1107-92-137 **Liwu Li*** (lwli@vt.edu), 970 Washington Street, Department of Biological Sciences, Blacksburg, VA 24061-0910. *Dynamic programming of innate immunity and inflammatory diseases.* Preliminary report.

Host macrophages can be pre-programmed into opposing primed or tolerant states depending upon the nature and quantities of external stimulants. The paradigm of priming and tolerance has significant implications in the pathogenesis and resolution of both acute and chronic inflammatory diseases. However, the responsible mechanisms are not well understood. Here, we report that super low dose bacterial endotoxin LPS primes the expression of pro-inflammatory mediators in macrophages upon a second high dose LPS challenge, although super low dose endotoxin itself does not trigger noticeable macrophage activation. Mice primed with super low dose LPS in vivo experience significantly elevated mortality following a second-hit high dose LPS as compared to saline-primed control mice. Mechanistically, we demonstrate that varying dosages of LPS primes macrophages by differentially modulating cellular and molecular switches inside the cells. The pathway switching and flipping induced by super low vs high dose LPS underscores the importance of competing intracellular circuitry during the establishment of macrophage priming and tolerance. (Received January 10, 2015)