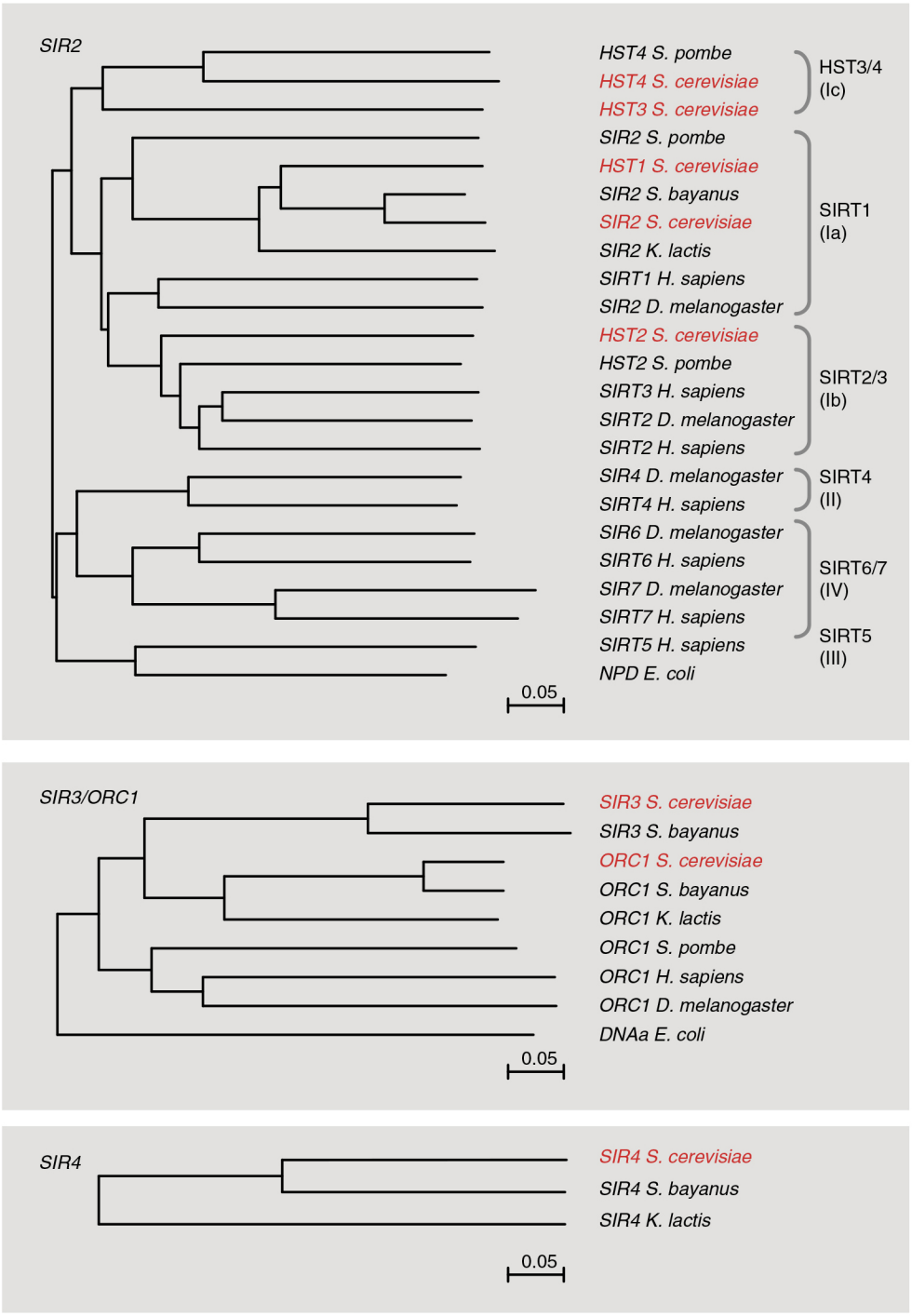

Figure 4. Sir protein family trees. Sir2 is the founding member of a large family of NAD-dependent deacetylases. The Sir2 family of proteins is highly conserved, found in multiple isoforms in organisms that range from bacteria to man. In the latter, there are both nuclear and cytoplasmic isoforms. Homologs of Sir2, Sir3, and Sir4 from *Saccharomyces bayanus*, *Kluyveromyces lactis*, *Schizosaccharomyces pombe*, *D. melanogaster*, and *Homo sapiens* were collected from UniProt and were aligned using ClustalW2 alignment. The phylogenetic tree was created using neighbor joining. Sir2 classification is according to Frye (2000). *K. lactis* has 4 *SIR2* orthologs (homologs to *S. cerevisiae* Sir2, Hst2, Hst3, and Hst4), but the *HST* homologs were omitted in the tree for clarity. For *S. bayanus*, only the Sir2 homolog is annotated to date. *S. cerevisiae* homologs are in red. Sir3 arose through a gene duplication of a gene encoding an ancient Orc1, and Sir4 is a rapidly evolving protein that is only found in related budding yeasts. The related proteins shown are not exhaustive, particularly for Sir2.