

Table 1. The metazoan toolkit of conserved functional components and processes: When did they first arise in evolution?

First arose in evolution	Conserved functional components and processes
Three billion years ago, in early prokaryotic organisms	Components of energy metabolism, biosynthesis of the 60 building blocks, DNA replication, DNA transcription to RNA, translation of RNA to protein, lipid membrane synthesis, transmembrane transport
Two billion years ago, in early eukaryotic cells	Components of the formation of microfilament and microtubule cytoskeletons, motor proteins moving materials along the cytoskeletons, contractility processes, movement of the cell by cilia and ruffling membrane action, shuttling of materials between intracellular organelles, phagocytosis, secretion, chromosome dynamics, a complex cell cycle driven by protein kinases and protein degradation, sexual reproduction with meiosis and cell fusion
One billion years ago, in early multicellular animal life forms	Components of 15–20 cell–cell signaling pathways, cell adhesion processes, apical basal polarization of cells, junction formation, epithelium formation, specialization of cells toward physiological ends, some developmental processes of the single-celled egg to the multicellular adult
Near pre-Cambrian, in animals with early body axes	Components of complex developmental patterning, such as anteroposterior axis formation (Wnt/Wnt antagonist gradients) and dorsoventral axis formation (Bmp/antagonist gradients), inductions, complex cell competence, additional specialized cell types, formation of the body plan’s map of selector gene compartments (both transcription factors and signaling proteins), various regulatory processes