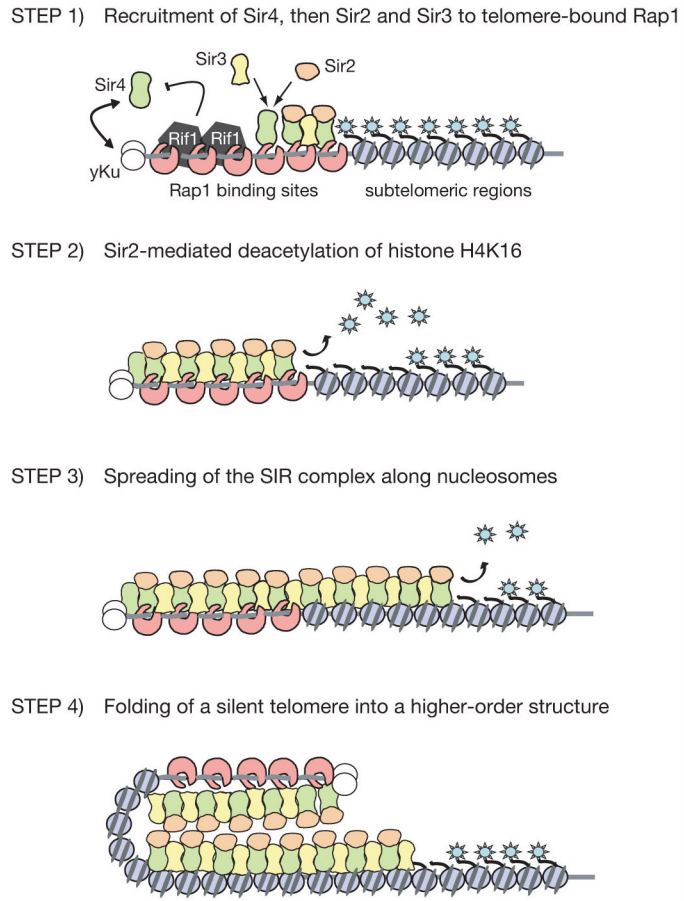

Figure 6. Steps in the Assembly of Telomeric Heterochromatin

(*Step 1*) At telomeres, Rap1 and yKu recruit Sir4 even in the absence of Sir2 or Sir3. Only Sir4 can be recruited, in the absence of the other Sir proteins, and its binding is antagonized by Rif1 and Rif2 (Mishra and Shore 1999). (*Step 2*) Sir4-Sir2 and Sir4-Sir3 interact strongly, creating Sir complexes along the TG repeats. Sir2 NAD-dependent histone deacetylase activity is stimulated by complex formation, and Sir2 deacetylates the acetylated histone H4 K16 residue in nearby nucleosomes. (*Step 3*) SIR complexes spread along the nucleosomes, perhaps making use of the O-acetyl ADP ribose intermediate produced by NAD hydrolysis (Liou et al. 2005). Sir3 and Sir4 bind the deacetylated histone H4 tails. Although the deacetylated histone H3 amino-terminal tail also binds Sir3 and Sir4 proteins, it is not shown here. (*Step 4*) The silent chromatin "matures" at the end of M phase to create an inaccessible structure. This may entail higher-order folding and sequestering at the nuclear envelope.