

Ovine Forestomach Matrix (Endoform™) Stimulates Cell Differentiation and Vascularization

Barnaby C. H. May, Stan Lum, Stephanie M. Irvine, Evan Fridlen, Brian R. Ward
Mesynthes Limited, 69 Greendale Road, Lower Hutt 5000, New Zealand

Abstract: We have generated a new biologically-derived extracellular matrix (ECM) termed Endoform™ to meet the need for a natural and emerging tissue for cell differentiation and vascularization. Endoform™ is a natural ECM (ECM) matrix derived from the ovine forestomach. It contains a variety of biological components including fibronectin, GAGs, laminin and EGF2. We have shown that extracts of OFM stimulate differentiation of rat pheochromocytoma cells (PC12), and that the stimulatory effect could be inhibited in part by an anti-EGF2 antibody. OFM produced a dramatic increase in microvasculature in a rat aortic ring study. Further in vivo studies in sheep demonstrated that OFM stimulates cell differentiation and increases the number of microvessels and has promising characteristics for clinical applications.

Summary: Endoform™ is a promising new material for clinical applications in wound care and tissue regeneration. Endoform's properties can be attributed to its complementary biochemical, architectural and biophysical properties, termed authentic complexity, which make it ideally suited for clinical applications.

Biochemical Characterization

The major and minor biochemical components of Endoform and OQS™ were analyzed using established techniques. Endoform was shown to be a rich biological matrix containing connective tissue adhesion and signaling proteins, all of which play central roles in cell adhesion, differentiation and growth. Endoform was also shown to contain a variety of GAGs and heparin. On the whole, Endoform had comparable biochemistry to OQS™ apart from elevated fibronectin concentrations (Table 2).

Table 2 Biochemical components of Endoform and OQS™

Component	Endoform TM (mg/g)	OQS TM (mg/g)	Relative Difference (mg/g)
Collagen I	10.22	9.81	0.41
Collagen III	10.22	9.81	0.41
Collagen IV	10.22	9.81	0.41
Decorin	10.22	9.81	0.41
Heparan sulfate	10.22	9.81	0.41
Fibronectin	10.22	9.81	0.41
Laminin	10.22	9.81	0.41
EGF2	10.22	9.81	0.41
Protein	10.22	9.81	0.41
Water	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Sulfur	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22	9.81	0.41
Iron	10.22	9.81	0.41
Copper	10.22	9.81	0.41
Zinc	10.22	9.81	0.41
Manganese	10.22	9.81	0.41
Selenium	10.22	9.81	0.41
Vanadium	10.22	9.81	0.41
Chlorine	10.22	9.81	0.41
Fluorine	10.22	9.81	0.41
Bromine	10.22	9.81	0.41
Iodine	10.22	9.81	0.41
Strontium	10.22	9.81	0.41
Barium	10.22	9.81	0.41
Lithium	10.22	9.81	0.41
Sodium	10.22	9.81	0.41
Potassium	10.22	9.81	0.41
Calcium	10.22	9.81	0.41
Magnesium	10.22		