Plants using ants as anti-herbivore agents are common in tropical regions. They provide ants with food and nesting sites, called domatia. Domatia are hollow structures that host ants and are key traits for the evolution of ant-plant interaction. However, the morphology and molecular mechanisms of domatia development have rarely been studied. We studied stem domatia of well-known ant plants, the genus Macaranga, using comparative transcriptomic and morphological analyses. The results indicated that programmed cell death, a suicide procedure in the ultimate step of cell-specific differentiation, developed hollow cavities. We also found three possible procedures of the domatia formation: (i) stem expansion, in which proliferates pith cells occur; (ii) programmed cell death, which forms cavities; and (iii) secondary cell wall deposition, which shapes the physical structure. These findings provide new evidence for the domatia development and enhance our understanding of protective ant-plant interaction.