1131-92-391 **Yusuf Talha Tamer** and **Haleh Abdizadeh**, Istanbul, **Tugce Altinusak Batur**, Istanbul, **Ali Rana Atilgan**, Istanbul, **Canan Atilgan**, Istanbul, and **Erdal Toprak***, 6001 Forest Park Rd, ND11.136D, Dallas, TX 75390-8597. *Predictability in Evolution of Antibiotic Resistance.* Preliminary report.

Antibiotic resistance is a growing public health problem. One of the most prevalent resistance mechanisms is increased antibiotic tolerance as a result of spontaneous mutations on the enzymes that are the targets of antibiotic molecules. In a custom made continuous culture device that we call the Morbidostat, we evolved several wild type Escherichia coli populations against trimethoprim under nearly constant drug induced growth inhibition. In the Morbidostat, trimethoprim resistance increased in a stepwise manner as a result of accumulation of multiple point mutations on folA gene coding for dihydrofolate reductase (DHFR) enzyme, following a quasi-deterministic order. We quantified the epistatic interactions in the adaptation landscape of DHFR enzyme by synthetically constructing and phenotyping all combinatorial alleles carrying up to six trimethoprim resistance-conferring mutations. Our results suggest that evolution of resistance depends on fitness constraints imposed by protein structure as well as environmental factors. (Received July 18, 2017)