Lindsay M. LaFave, Ph.D.

Positions:
Assistant Professor, Department of Cell Biology
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Research interests:

Our group aims to decipher the gene regulatory mechanisms that control stemness in lung cells and how these programs are co-opted in lung cancers. Rare subpopulations of alveolar type 2 (AT2) cells, the surfactant secreting cells that partially comprise the air sacs (alveoli) in the lungs, can function as stem cells under normal tissue homeostatic conditions. Importantly, AT2 cells demonstrate enhanced stem cell activity in the context of injury and disease; however, very little is known about how these cells adopt altered stemness in these settings. AT2 cells are also a cell-of-origin for lung adenocarcinoma, and transformation of this cell population leads to substantial cell state diversification. We seek to investigate the underlying context-specific epigenetic mechanisms that mediate alveolar stemness and how these programs are disrupted in diseases such as lung cancer. To address these questions, we pair lung cancer modeling with epigenomic technologies (including single-cell ATAC-sequencing and spatial approaches) to dissect mechanisms important for the acquisition and maintenance of dysregulated cell states in lung cancer. We flexibly utilize genetically engineered mouse models, alveolar human and murine organoids, and cell-based assays to perform functional studies. We continue to expand our technological and modeling toolkit to study normal lung stem cell biology and lung cancer with the overarching goal of better targeting lung cancer progression.
For more information on our research, please visit: https://www.lafavelab.org/.

Current grant funding:

K22CA258957 (PI: LaFave) 09/01/21-08/31/24 NCI
Title: Investigating the role of RUNX2 activation across cancer evolution in lung adenocarcinoma

Recent publications (selected):

#Indicates Equal contribution; *Indicates Co-corresponding authors

1. Concepcion C, Ma S#, **LaFave LM**#, Bhutkar A#, Liu M, DeAngelo LP, Kim JY, Del Priore I, Schoenfeld AJ, Miller M, Kartha VK, Westcott PMK, Sanchez-Rivera FJ, Meli K, Gupta M, Bronson RT, Riely GJ, Rekhtman N, Rudin CM, Kim CF, Regev A, Buenrostro JD, JacksT. Smarca4 inactivation promotes lineage-specific transformation and early metastatic features in the lung. *Cancer Discovery*. 2021 Sep 24:candisc.0248.2021.

2. Del Priore I#, Ma S#, Strecker J, Jacks T, **LaFave LM***, Buenrostro JD*. Protocol for single-cell ATAC sequencing using combinatorial indexing in mouse lung adenocarcinoma. *STAR Protocols*. 2021 Jun3;2(2):100583. doi: 10.1016/j.xpro.2021.100583.

3. Ma S, Zhang B, **LaFave LM**, Chiang Z, Hu Y, Ding J, Brack A, Kartha V, Law T, Lareau C, Hsu Y, Regev A*, Buenrostro JD*. Chromatin-mediated lineage priming and chromatin potential identified by shared single cell profiling of RNA and chromatin. *Cell*. 2020 Oct 20:S0092-8674(20)31253-8.

4. **LaFave LM**, Kartha VK#, Ma S#, Meli K, Del Priore I, Lareau C, Naranjo S, Westcott P, Duarte FM, Sankar V, Chiang Z, Brack A, Law T, Hauck H, Okimoto A, Regev A, Buenrostro JD*, Jacks T*. Epigenomic state transitions characterize tumor progression in mouse lung adenocarcinoma. *Cancer Cell.* 2020 Aug 10;38(2):212-228.e13.

5. LaFave LM, Béguelin W, Koche R, Teater M, Spitzer B, Chramiec A, Papalexi E, Keller M, Hricik T, Konstantinoff K, Micol JB, Durham B, Knutson SK, Campbell JE, Blum G, Shi X, Doud EH, Krivtsov A, Chung YR, Khodos I, DeStanchina A, Ouerfelli O, Adusumilli P, Thomas PM, Kelleher NL, Luo M, Keilhack H, Abdel-Wahab O, Melnick A, Armstrong S, Levine RL. Bap1 loss leads to EZH2-dependent transformation. *Nature Medicine.* 2015 Nov (21); 1344-1349.

6. Abdel-Wahab O#, Adli M#, **LaFave LM**#, Gao, J, Hricik T, Shih AH, Pandey S, Patel J, Perna F, Zhao X, Taylor JE, Park CY, Carrol M, Melnick A, Nimer SD, Jaffe JD, Aifantis I, Bernstein BE, Levine RL. ASXL1 Mutations Promote Myeloid Transformation Through Loss of PRC2-Mediated Gene Repression. *Cancer Cell.* 2012 Aug 14; 22(2):180-93.