CRISPR genome editing has become a widely-used tool to easily and efficiently modify a genome of interest in a programmable way and could be a promising therapeutic modality to produce beneficial genetic changes in patient cells. However, off-targets (i.e., unwanted cleavages at sites with high homology with the desired target sequence) may occur. It is important to consider the efficiency of the guide RNA at these off-target sites, especially when multiple guides are considered for a given application in order to maximize the editing outcomes and assess safety.

Although several websites have been developed to aid the design of single-guide RNAs (sgRNAs) and to predict outcomes of specific sgRNAs, these tools do not explicitly account for personal genetic variants and are therefore limited in assessing efficiency, specificity, and safety of sgRNAs. In fact, their on and off-target scores are calculated based on reference genomes only.

To overcome these limitations, we present CRISPRme, a web application that extends CRISPRitz (Cancellieri et al, Bioinformatics 2020) with a user-friendly interface to enumerate on- and off-target sites accounting for mismatches, DNA/RNA bulges, and common genetic variants.

Importantly, CRISPRme performs genomic scanning while accounting for existing haplotypes, instead of enumerating combinations of genetic variants that may not exist in a given population.

CRISPRme analyzes super populations (based on variants from the 1000 Genome Project) as well as personal genomes, and produces reports to quickly assess the potential risk of off-target editing.

CRISPRme can be easily deployed on any machine and customized with personal genomes (user-defined reference genome and/or variants from personal VCFs) to maintain personal genome privacy and security.