**Predicting the Efficiencies of Genome Editing Tools**

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We developed high-throughput methods for evaluating activities of AsCas12a, SpCas9 including the high-fidelity variants and variants with different protospacer-adjacent motif compatibilities, base editors, and prime editor 2. Based on the large data sets of these genome editing tool activities, we developed computational models that predict the activities and, in some cases, editing outcomes of these genome editing tools based on target sequence composition in mammalian cells. Applications of prime editing are often limited due to insufficient efficiencies, and it can require substantial time and resources to determine the most efficient pegRNAs and prime editors (PEs) to generate a desired edit under various experimental conditions. Here, we evaluated prime editing efficiencies for a total of 338,996 pairs of pegRNAs including 3,979 epegRNAs and target sequences in an error-free manner. These datasets enabled a systematic determination of factors affecting prime editing efficiencies. Then, we developed computational models, named DeepPrime and DeepPrime-FT, that can predict prime editing efficiencies for eight prime editing systems in seven cell types for all possible types of editing of up to 3 base pairs. We also extensively profiled the prime editing efficiencies at mismatched targets and developed a computational model predicting editing efficiencies at such targets. These computational models, together with our improved knowledge about prime editing efficiency determinants, will greatly facilitate prime editing applications.