The cell differentiation process plays a crucial role in the prenatal development of multicellular organisms. Recent advances in the research on stem cell properties and embryonic development have uncovered several steps in the differentiation process [1–8]. Single and multiple sequences of cell differentiation have been identified through in-vivo observations of a particular embryo during early stages of development and through pathology studies of miscarriages during late stages of the process. While the identification of each cell differentiation step has been the subject of intense research, an integrated view of this complex process is still missing. Such a global view promises to reveal features associated with the large-scale modular organization of the cell types [5–7, 9–13] with the purpose of discovering new functional modules between cell types using novel theoretical network analysis for community detection [10–12]. In this letter, we take advantage of the current knowledge on the sequence of cell differentiation processes, which is spread over a vast specialized literature [1–6, 14–28] (see the Supplementary Information SI-Table I and references therein), to reveal and characterize the topological and dynamical features associated with the network of human cell differentiation (NHCD).

I. RESULTS

We construct the NHCD by systematically gathering the scattered information on the evolution of each cell type present in the embryo and fetus from a predecessor with a higher degree of differentiation potential into a more specialized type. The process of cell differentiation is then mapped onto a complex network which consists of 873 nodes connected through 977 edges. The nodes in the network represent distinct cell types reported in the literature [1–6, 14–28] and the edges represent the association between two cell types through a differentiation event.

The initial steps of the NHCD are shown in the inset of Fig. 1, while the resulting network structure is shown in the main panel of Fig. 1 (see also SI-Figs. 5a and 5b). The fertilized egg is followed by the ball stage, and the formation of the primary germ cell layers. Currently, it is known that until the ball stage, cell division is symmetric and produces further totipotent stem cells [1]. These cells then give rise to all the differentiated tissues of the organism as well as the extra-embryonic tissues (placenta, umbilical cord, etc.). Moreover, in the course of the entire process of organism formation, there is a monotonic decrease in the differentiation