Microbial hosts are preferentially employed for recombinant protein production, as clone generation is easier relative to eukaryotic host systems. Also, methods for manipulation of microbial genomes are generally more straightforward. Using *E.coli* as a model, we demonstrate a rapid genome engineering method named FAST-GE and compare this method to several other common techniques. Examples of protein expression host genome modification are highlighted where the final objective is isolation of highly pure target protein.

Host cell protein (HCP) analysis is a highly sensitive quality assurance test and is a standard during the purification of therapeutic proteins. In some cases, host genome modification may be necessary to eliminate specific contaminating proteins since contaminant removal by conventional chromatography methods reduces target protein yield too severely. The NiCo21(DE3) strain of *E.coli* is a BL21(DE3) derivative engineered to aid in the isolation of poly-histidine tagged recombination protein. The advantages of employing NiCo21(DE3) for recombinant protein expression will be described.