

6 Barcoded viral platform for multiplexed functional validation of oncogenic cancer mutations in vivo and uses thereof

Researchers at Stanford University have developed a method which integrates cell barcoding and high-throughput sequencing to quantify tumor growth in genetically engineered mouse models of human cancer (called 'Tuba-seq' for Tumor barcoding coupled with sequencing). Unlike existing methods, this platform allows measurement of parameters of population (tumor) growth for a very large number of independent clonal populations (tumors) within the same mouse, providing exquisitely precise, cheap, and rapid estimate of effects of tumor-suppressors function modification on tumor growth *in vivo*. Because Tuba-seq enables the analysis of multiple pathways in the same animal using a very large number of independent tumors, it is much faster, much more precise, and is a much less expensive way to investigate tumor-suppressor function as well as genotype-specific therapeutic responses. This method is naturally adaptable for high-throughput profiling of drug responses of many tumor types growing *in vivo*.

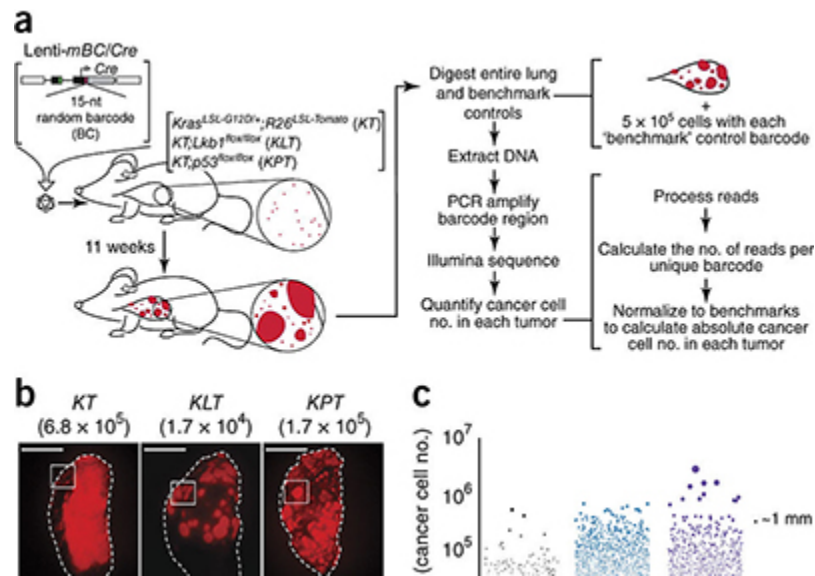


Figure 1. (a) Schematic of Tuba-seq pipeline to assess lung tumor size distributions. (b) Fluorescence dissecting scope images of lung lobes from KT, KLT, and KPT mice with Lenti-mBC/Cre⁺initiated tumors. (c) Tumor size distributions in KT, KLT, and KPT mice.

Figure adapted from: Rogers, Z. N. et al. A quantitative and multiplexed approach to uncover the fitness landscape of tumor suppression *in vivo*. *Nature Methods* (2017). doi:10.1038/nmeth.4297

Applications

- Interrogation of gene function in mouse models of human cancer
- Profiling therapeutic effects of compounds/treatments on many major tumors genotypes in parallel, cheaply, rapidly, and precisely

Advantages

- Rapid, quantitative method to determine functional importance of putative tumor suppressors on cancer growth *in vivo*
- Ability to generate tumors in mice with different loss- and gain-of-function mutations, thus greatly reducing costs and time associated with pre-clinical testing *in vivo*
- Provides sensitivity to identify tumor suppressors of small effect

Publications

- Rogers, Z. N., McFarland, C. D., Winters, I. P., Naranjo, S., Chuang, C., Petrov, D., and Monte M. Winslow. [A quantitative and multiplexed approach to uncover the fitness landscape of tumor suppression *in vivo*](#). *Nature Methods*, 14: 737-742 (2017).

Patents

- Published Application: [20180282720](#)
- Published Application: [WO2018187156](#)
- Published Application: [20190367908](#)
- Published Application: [WO2020072531](#)
- Published Application: [20210009992](#)
- Published Application: [20210062184](#)
- Published Application: [20220304285](#)
- Published Application: [20240287503](#)
- Issued: [10,801,021 \(USA\)](#)
- Issued: [10,738,300 \(USA\)](#)

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