Peptidyl-proline isomerases alter protein substrates by altering their shape at prolyl-peptide bonds. This post-translational modification controls a variety of processes from de novo folding to signaling and enzyme activity. While several isomerases are localized to the nucleus, their substrates and functions have remained fairly uncharacterized. We have uncovered a role for the human prolyl-isomerase FKBP25 in ribosomal RNA (rRNA) biogenesis. FKBP25 occupies rDNA chromatin and mediates RNA Pol I transcription. FKBP25-interacting proteins include several enzymes that modify rDNA chromatin, which implicates proline isomerization in the epigenetic regulation of nucleolar chromatin. The mechanisms by which FKBP25 modulates Pol I transcription will be discussed, as will insights into how peptidyl-proline isomerase activity itself may be regulated in response to proliferation signals. Together these results identify prolyl-isomerases in the coordination of cell growth signals via the expression of rRNAs needed for ribosome biogenesis.