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Vascularity of a Tissue-Engineered Model of Human Phalanges

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Methods for tissue engineering have led to many advances in the growth and development of a variety of cell types on biodegradable scaffolds. Resulting cell-polymer constructs hold great promise ultimately as vehicles for generating new tissue in the human body. As an example in this context, models of human phalanges have been fabricated by suturing three different cell-polymer constructs to produce a distal phalanx, a middle phalanx, and a distal interphalangeal joint [1]. Bovine periosteum, cartilage, and tendon were obtained as a source of osteoblasts, chondrocytes, and tenocytes, respectively. Periosteal sheets were wrapped about a biodegradable co-polymer of polyglycolic acid (PGA) and poly-L-lactic acid (PLLA), and isolated chondrocytes and tenocytes were separately seeded on PGA scaffolds [1]. The three phalanx constructs were cultured for one week and then implanted in athymic (nude) mice for up to 60 weeks. On retrieval of constructs after 20 and 40 weeks of implantation, histology [1] or in situ hybridization [2] showed that bone, cartilage and tendon had developed with intact interfaces between the cell types; models maintained original shapes of human phalanges; a putative cartilaginous growth plate appeared in phalanx models; the initial bovine phenotype of models persisted over time; and the bone of models was vascularized in rudimentary fashion by the host nude mice. The latter observation was investigated more completely by transmission electron microscopy to gain insight into possible means by which phalanx models were supported in their nutrition and growth.

Tissue-engineered middle phalanx constructs were dissected following implantation for 20 weeks in nude mice, fixed in paraformaldehyde, dehydrated in graded ethanols, and embedded in Spurr resin. Thin sections (80 nm) stained with uranyl acetate and lead citrate were examined and photographed in a JEOL 100S electron microscope, operated at 60-80 kV. Microscopy revealed that portions of the periosteum and cancellous bone of middle phalanx models contained capillaries, small muscular arteries, and other vessels demonstrating vascular invasion of the constructs (Figs. 1,2). Erythrocytes within capillaries (Fig. 1) and endothelial and smooth muscle cells adjacent to elastic laminae of small muscular arteries were common (Fig. 2). Collagen fibrils were present as well as macrophages and other cells originating with vasculature and apparently involved in degradation of scaffold polymer (Fig. 1). This electron microscopic evidence shows more definitively than previous histology [1] that vascularity develops from host mice in these tissue-engineered models of human phalanges. Vascularity is accompanied by cells capable of providing oxygen, nutrition and mechanical integrity to the constructs as well as resorption of extraneous polymer components [3].

References

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[2] W. Landis et al., Trans. Fourth Combined Mtg. Orthop. Res. Soc. USA, Canada, Europe, Japan (2001) 197.
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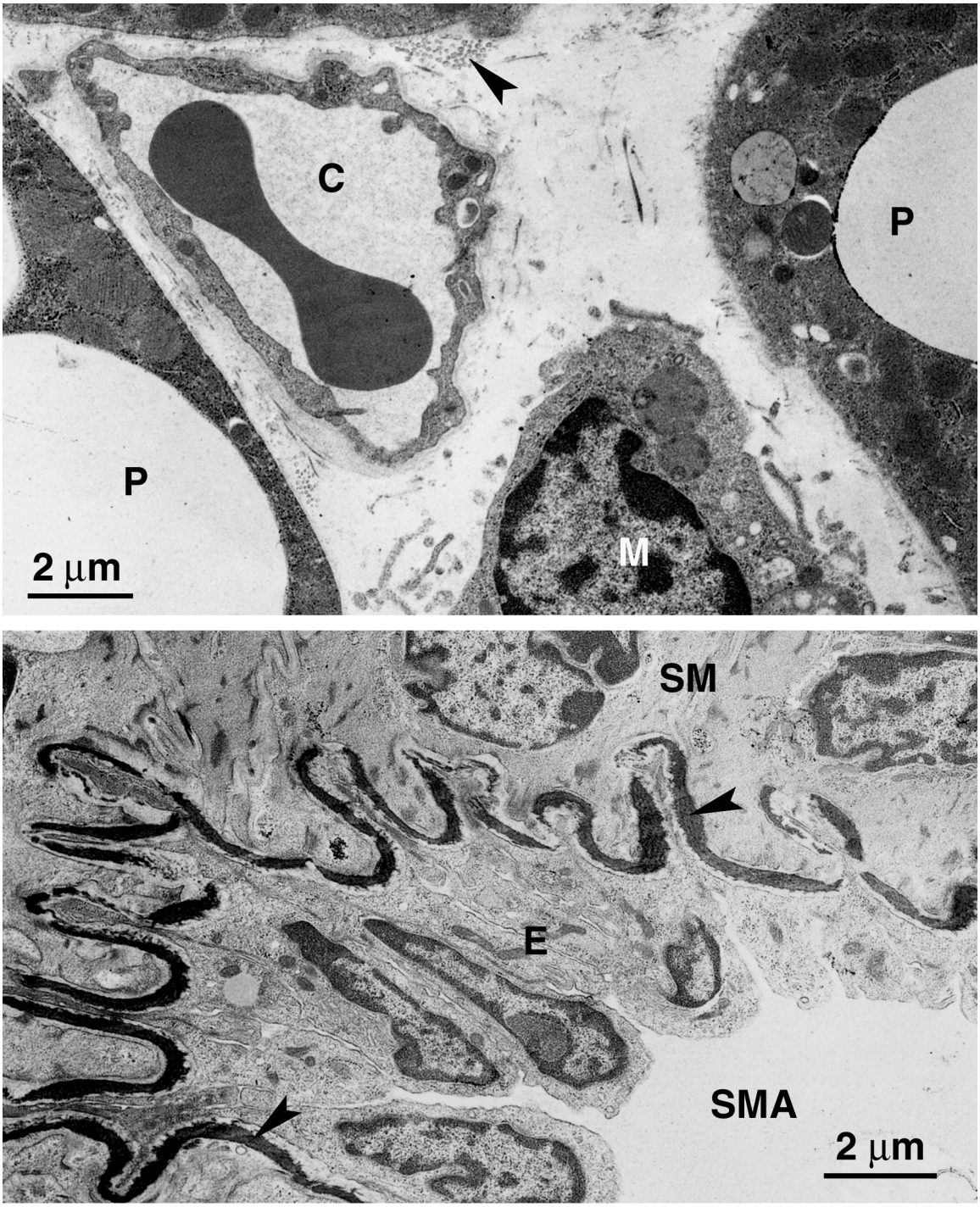

FIG. 1 (top). A middle phalanx showing a capillary (C) containing an erythrocyte in transverse profile, a small cluster of collagen fibrils (arrowhead), and macrophages (M) adjacent to scaffold polymer (P) of the constructs.

FIG. 2 (bottom). Portion of a small muscular artery (SMA) in a middle phalanx construct. Densely stained elastic lamina (arrowheads) is bound by epithelial (E) and smooth muscle (SM) cells.

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