD                        | 12/2001                | Medicine   |
| Universidad de Antioquia, Bogota, Distrito Capital                     | MS                        | 04/2007                | Epidemiology (45 credits)                        |
| Universitat Pompeu Fabra, Barcelona, Catalonia                         | MPH                       | 09/2011                | Public Health (Environmental Health), 60 credits |
| Universitat Pompeu Fabra, Barcelona, Catalonia                         | PHD                       | 07/2015                | Biomedicine                                      |
| Centre of Research in Environmental Epidemiology, Barcelona, Catalonia | Postdoctoral Fellow       | 09/2015                | Environmental Epigenetics                        |
| Geisel School of Medicine at Dartmouth, Lebanon, NH                    | Postdoctoral Fellow       | 11/2018                | Cancer epigenetics                               |

**A. Personal Statement**

My research interests include cancer epigenetics, environmental health, and cell heterogeneity, and the integration of molecular biomarkers to population health. As such I have led or collaborated in diverse efforts to understand the role of DNA methylation and miRNA changes in cancer cell heterogeneity. Specifically, I have the expertise in designing and analyzing EWAS (Epigenome Wide Association Studies) and Transcriptome Wide Association studies (TWAS) and in the developing and application of reference-based cell deconvolution using DNA methylation data. I have also successfully developed and validated predictive DNA methylation biomarkers. In academia, I have the experience of learning and teaching in multicultural backgrounds. Since 2012, I have been a lecturer and regular faculty for different medical, graduate, and post-graduate-level courses (epidemiology, biostatistics, bioinformatics and community health, molecular epidemiology) which position me to support the development of seminars within this project. I have lectured on specialized courses in four different countries (Colombia, Spain, USA, and China) in three different languages and faced the hurdles of teaching different levels of experts in clinical and research topics. The current application builds logically on my prior work. My medical background provided me solid bases in human pathophysiology, pharmacology, and toxicology. I have also hands-on experience in cancer registries, cancer surveillance, social and environmental epidemiology, bioinformatics, and biostatistics. I was also trained as a research project manager including field planning and execution, research project follow-ups (e.g. staffing, research protections, budget), and data processing and analysis in complex epidemiological settings.

1. **Salas LA**, Johnson KC, Koestler DC, O'Sullivan DE, Christensen BC. Integrative epigenetic and genetic pan-cancer somatic alteration portraits. *Epigenetics*. 2017 Jul 3;12(7):561-574. PubMed PMID: [28426276](https://pubmed.ncbi.nlm.nih.gov/28426276/); PubMed Central PMCID: [PMC5687331](https://pubmed.ncbi.nlm.nih.gov/PMC5687331/).
2. **Salas LA**, Koestler DC, Butler RA, Hansen HM, Wiencke JK, Kelsey KT, Christensen BC. An optimized library for reference-based deconvolution of whole-blood biospecimens assayed using the Illumina HumanMethylationEPIC BeadArray. *Genome Biol*. 2018 May 29;19(1):64. PubMed PMID: [29843789](https://pubmed.ncbi.nlm.nih.gov/29843789/); PubMed Central PMCID: [PMC5975716](https://pubmed.ncbi.nlm.nih.gov/PMC5975716/).

3. Zhang Z, Wiencke JK, Koestler DC, **Salas LA**, Christensen BC, Kelsey KT. Absence of an embryonic stem cell DNA methylation signature in human cancer. BMC Cancer. 2019 Jul 19;19(1):711. PubMed PMID: [31324166](#); PubMed Central PMCID: [PMC6642562](#).
4. **Salas LA**, Baker ER, Nieuwenhuijsen MJ, Marsit CJ, Christensen BC, Karagas MR. Maternal swimming pool exposure during pregnancy in relation to birth outcomes and cord blood DNA methylation among private well users. Environ Int. 2019 Feb;123:459-466. PubMed PMID: [30622071](#); PubMed Central PMCID: [PMC6599635](#).

## B. Positions and Honors

### Positions and Employment

|             |   |
|-------------|---|
| 2000 - 2001 | Medical intern, Fundacion Santa Fe de Bogota, Education division, Bogota  |
| 2002 - 2003 | Research assistant, Fundacion Santa Fe de Bogota, Education division, Bogota  |
| 2003 - 2003 | Emergency room physician, Fundacion Santa Fe de Bogota, University Hospital, Bogota   |
| 2003 - 2005 | Family physician, Hospital Centro Oriente II nivel, Bogota  |
| 2005 - 2007 | Cancer registry physician, Instituto Nacional de Cancerologia Colombia, Research and public health division, Cancer Surveillance Team, Bogota |
| 2007 - 2010 | Project manager, Fundacion Santa Fe de Bogota, Community Health Division, Bogota  |
| 2010 - 2011 | Research internship, Centre of Research in Environmental Epidemiology (CREAL), Barcelona  |
| 2011 - 2015 | PhD researcher, Centre of Research in Environmental Epidemiology (CREAL), Barcelona   |
| 2015 - 2015 | Graduate Assistant Professor, Universitat Pompeu Fabra, Medical School, Barcelona   |
| 2015 - 2015 | Postdoctoral fellow, Centre of Research in Environmental Epidemiology (CREAL), Barcelona  |
| 2015 - 2018 | Postdoctoral Research Associate B, Dartmouth College, Department of Epidemiology, Christensen lab, Lebanon, NH                                |
| 2018 - 2019 | Research Scientist, Dartmouth College, Department of Epidemiology, Christensen lab, Lebanon, NH   |
| 2020 -      | Assistant Professor, Geisel School of Medicine at Dartmouth, Department of Epidemiology, Lebanon, NH  |

### Other Experience and Professional Memberships

|        |   |
|--------|---|
| 2015 - | Member, International Society of Environmental Epidemiology (ISEE)                            |
| 2016 - | Associate Member, American Association of Cancer Research (AACR)                              |
| 2018 - | Member, Society of Epidemiologic Research (SER)   |
| 2018 - | Member, International Society for Developmental Origins of Health and Disease (DoHAD Society) |

### Honors

|             |  |
|-------------|--|
| 1996 - 2001 | Best National High School Graduates scholarship program, Universidad Nacional de Colombia  |
| 2001        | Best ECAES (currently best "Saber Pro"), , Sixth national place in the standardized test of medical sciences knowledge, among Medical students in Colombia |
| 2011        | Cum Laude ("Matrícula de honor") . Acknowledgment for the best master's thesis work MPH 2010-2011., Universitat Pompeu Fabra.                              |

## C. Contribution to Science

1. Epigenetics methods and biomarkers. The core of my research is the development and application of epigenetics methods and biomarkers to cancer. I have worked in the application of global DNA methylation dysregulation biomarkers (Methylation dysregulation index, MDI). I developed the Fetal cell of origin biomarker (FCO) to trace human stem cell lineage. Finally, I developed a DNA methylation biomarker to trace the neutrophil to lymphocyte ratio in glioma patients.
  - a. **Salas LA**, Lundgren SN, Browne EP, Punska EC, Anderton DL, Karagas MR, Arcaro KF, Christensen BC. Prediagnostic breast milk DNA methylation alterations in women who develop breast cancer. Hum

Mol Genet. 2020 Mar 13;29(4):662-673. PubMed PMID: [31943067](#); PubMed Central PMCID: [PMC7068171](#).

- b. Zhang Z, Wiencke JK, Koestler DC, **Salas LA**, Christensen BC, Kelsey KT. Absence of an embryonic stem cell DNA methylation signature in human cancer. *BMC Cancer*. 2019 Jul 19;19(1):711. PubMed PMID: [31324166](#); PubMed Central PMCID: [PMC6642562](#).
  - c. **Salas LA**, Wiencke JK, Koestler DC, Zhang Z, Christensen BC, Kelsey KT. Tracing human stem cell lineage during development using DNA methylation. *Genome Res*. 2018 Sep;28(9):1285-1295. PubMed PMID: [30072366](#); PubMed Central PMCID: [PMC6120629](#).
  - d. Wiencke JK, Koestler DC, **Salas LA**, Wiemels JL, Roy RP, Hansen HM, Rice T, McCoy LS, Bracci PM, Molinaro AM, Kelsey KT, Wrensch MR, Christensen BC. Immunomethylomic approach to explore the blood neutrophil lymphocyte ratio (NLR) in glioma survival. *Clin Epigenetics*. 2017;9:10. PubMed PMID: [28184256](#); PubMed Central PMCID: [PMC5288996](#).
2. Although cancer is the main focus of my research, I remain active in the field of Epigenome Wide Association Studies (EWAS) and Developmental origins of Health and disease. I have worked with several large birth cohorts (e.g., INMA, Spain and the New Hampshire Birth Cohort (NHBC), USA). I am an active participant in the multinational Pregnancy and Childhood Epigenetics (PACE) Consortium.
- a. Merid SK, Novoloaca A, Sharp GC, Küpers LK, Kho AT, Roy R, Gao L, Annesi-Maesano I, Jain P, Plusquin M, Kogevinas M, Allard C, Vehmeijer FO, Kazmi N, **Salas LA**, Rezwani FI, Zhang H, Sebert S, Czamara D, Rifas-Shiman SL, Melton PE, Lawlor DA, Pershagen G, Breton CV, Huen K, Baiz N, Gagliardi L, Nawrot TS, Corpeleijn E, Perron P, Duijts L, Nohr EA, Bustamante M, Ewart SL, Karmaus W, Zhao S, Page CM, Herceg Z, Jarvelin MR, Lahti J, Baccarelli AA, Anderson D, Kachroo P, Relton CL, Bergström A, Eskenazi B, Soomro MH, Vineis P, Snieder H, Bouchard L, Jaddoe VW, Sørensen TIA, Vrijheid M, Arshad SH, Holloway JW, Håberg SE, Magnus P, Dwyer T, Binder EB, DeMeo DL, Vonk JM, Newnham J, Tantisira KG, Kull I, Wiemels JL, Heude B, Sunyer J, Nystad W, Munthe-Kaas MC, Räikkönen K, Oken E, Huang RC, Weiss ST, Antó JM, Bousquet J, Kumar A, Söderhäll C, Almqvist C, Cardenas A, Gruziova O, Xu CJ, Reese SE, Kere J, Brodin P, Solomon O, Wielscher M, Holland N, Ghantous A, Hivert MF, Felix JF, Koppelman GH, London SJ, Melén E. Epigenome-wide meta-analysis of blood DNA methylation in newborns and children identifies numerous loci related to gestational age. *Genome Med*. 2020 Mar 2;12(1):25. PubMed PMID: [32114984](#); PubMed Central PMCID: [PMC7050134](#).
  - b. Howe CG, Cox B, Fore R, Jungius J, Kvist T, Lent S, Miles HE, **Salas LA**, Rifas-Shiman S, Starling AP, Yousefi P, Ladd-Acosta C, Baccarelli A, Binder EB, Chatzi VL, Czamara D, Dabelea D, DeMeo DL, Ghantous A, Herceg Z, Kajantie E, Lahti JMT, Lawlor DA, Litonjua A, Nawrot TS, Nohr EA, Oken E, Pizzi C, Plusquin M, Räikkönen K, Relton CL, Sharp GC, Sørensen TIA, Sunyer J, Vrijheid M, Zhang W, Hivert MF, Breton CV. Maternal Gestational Diabetes Mellitus and Newborn DNA Methylation: Findings From the Pregnancy and Childhood Epigenetics Consortium. *Diabetes Care*. 2020 Jan;43(1):98-105. PubMed PMID: [31601636](#); PubMed Central PMCID: [PMC6925578](#).
  - c. Küpers LK, Monnereau C, Sharp GC, Yousefi P, **Salas LA**, Ghantous A, Page CM, Reese SE, Wilcox AJ, Czamara D, Starling AP, Novoloaca A, Lent S, Roy R, Hoyo C, Breton CV, Allard C, Just AC, Bakulski KM, Holloway JW, Everson TM, Xu CJ, Huang RC, van der Plaats DA, Wielscher M, Merid SK, Ullemer V, Rezwani FI, Lahti J, van Dongen J, Langie SAS, Richardson TG, Magnus MC, Nohr EA, Xu Z, Duijts L, Zhao S, Zhang W, Plusquin M, DeMeo DL, Solomon O, Heimovaara JH, Jima DD, Gao L, Bustamante M, Perron P, Wright RO, Hertz-Picciotto I, Zhang H, Karagas MR, Gehring U, Marsit CJ, Beilin LJ, Vonk JM, Jarvelin MR, Bergström A, Örtqvist AK, Ewart S, Villa PM, Moore SE, Willemsen G, Standaert ARL, Håberg SE, Sørensen TIA, Taylor JA, Räikkönen K, Yang IV, Kechris K, Nawrot TS, Silver MJ, Gong YY, Richiardi L, Kogevinas M, Litonjua AA, Eskenazi B, Huen K, Mbarek H, Maguire RL, Dwyer T, Vrijheid M, Bouchard L, Baccarelli AA, Croen LA, Karmaus W, Anderson D, de Vries M, Sebert S, Kere J, Karlsson R, Arshad SH, Hämäläinen E, Routledge MN, Boomsma DI, Feinberg AP, Newschaffer CJ, Govarts E, Moisse M, Fallin MD, Melén E, Prentice AM, Kajantie E, Almqvist C, Oken E, Dabelea D, Boezen HM, Melton PE, Wright RJ, Koppelman GH, Trevisi L, Hivert MF, Sunyer J, Munthe-Kaas MC, Murphy SK, Corpeleijn E, Wiemels J, Holland N, Herceg Z, Binder EB, Davey Smith G, Jaddoe VWV, Lie RT, Nystad W, London SJ, Lawlor DA, Relton CL, Snieder H, Felix JF. Meta-analysis of epigenome-wide association studies in neonates reveals widespread differential DNA

methylation associated with birthweight. *Nat Commun.* 2019 Apr 23;10(1):1893. PubMed PMID: [31015461](#); PubMed Central PMCID: [PMC6478731](#).

- d. Vilahur N, Bustamante M, Morales E, Motta V, Fernandez MF, **Salas LA**, Escaramis G, Ballester F, Murcia M, Tardon A, Riaño I, Santa-Marina L, Ibarluzea J, Arrebola JP, Estivill X, Bollati V, Sunyer J, Olea N. Prenatal exposure to mixtures of xenoestrogens and genome-wide DNA methylation in human placenta. *Epigenomics.* 2016 Jan;8(1):43-54. PubMed PMID: [26679211](#).
3. Molecular mechanisms of disinfection by-products and cancer. This work laid the foundations of molecular mechanisms of these toxicants in long and short-term exposure in human populations.
    - a. **Salas LA**, Font-Ribera L, Bustamante M, Sumoy L, Grimalt JO, Bonnin S, Aguilar M, Mattlin H, Hummel M, Ferrer A, Kogevinas M, Villanueva CM. Gene expression changes in blood RNA after swimming in a chlorinated pool. *J Environ Sci (China).* 2017 Aug;58:250-261. PubMed PMID: [28774616](#).
    - b. **Salas LA**, Bustamante M, Gonzalez JR, Gracia-Lavedan E, Moreno V, Kogevinas M, Villanueva CM. DNA methylation levels and long-term trihalomethane exposure in drinking water: an epigenome-wide association study. *Epigenetics.* 2015;10(7):650-61. PubMed PMID: [26039576](#); PubMed Central PMCID: [PMC4622514](#).
    - c. **Salas LA**, Villanueva CM, Tajuddin SM, Amaral AF, Fernandez AF, Moore LE, Carrato A, Tardón A, Serra C, García-Closas R, Basagaña X, Rothman N, Silverman DT, Cantor KP, Kogevinas M, Real FX, Fraga MF, Malats N. LINE-1 methylation in granulocyte DNA and trihalomethane exposure is associated with bladder cancer risk. *Epigenetics.* 2014 Nov;9(11):1532-9. PubMed PMID: [25482586](#); PubMed Central PMCID: [PMC4622716](#).
    - d. **Salas LA**, Cantor KP, Tardon A, Serra C, Carrato A, Garcia-Closas R, Rothman N, Malats N, Silverman D, Kogevinas M, Villanueva CM. Biological and statistical approaches for modeling exposure to specific trihalomethanes and bladder cancer risk. *Am J Epidemiol.* 2013 Aug 15;178(4):652-60. PubMed PMID: [23648803](#); PubMed Central PMCID: [PMC3736753](#).
  4. Open source methods for molecular epidemiology. I updated the methods for DNA methylation for adult and umbilical cord blood cell deconvolution. I have collaborated in the development of multiple open source bioinformatic software for the analysis of molecular markers (cell deconvolution) and digital pathology. Among others: FlowSorted.Blood.EPIC, FlowSorted. CordBloodCombined.450k, PyMethylProcess and PathFlowAI.
    - a. Levy JJ, **Salas LA**, Christensen BC, Sriharan A, Vaickus LJ. PathFlowAI: A High-Throughput Workflow for Preprocessing, Deep Learning and Interpretation in Digital Pathology. *Pac Symp Biocomput.* 2020;25:403-414. PubMed PMID: [31797614](#); PubMed Central PMCID: [PMC6919317](#).
    - b. Gervin K, **Salas LA**, Bakulski KM, van Zelm MC, Koestler DC, Wiencke JK, Duijts L, Moll HA, Kelsey KT, Kobor MS, Lyle R, Christensen BC, Felix JF, Jones MJ. Systematic evaluation and validation of reference and library selection methods for deconvolution of cord blood DNA methylation data. *Clin Epigenetics.* 2019 Aug 27;11(1):125. PubMed PMID: [31455416](#); PubMed Central PMCID: [PMC6712867](#).
    - c. Levy JJ, Titus AJ, **Salas LA**, Christensen BC. PyMethylProcess-convenient high-throughput preprocessing workflow for DNA methylation data. *Bioinformatics.* 2019 Dec 15;35(24):5379-5381. PubMed PMID: [31368477](#); PubMed Central PMCID: [PMC6954637](#).
    - d. **Salas LA**, Koestler DC, Butler RA, Hansen HM, Wiencke JK, Kelsey KT, Christensen BC. An optimized library for reference-based deconvolution of whole-blood biospecimens assayed using the Illumina HumanMethylationEPIC BeadArray. *Genome Biol.* 2018 May 29;19(1):64. PubMed PMID: [29843789](#); PubMed Central PMCID: [PMC5975716](#).
  5. Developing of biomarkers and identification of epigenetic signatures using DNA methylation information in cancer and other chronic diseases.
    - a. Muse ME, Titus AJ, **Salas LA**, Wilkins OM, Mullen C, Gregory KJ, Schneider SS, Crisi GM, Jawale RM, Otis CN, Christensen BC, Arcaro KF. Enrichment of CpG island shore region hypermethylation in

epigenetic breast field cancerization. Epigenetics. 2020 Oct;15(10):1093-1106. PubMed PMID: [32255732](#).

- b. **Salas LA**, Lundgren SN, Browne EP, Punska EC, Anderton DL, Karagas MR, Arcaro KF, Christensen BC. Prediagnostic breast milk DNA methylation alterations in women who develop breast cancer. Hum Mol Genet. 2020 Mar 13;29(4):662-673. PubMed PMID: [31943067](#); PubMed Central PMCID: [PMC7068171](#).
- c. Chen Y, Wang Y, **Salas LA**, Miller TW, Mark K, Marotti JD, Kettenbach AN, Cheng C, Christensen BC. Molecular and epigenetic profiles of BRCA1-like hormone-receptor-positive breast tumors identified with development and application of a copy-number-based classifier. Breast Cancer Res. 2019 Jan 25;21(1):14. PubMed PMID: [30683142](#); PubMed Central PMCID: [PMC6347811](#).
- d. Chen Y, Armstrong DA, **Salas LA**, Hazlett HF, Nymon AB, Dessaint JA, Aridgides DS, Mellinger DL, Liu X, Christensen BC, Ashare A. Genome-wide DNA methylation profiling shows a distinct epigenetic signature associated with lung macrophages in cystic fibrosis. Clin Epigenetics. 2018 Dec 10;10(1):152. PubMed PMID: [30526669](#); PubMed Central PMCID: [PMC6288922](#).

## **D. Additional Information: Research Support and/or Scholastic Performance**

### **Ongoing Research Support**

W81XWH-20-1-0778, Congressionally Directed Medical Research Programs/Department of Defense

Salas Diaz, Lucas A (PI)

09/01/20-08/31/24

Epigenetic modifications of cytosines in clear cell kidney carcinogenesis and survival

This proposal aims to investigate differential DNA methylation and hydroxymethylation patterns in clear cell renal carcinomas and normal adjacent kidney tissue from the Renal Tumor Bank at Dartmouth, and their relation with survival and gene expression patterns (mRNA and miRNA) in the tumor tissue.

Role: PI