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The relationship between genotype/phenotype and fitness under a given environment is complex, but its structure allows the explanation and prediction of evolutionary trajectories. In this study, we infer the phenotype-based fitness landscape for antibiotic resistance evolution by quantifying the phenotypic changes to develop a fitness landscape capable of predicting evolution for the whole cell. We show that different peaks of the landscape correspond to different drug resistance mechanics, thus supporting the landscape’s validity. This approach links phenotypic/genotypic changes and fitness, helping to a better understanding of drug resistance evolution.