Is the Fetal Heart a Hematopoietic Organ?

To the Editor:

The article by Tomanek et al1 presents well the in vivo data on the requirement of VEGF family members for tubulogenesis and coronary artery formation. The authors observed that VEGF-Trap (a chimera of R1 and R2), apart from precluding formation of coronary arteries, causes a massive accumulation of erythrocytes in the subepicardium and in the interventricular septum. The important finding of this study was that erythrocytes that are components of blood islands derive from epicardial-derived precursors. The authors assume that proepicardial cells include a hemangioblast population. From this observation a conclusion can be drawn that either the proepicardium or the fetal heart exhibits a hematopoietic activity.

Considering the topic of blood island derivation in the embryonic heart I would like to comment that although the derivation of the endothelial cell component in these structures has been proven, the origin of erythrocytes is ambiguous and has not yet been resolved. Quail-chicken chimera and retrovirus-infected proepicardial organ studies revealed that endothelial cells of coronary vasculature derive from the proepicardium and subsequently from the epicardium.1,2,3 Angiogenic potential of the proepicardium has been confirmed several times.4 With regard to derivation of the blood cell component, one of the theories implies that fetal heart hemoblasts (erythroblasts) derive in situ from migrating angioblasts or hemangioblasts.5 This situation would be similar to that seen in developing yolk sac, indicative of the presence of a presumptive hemangioblast.6 An article by Kattan et al7 indicates that commitment to the hematopoietic lineage appears to precede the formation of blood islands in the fetal quail heart. Thus, blood island formation in the avascular embryonic heart derives from systemic circulation (yolk sac) and not at earlier stages of erythroblast differentiation. In fact, the morphological differences between erythroblasts and erythrocytes in birds are possibly not pronounced. Contrary to mammals, in which erythrocytes are enucleated (circulating NRBCs in mice start to lose nuclei on E12), in birds both erythroblasts and erythrocytes contain nuclei. Thus, the heart seems not to be a hematopoietic organ, at least not in mammals. The derivation of NRBCs in blood islands may be different in birds as compared with mammals, or both ways of NRBC derivation are possible: in situ differentiation from hemangioblasts and diapedesis via the endocardium. In either case more studies are required to resolve the ambiguous issue of NRBC origin in the avascular heart and to reconcile these discrepant results.

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