Implantation is a critical developmental milestone for early human embryogenesis and successful pregnancy. During implantation, the pluripotent epiblast gives rise to the squamous amniotic ectoderm and the columnar embryonic disc, which together enclose the amniotic cavity to form an asymmetric cystic structure termed the amniotic sac (Figure 1a). The development of the amniotic sac is the keystone for post-implantation human embryogenesis, as the columnar epiblast and the squamous amniotic ectoderm eventually develop into the embryo proper and the enveloping amniotic membrane, respectively, which together constitute the core of a human embryo. Despite its fundamental and clinical significance, the development of the amniotic ectoderm and the amniotic sac in humans is poorly understood due to the technical and ethical challenges of harvesting and/or culturing early embryo specimens for study. Here, we report the first in vitro model for multiple post-implantation human embryogenic events centered around the amniotic sac development, by culturing human pluripotent stem cells (hPSC) in a bioengineered niche that mimics the mechanical softness and the physical dimensionality of the implantation microenvironment (Figure 1b) [1,2]. Specifically, we find that hPSC can self-organize to form three-dimensional asymmetric cystic structure - herein termed the post-implantation amniotic sac embryoid (PASE) - that recapitulates the differentiation of amniotic ectoderm, and further, the asymmetric morphogenesis and bipolar amniotic ectoderm-epiblast patterning seen in human amniotic sac development in vivo (Figure 1c). Intriguingly, our findings show that biomimetic physical niche cues are both necessary and sufficient for the amniotic induction that is indispensable for the development of PASE. Upon further development, the PASE initiates a process that resembles posterior primitive streak (PS) development at early gastrulation (Figure 1d&e). We also unveil an endogenous activation and self-patterning of BMP-SMAD signaling during PASE development in vitro (Figure 1f). Together, Our findings reveal an unexplored developmental potential of hPSC and highlight the self-organizing nature of post-implantation human embryogenesis. This study provides a novel hPSC-based in vitro platform for advancing our fundamental understanding of early human development.

**Figure 1.** (a) Schematic of a human embryo during implantation. (b) Schematic of the biomimetic 3D culture system. (c) Images of PASE. Section image (right) shows a day 12 human amniotic sac. (d) Image of a PASE showing migratory cells disseminating from the columnar embryonic disc, resembling PS initiation in day 16 embryo (arrow heads). (e) Images showing PS markers in PASE. (f) Bipolar patterning of phosphorylated SMAD1/5 in PASE.