Estrogen receptor alpha (ERα) activity is associated with increased proliferation and high Gleason grade in prostate cancer. Studies aiming to understand the impact of ERα on cancer associated phenotypes have largely been limited to its activity as a transcription factor. Herein, we demonstrate that ERα also selectively modulates mRNA translation, whereby ERα-dependent transcriptional and translational programs in prostate cancer cells are coordinated. For a large number of genes, ERα-driven alterations in the transcriptome are buffered at the level of mRNA translation, in such manner that the amount of translated mRNA and protein levels are maintained despite changes in total mRNA abundance. Transcripts whose levels are reduced following ERα depletion, but translationally buffered, lack features known to limit translational efficiency including structured 5'UTRs and miRNA target sites. In contrast, mRNAs that are induced upon ERα depletion and are translationally buffered exhibit increased requirement for U34 tRNA modifications. Consistently, ERα regulates levels of U34-modification enzymes whilst alterations in their expression disrupt translational buffering. Altogether, we unravel a hitherto unprecedented mechanism of ERα-dependent coordination of gene expression, and demonstrate that translational buffering is a pervasive mechanism of proteome maintenance in hormone-dependent cancers.