Abstract Submitted for the MAR17 Meeting of The American Physical Society

Rapid emergence and mechanisms of resistance by U87 glioblastoma cells to doxorubicin in an in vitro tumor microfluidic $ecology^1$ ROBERT AUSTIN, Princeton University, SANGHYUK LEE, cEwha Research Center for Systems Biology (ERCSB), Ewha Womans University, Seoul, Korea, SUNGSU PARK, aSchool of Mechanical Engineering, Sungkyunkwan University, Suwon, Korea — We have developed a microfluidic device consisting of approximately 500 hexagonal micro-compartments which provides a complex ecology with wide ranges of drug and nutrient gradients and local populations. This ecology of a fragmented metapopulation induced the drug resistance in stage IV U87 glioblastoma cells to doxorubicin in seven days. Exome and transcriptome sequencing of the resistant cells identified mutations and differentially expressed genes. Gene ontology and pathway analyses of the genes identified showed that they were functionally relevant with the established mechanisms of doxorubicin action. Functional experiments support the in silico analyses and together demonstrate the effects of these genetic changes. Our findings suggest that given the rapid evolution of resistance and the focused response, this technology could act as a rapid screening modality for genetic aberrations leading to resistance to chemotherapy as well as counter-selection of drugs unlikely to be successful ultimately.

¹Technology Innovation Program of the Ministry of Trade, Industry and Energy, Republic of Korea (10050154 to S.L. and S.P.), the National Research Foundation of Korea (NRF-2014M3C9A3065221 to S.L., NRF-2015K1A4A3047851 to J.K. and S.L.) funded by the Minis

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Date submitted: 17 Nov 2016

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