Figure S1. Structural characterization of the TLE Q-domain.

A. Electron density maps of the TLE Q-domain. 2Fo-Fc density contoured at 2σ of the N-terminal domain shown in gold, Fo-Fc map contoured at 2.5σ showed in green. Top left panel shows the N-terminal domain of the TLE1-156, top right panel shows the N-terminal tetramerization domain of the TLE20-156 structure. Bottom left and right panels show representative densities of the TLE1-156 and the TLE20-156 structure respectively.

B. TLE120-156 crystal packing. The crystallographic asymmetric unit contains four protomers, and two potential tetramers are seen in the crystal lattice. In the first, hydrophobic residues present at the N-terminal of the dimer associate in an antiparallel orientation with the equivalent residues of another dimer to form a 212 Å elongated dimer of dimers (red box; see also Fig. 1A). This interaction buries 3320 Å² of surface area. A second dimer-dimer association occurs between the C-terminal portion of α3 from one dimer and the C-terminal region of α1 from another, antiparallel dimer (black box), and comprises mostly polar interactions. This interface is smaller, burying a surface area of 655 Å².

C. Sequence alignments. The Q-domains of selected TLE/Groucho family members are aligned based on the crystal structure of human TLE1. White letters on black background indicate invariant residues. Red box indicates the tetramerization region in the TLE1 structure. Despite strong sequence homology between the tetramerization domains of TLE1 and yeast Tup1, the structure of the TLE1 tetramerization domain differs greatly
from that reported for Tup1. The crystal structure of Tup1 shows an antiparallel 135Å long four-helix bundle with a large, water-filled interface (Matsumura et al, 2012). In contrast, TLE1 forms a 212Å long dimer of dimers with a short, antiparallel tetramer interface at the N-terminus mediated by hydrophobic packing. The origin of this difference is unclear, and we cannot rule out that differences in crystallization conditions, most notably pH 4.6 for Tup1 and 7.0 for TLE1, gave rise to the different structures.