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Letter to the Editor

A novel function for amniotic fluid: Original or authentic?

Dear Editor,

The recent review by Tong[1] in this journal suggested that amniotic fluid (AF) acts as a transporting pathway for signaling molecules and stem cells during the embryonic development of amniotes. Single-author manuscripts are relatively rare, and the title seems to address something already understood within the medical community. Therefore, is this hypothesis simply an original individual opinion, or an authentic depiction of a previously understood concept?

Amniotes, tetrapod mammals, and reptiles (including birds) likely became dominant land vertebrates because they could reproduce on dry land. An important aspect of this reproductive adaptation was evolution of the amniotic sac membrane, which surrounds the fetus and encapsulates fluid that provides the fetus with both physical cushioning and nutrients. By careful examination of particular details of this evolutionary process, Tong[1] invites renewed exploration of existing assumptions.

The interdependence of cellular interactions with fetal development involves the induction of cell specialization through the activation of intracellular pathways via extracellular signaling molecules. The sources of these extracellular signals include fetus-derived factors released into the amniotic cavity.

When molecular flow was traced in chick embryos or sheep, a rapid exchange (within minutes) was detected between AF and fetal tissues. Moreover, a reciprocal relationship was apparent between local concentrations indicating a bi-directional exchange of solutes involving fetal tissue and AF. The constituents of AF vary with fetal development, featuring a profile significantly different from maternal plasma as confirmed via proteomic analysis. Fundamental qualities of its composition have suggested that AF is an independent fluid pool rather than a blood filtrate.

Strict interdependency between chick development and AF composition, as shown by partial substitution with isotonic saline,[1] suggests molecular candidates; it has long been appreciated that there is a dynamic regulation of insulin-like growth factors in amniotic fluid.[2]

Some arguments presented in Tong's[1] hypothesis could be questioned. Most AF proteins and polypeptides mapped by two-dimensional electrophoresis had low molecular weights, yet proteomic experiments need to be interpreted cautiously, as different isolation platforms can bias outcome. Finding that AF extracts arrest murine H22 hepatoma growth with an induction of cell differentiation just provides indirect, rather than direct evidence that AF functions as an orchestrator of differentiation in the fetus.

Determining specifically where, how, and when AF influences embryonic development represents the least clarified aspect of Tong's hypothesis, especially since we know relatively little about the ontogenesis of stem cell niches. Nonetheless, it is encouraging to recognize that we are gaining an understanding of how fetal cortical and mesenchymal cells participate in the establishment of progenitor cell niches.[3] Denuded amniotic membrane can provide a supportive niche for limbal epithelial progenitors,[4] and processed AF remains bioactive for the enhancement of diabetically-impaired wound healing.[5] There is growing recognition that AF is a rich source of stem cells with potential applications ranging from intestinal disease[6] and neuronal regeneration[7] to cancer therapy.[8]

Tong's[1] review title may lack a sense of originality, but it is more important to be authentic. The hypothesis that is presented is both supported by reasonable observations of the author and timely, given our improved ability to characterize signaling organelles in body fluids[9] and the potential for molecular characterization to predict critical events, including the health of the fetus and integrity of the amniotic membrane.[10] Accordingly, existing evidence supports further pursuit of this hypothesis.

Conflicts of interest

The authors declare that there are no conflicts of interest related to the subject matter or materials discussed in this article.

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