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Advances in sequencing technology have led to the identification of millions of missense mutations in the human genome. However, the pathogenicity or functional consequence of >99% of these mutations remains unknown. We used CRISPR-Cas9 base editor screens to identify mutations with a detrimental effect on cell proliferation in a high-throughput manner. We performed a pooled CRISPR-Cas9 cytosine base editor screen targeting 2000 different sites in 9 essential genes with a role in transcription, translation, or DNA replication. We tracked the change in abundance of mutants in cell pools over time at three different temperatures: 35, 37, and 39°C. This allowed us to classify mutants as either unconditional detrimental if a proliferation defect was observed at all temperatures, or as hypomorphic (partial loss-of-function) if the defect was only detected under temperature stress. In total, 25% of all tested gRNAs led to a proliferation defect in our screen, including 5% that caused an unconditional detrimental phenotype and 20% that were hypomorphic. We found that deleterious variants were enriched in specific protein domains and that the frequency of the various types of deleterious variants was gene-dependent. For example, mutations in DDX3X frequently showed a cold-sensitive phenotype, whereas RCC1 mutations were more likely to be unconditionally detrimental. Moreover, we identified known disease-associated mutations with a hypomorphic phenotype that can be used to further characterize these variants. To conclude, we show that base editor screens can be used to identify unconditionally detrimental and hypomorphic mutations, and can highlight critical residues and domains within essential genes.