Docket #: S16-338

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*.

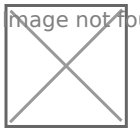

Figure 1. (**a**) Schematic of Tuba-seq pipeline to assess lung tumor size distributions. (**b**) Fluorescence dissecting scope images of lung lobes from KT, KLT, and KPT mice with Lenti-mBC/Cre?initiated tumors. (**c**) Tumor size distributions in KT, KLT, and KPT mice.

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
- Issued: 10,801,021 (USA)

- Issued: 10,738,300 (USA)

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