

Intestinal Engineering for the Treatment of Pediatric Patients with Short Bowel Syndrome



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INTESTINAL FAILURE

- 40,000 patients in the U.S.
- Gastroschisis, NEC, atresia, volvulus, etc.
- 4 billion dollars for parenteral nutrition
- Liver failure
- Transplantation



Dunn, Nature CPGH, 2008



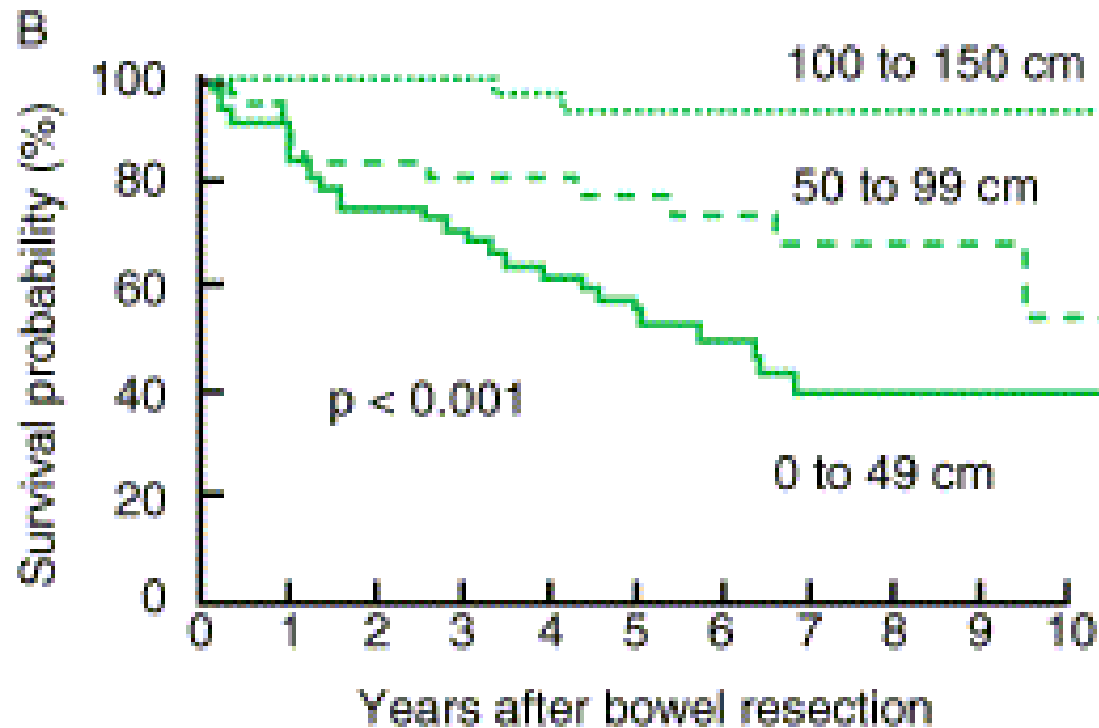
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INTESTINAL LENGTH



Messing et al., Gastroenterology, 1999



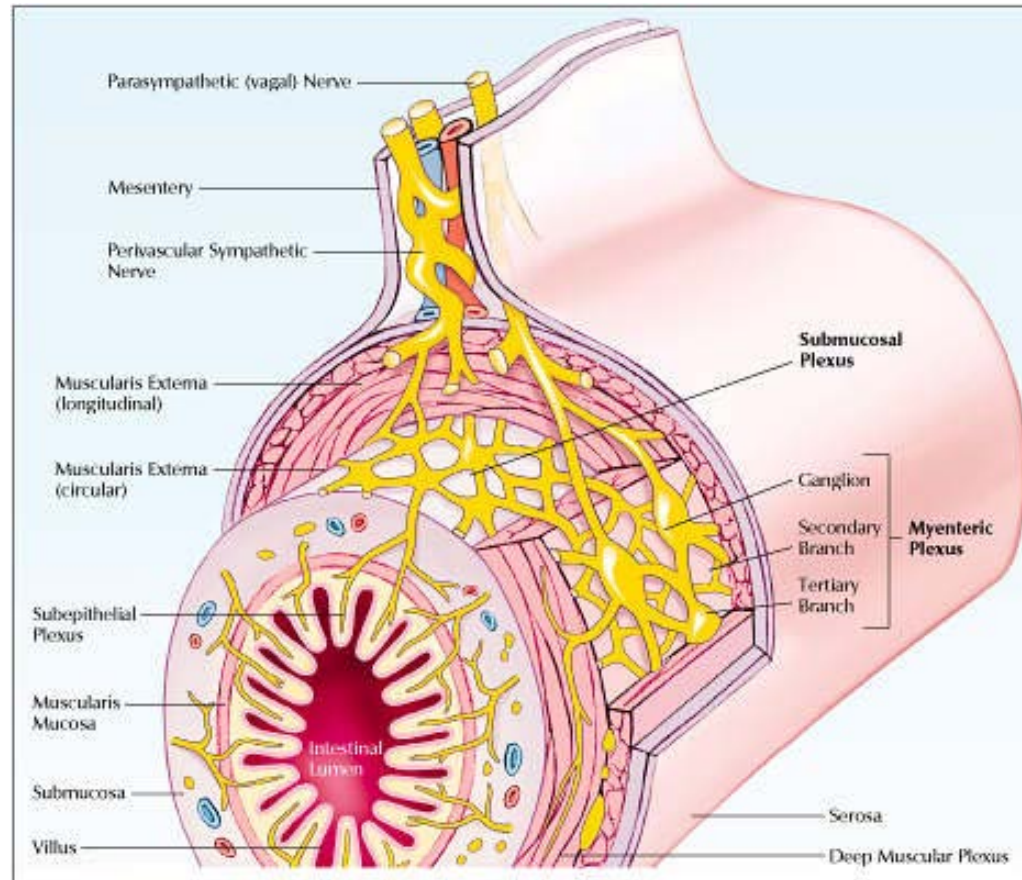
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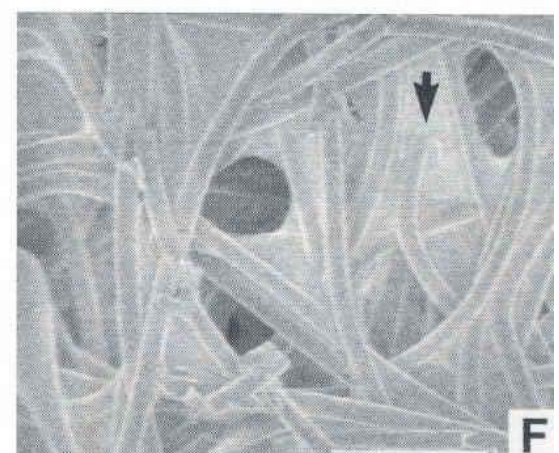
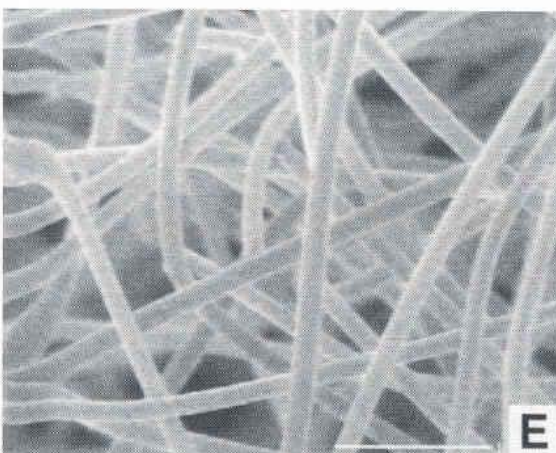
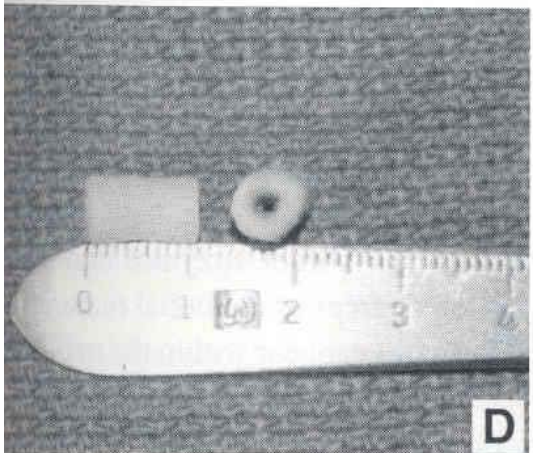
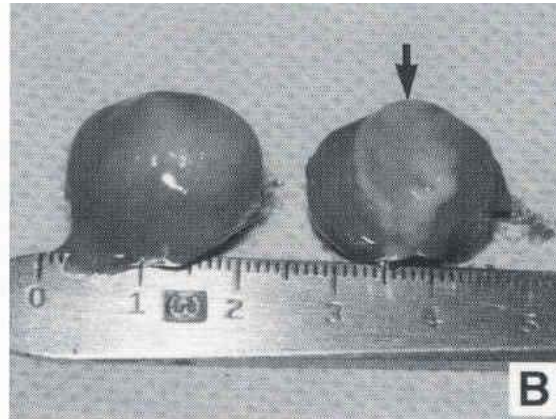
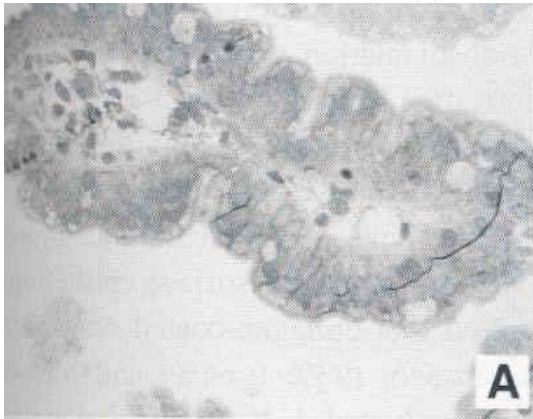


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SMALL INTESTINE



NEONATAL ORGANOID



Choi et al., J Pediatr Surg, 1998

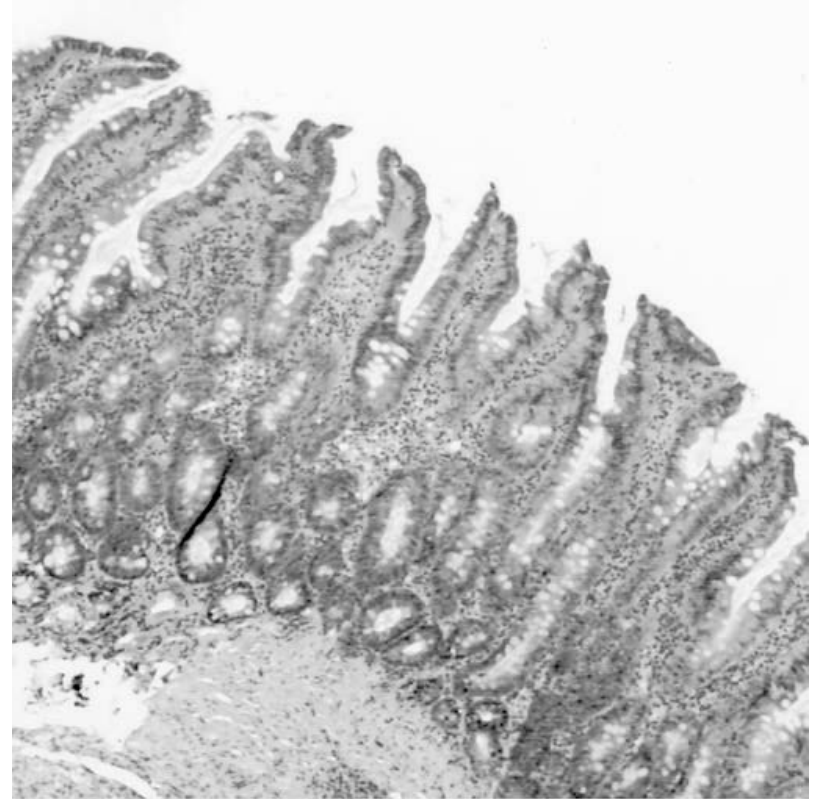


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NEOMUCOSA



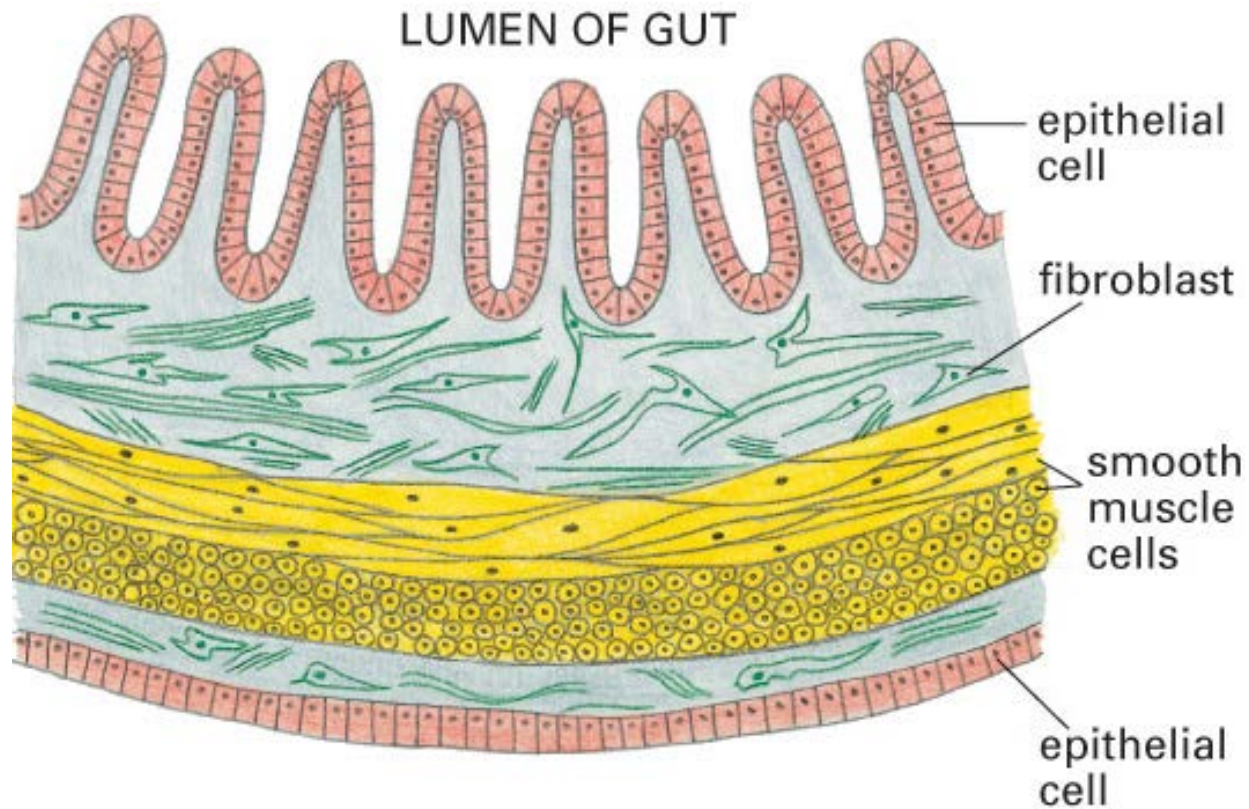
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INTESTINAL LAYERS



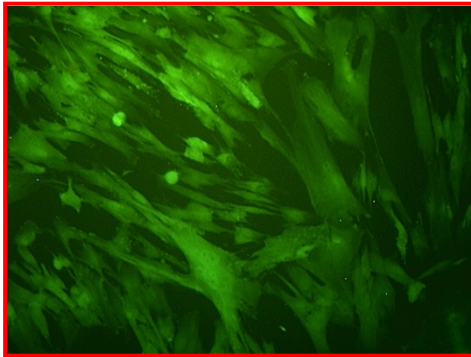
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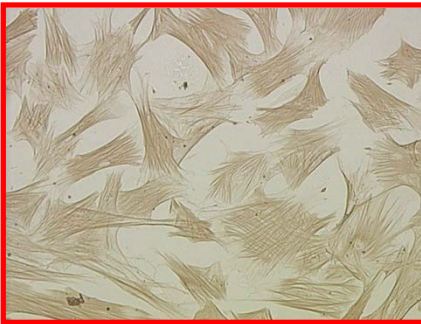
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SMOOTH MUSCLE CELLS



small intestinal smooth muscle cells

GFP-transgenic Lewis rats



Smooth muscle actin



Calponin



Myosin heavy chain

Lee et al., Biomaterials, 2007



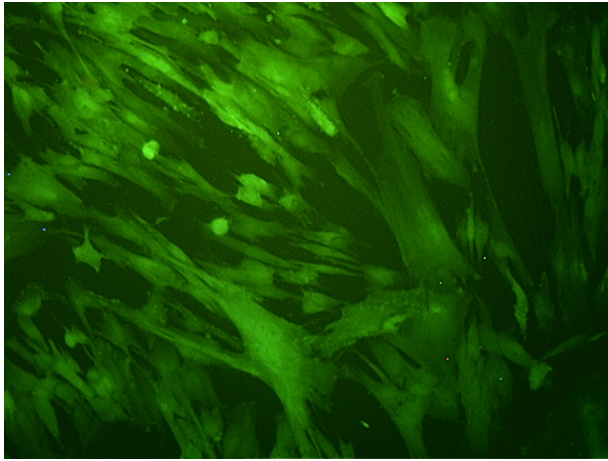
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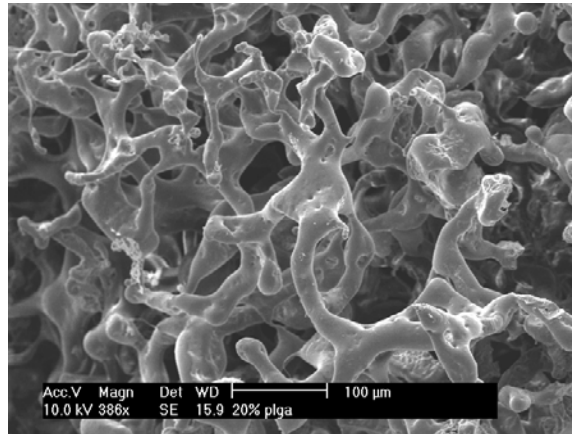
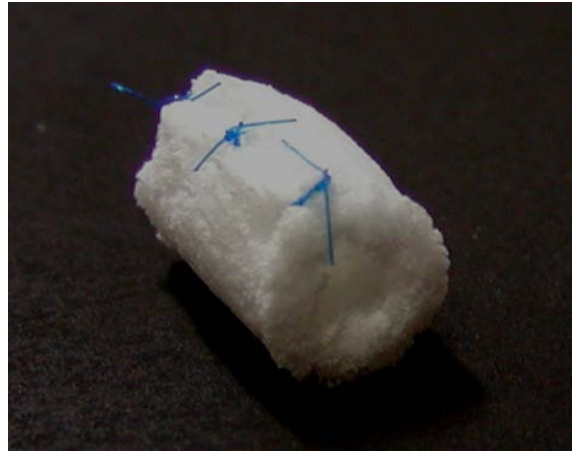


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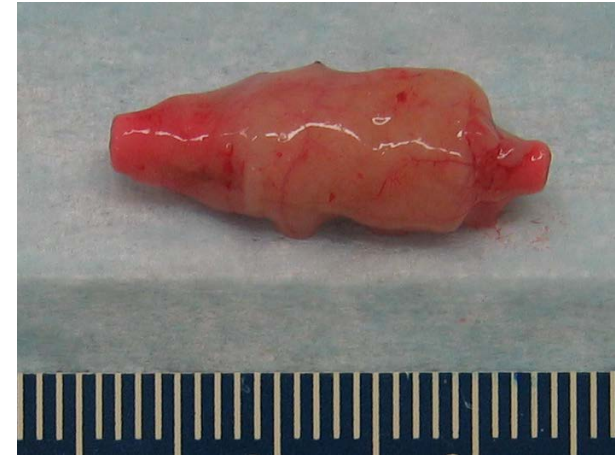
CELL-SCAFFOLD IMPLANT



Smooth muscle cells



Porous scaffold



Implantation



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GFP TRACKING

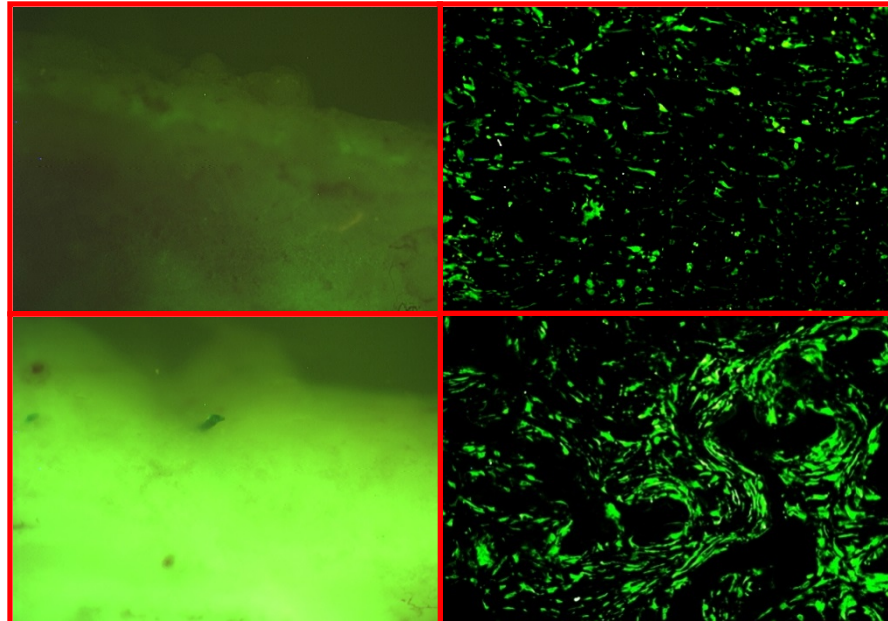


4 days

14 days

fluorescence

anti-GFP



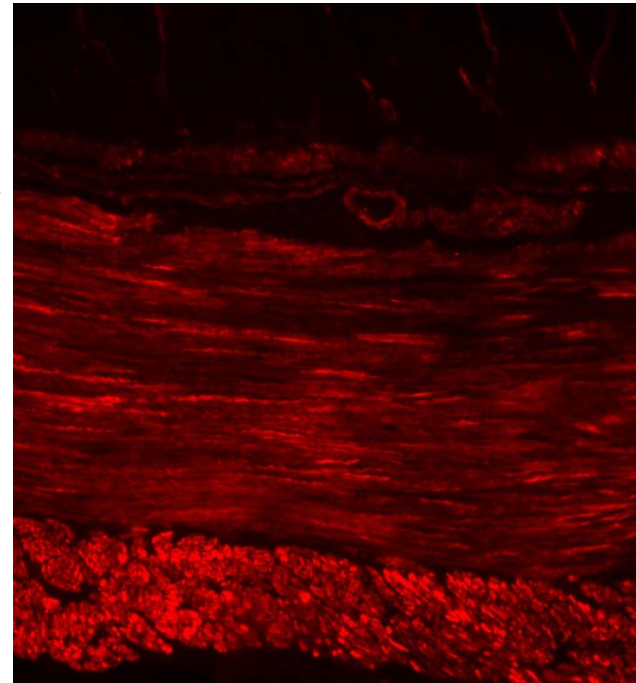
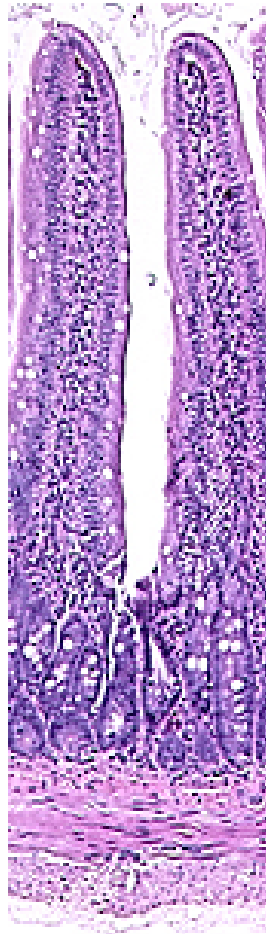
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ORTHOGONAL ORIENTATION



anti-SMA



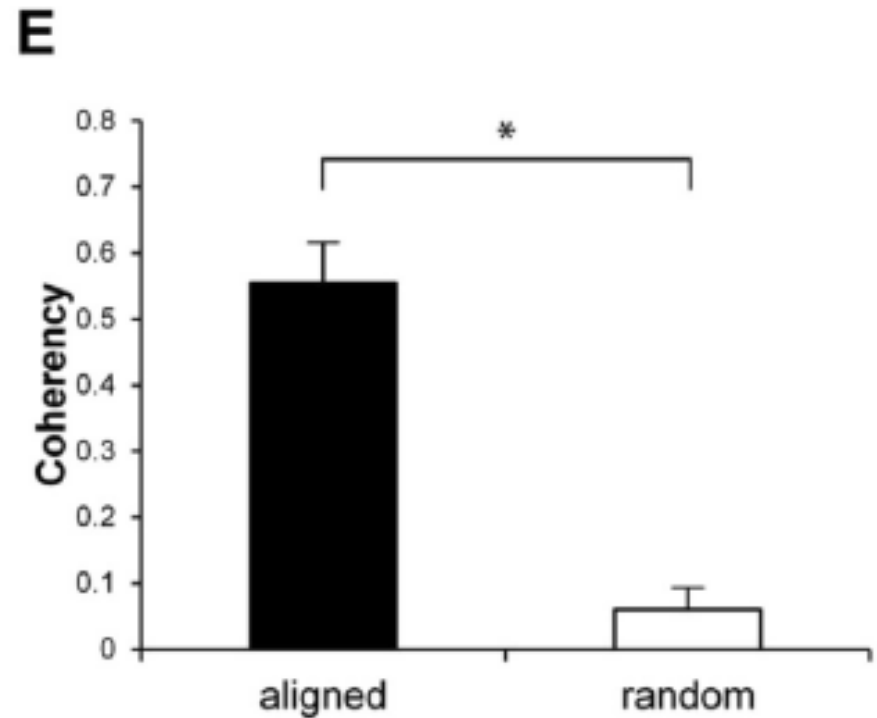
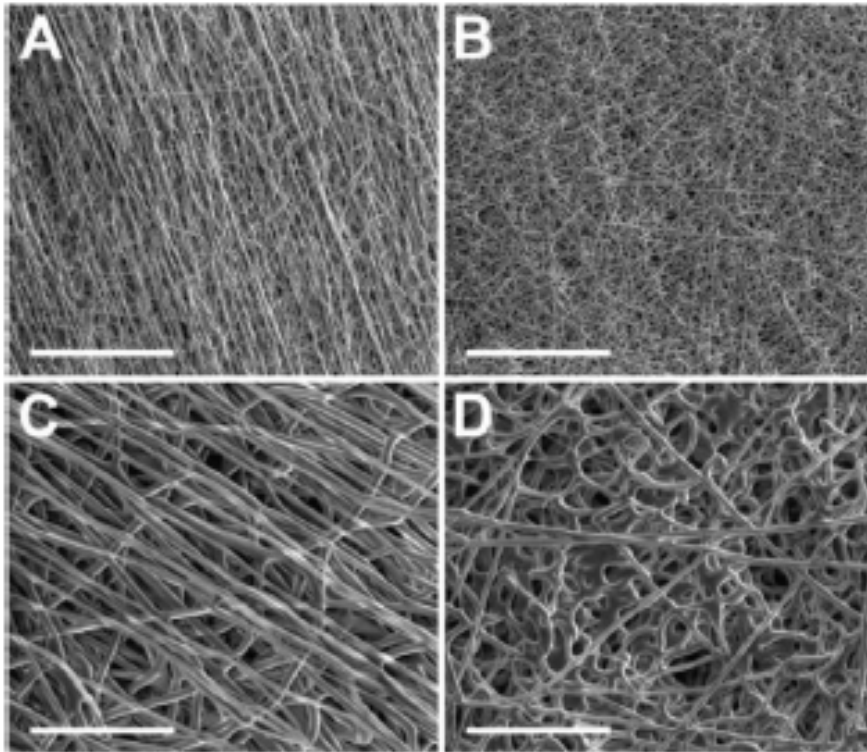
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ORIENTED FIBERS



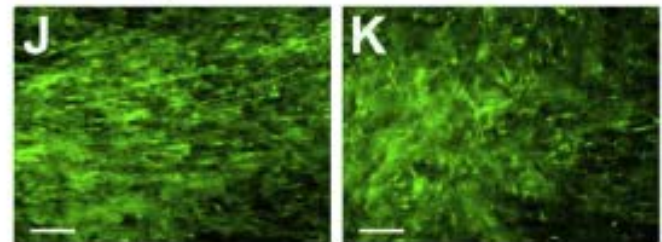
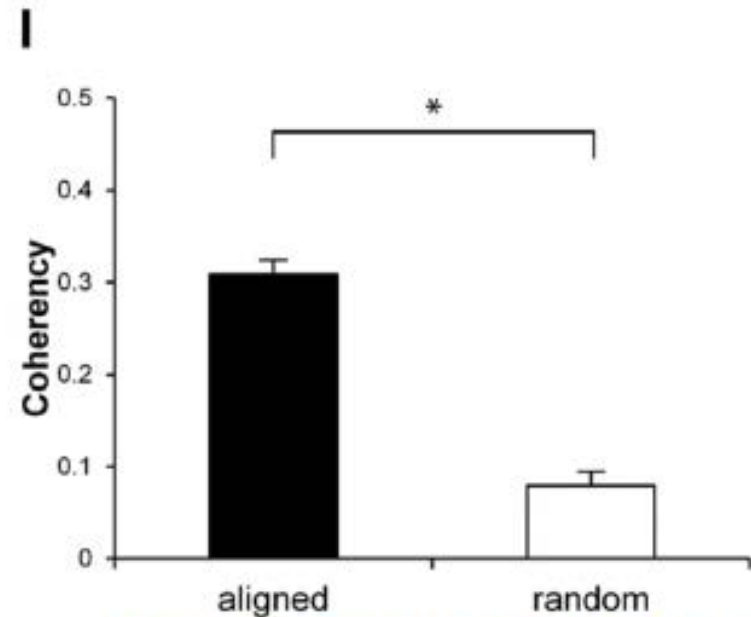
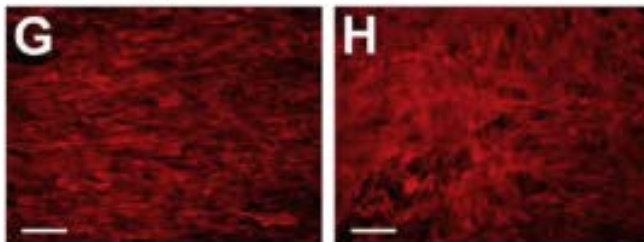
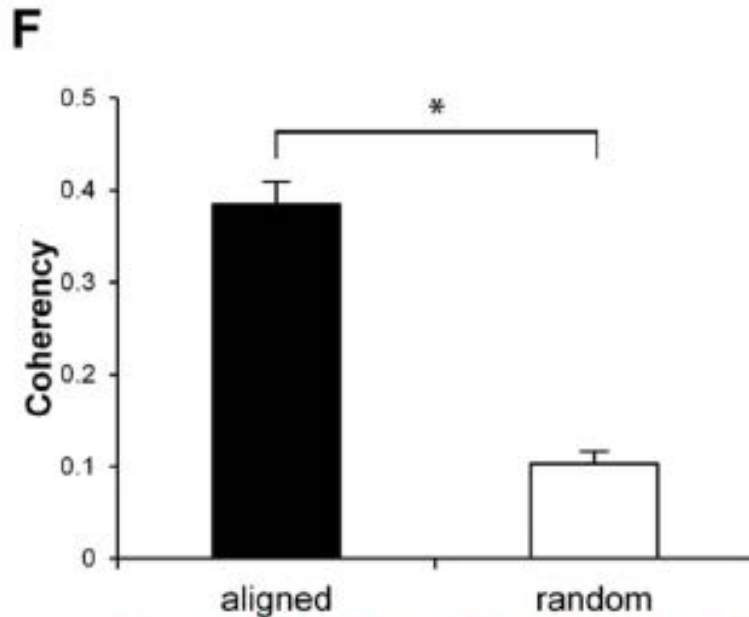
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ALIGNED CELLS

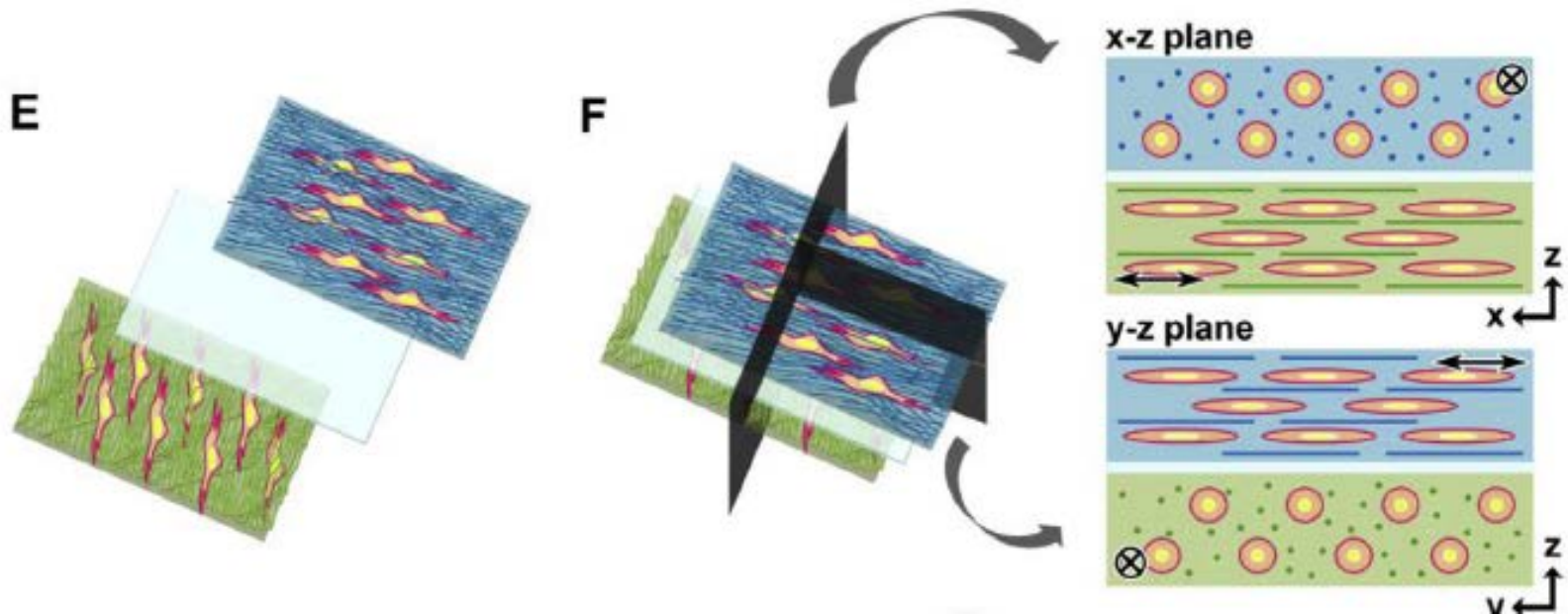


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ORTHOGONAL FIBERS



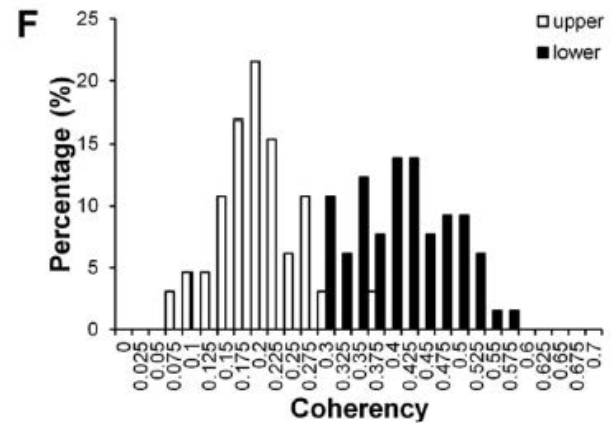
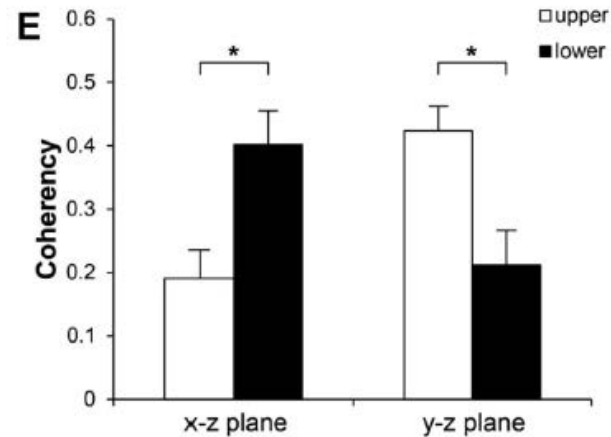
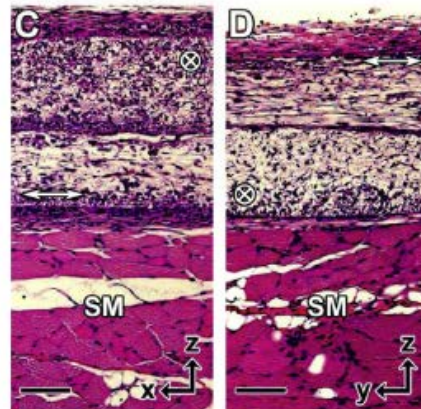
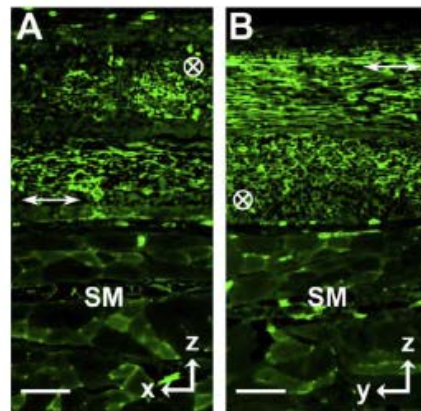
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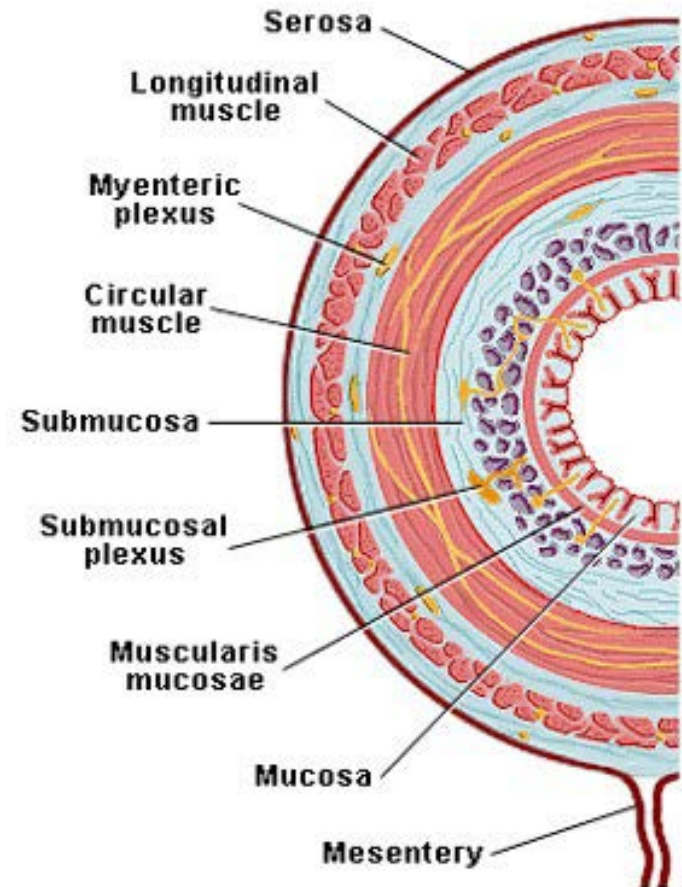
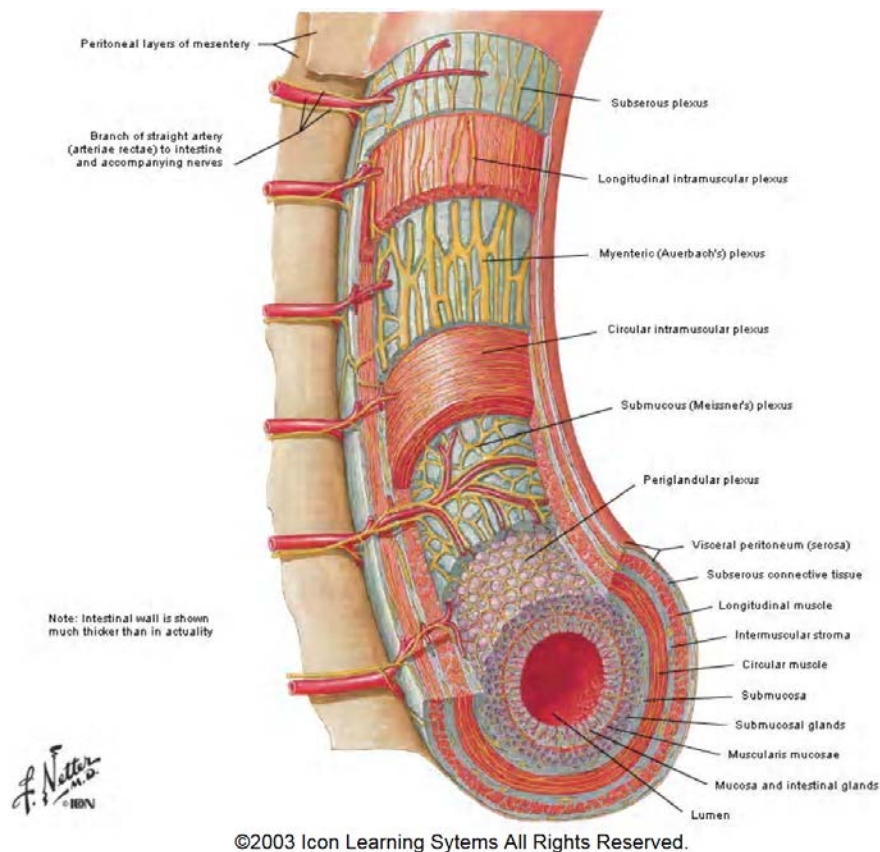


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ORTHOGONAL LAYERS



MULTIPLE LAYERS



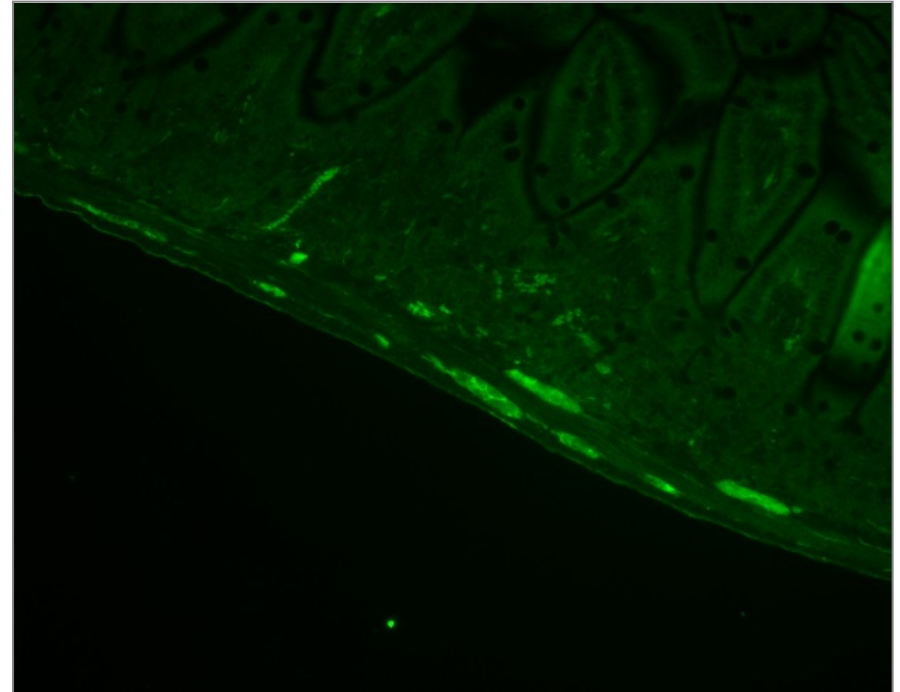
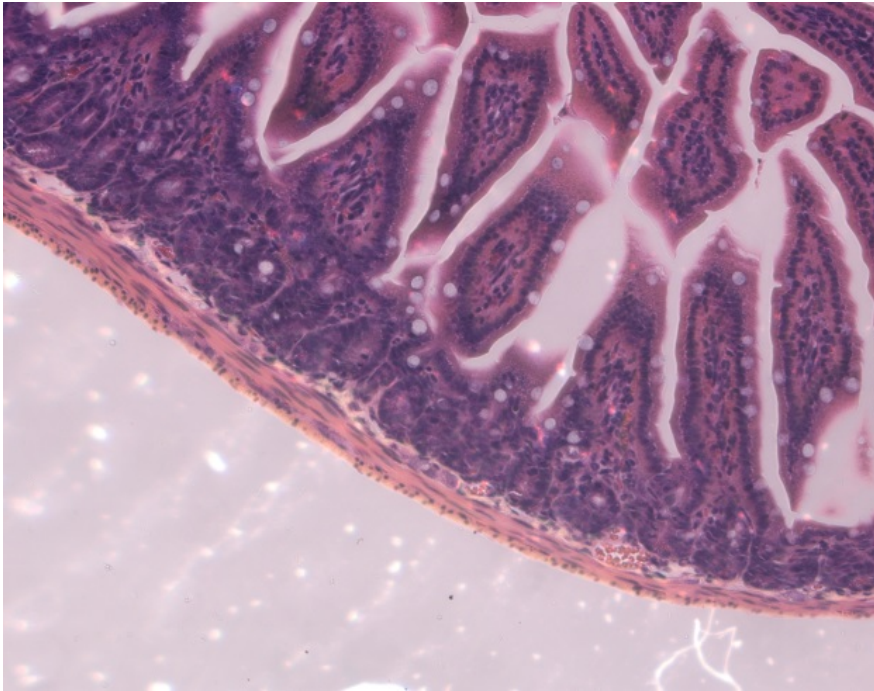
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ENTERIC NERVOUS SYSTEM



anti-peripherin



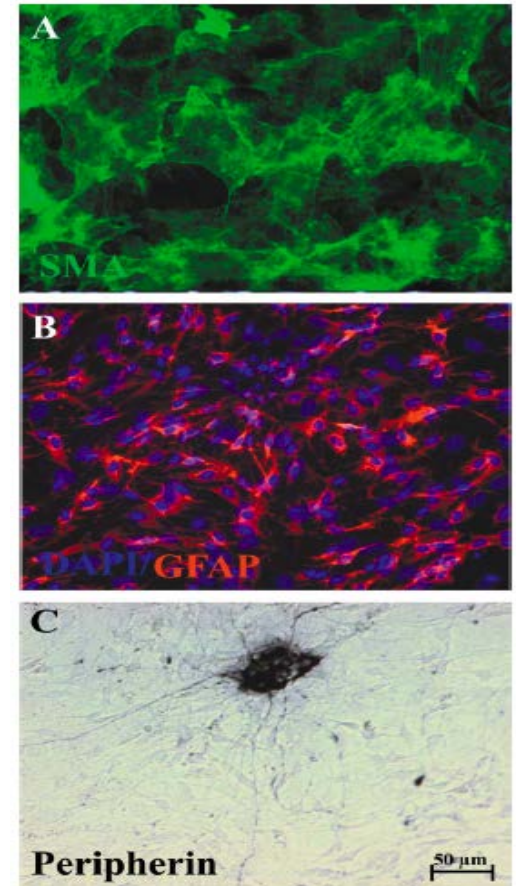
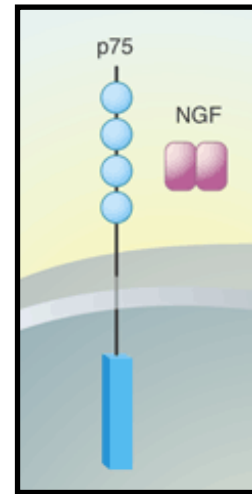
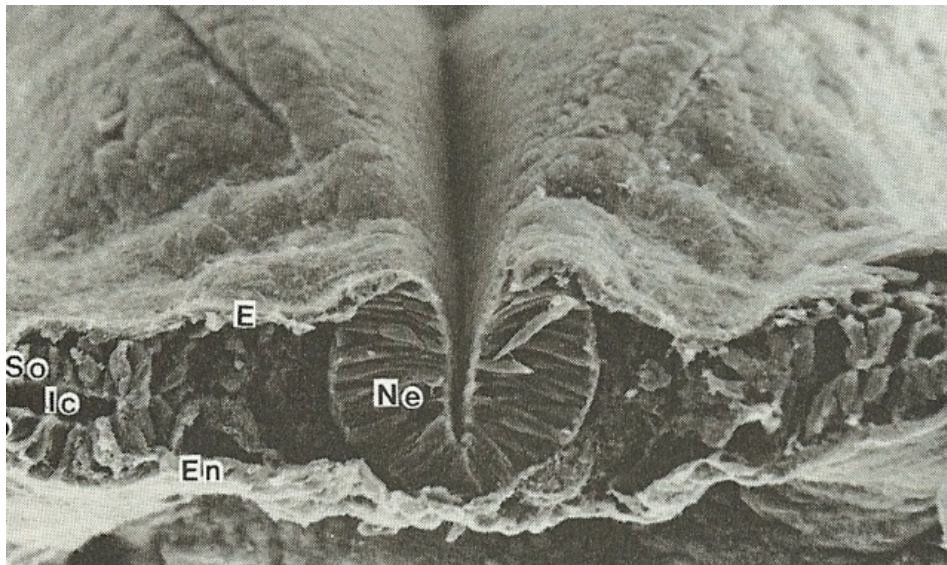
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NEURAL CREST STEM CELLS



Kruger et al., Neuron 35, 2002



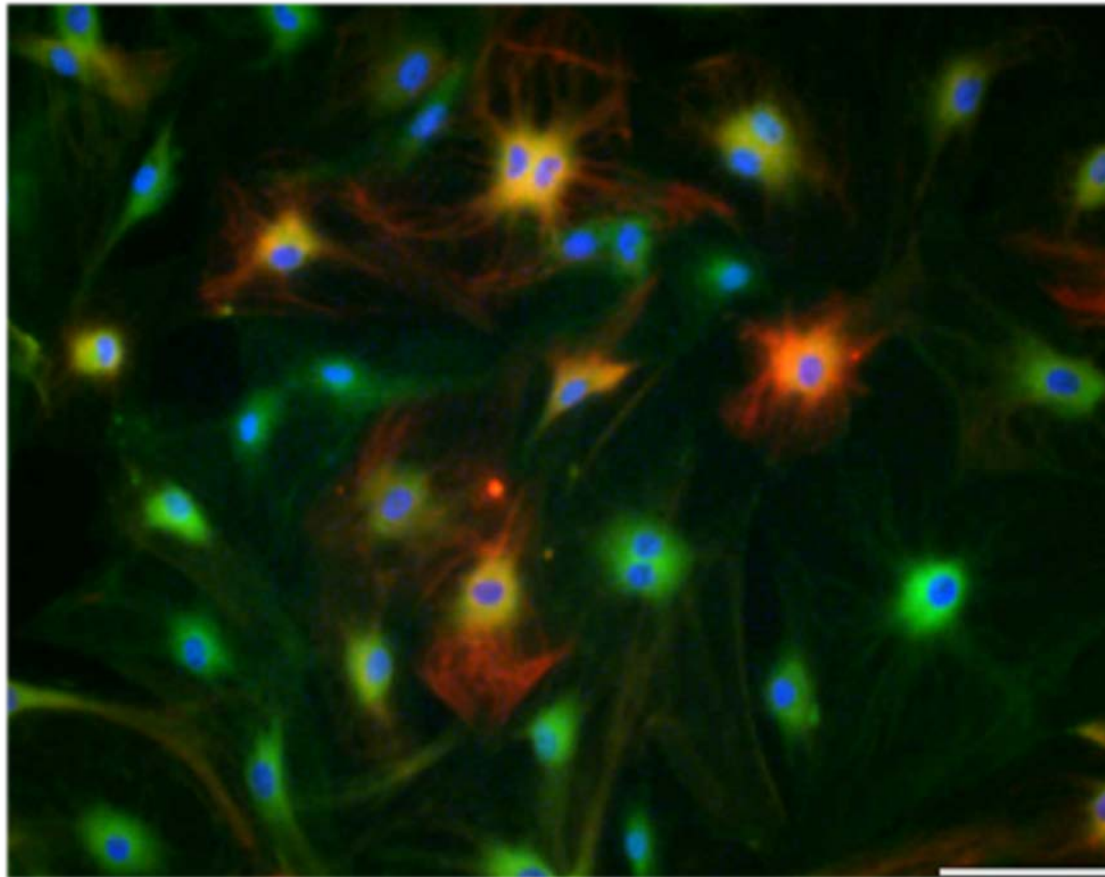
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SKIN-DERIVED PRECURSORS

DAPI
S100
Nestin



scale bar = 100 μ m



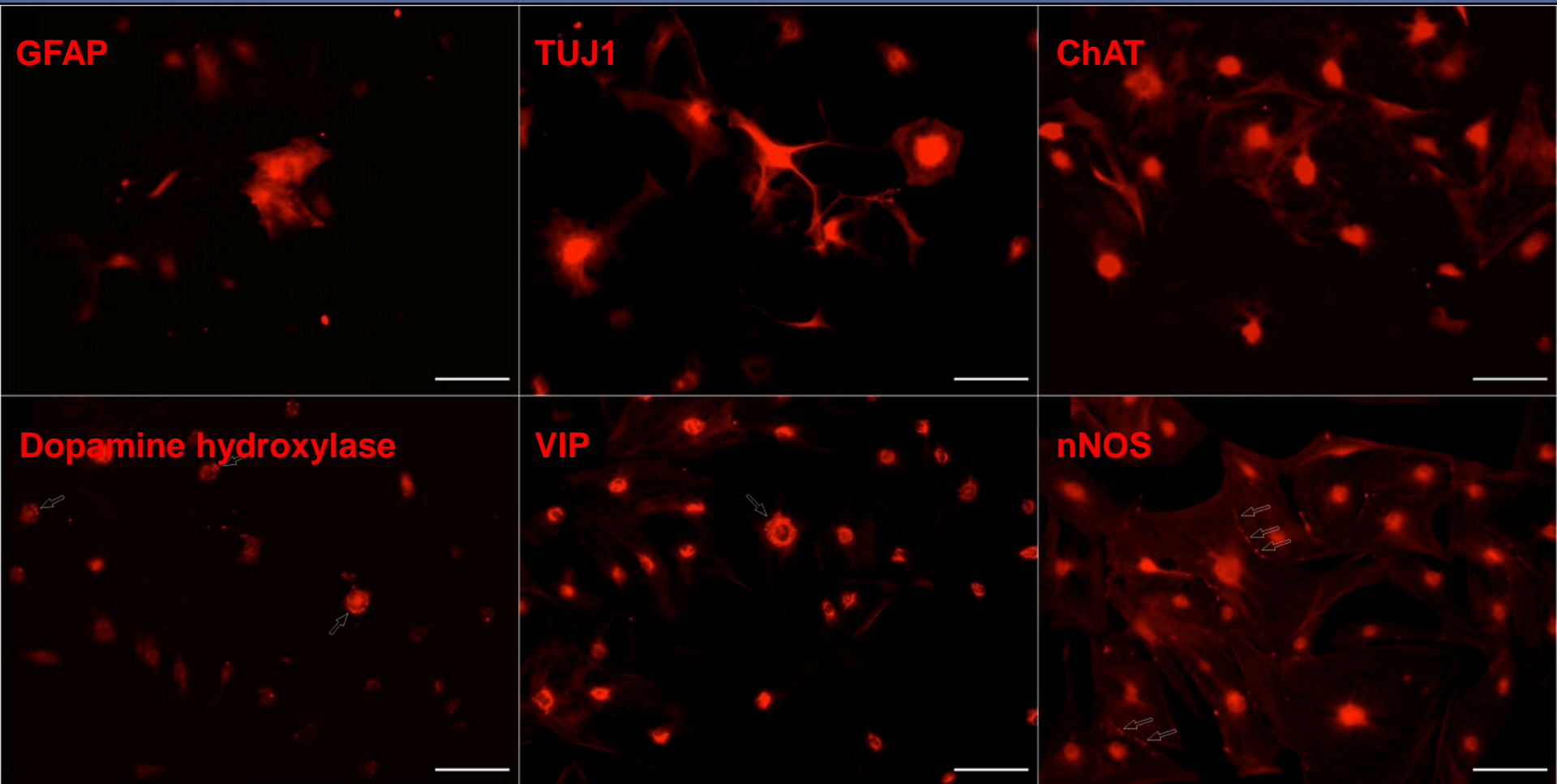
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SKP DIFFERENTIATION



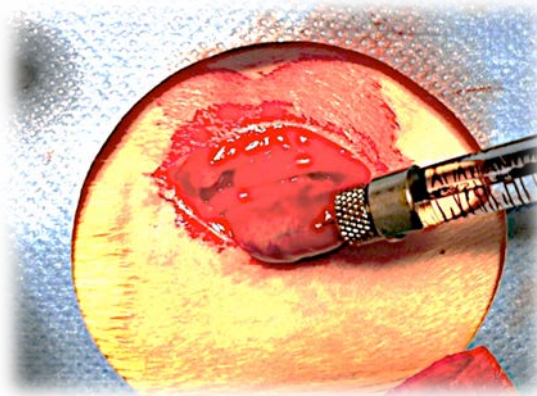
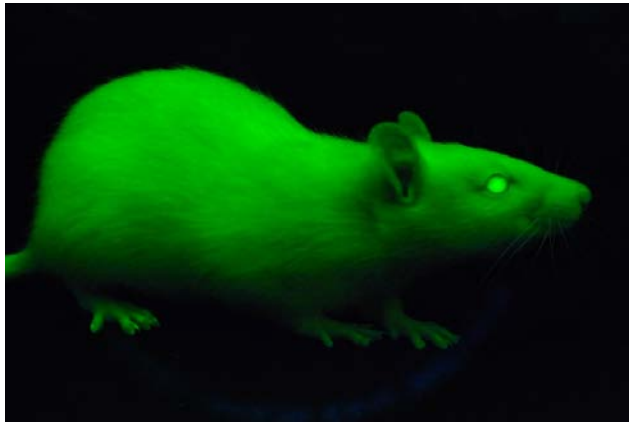
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SKP DELIVERY



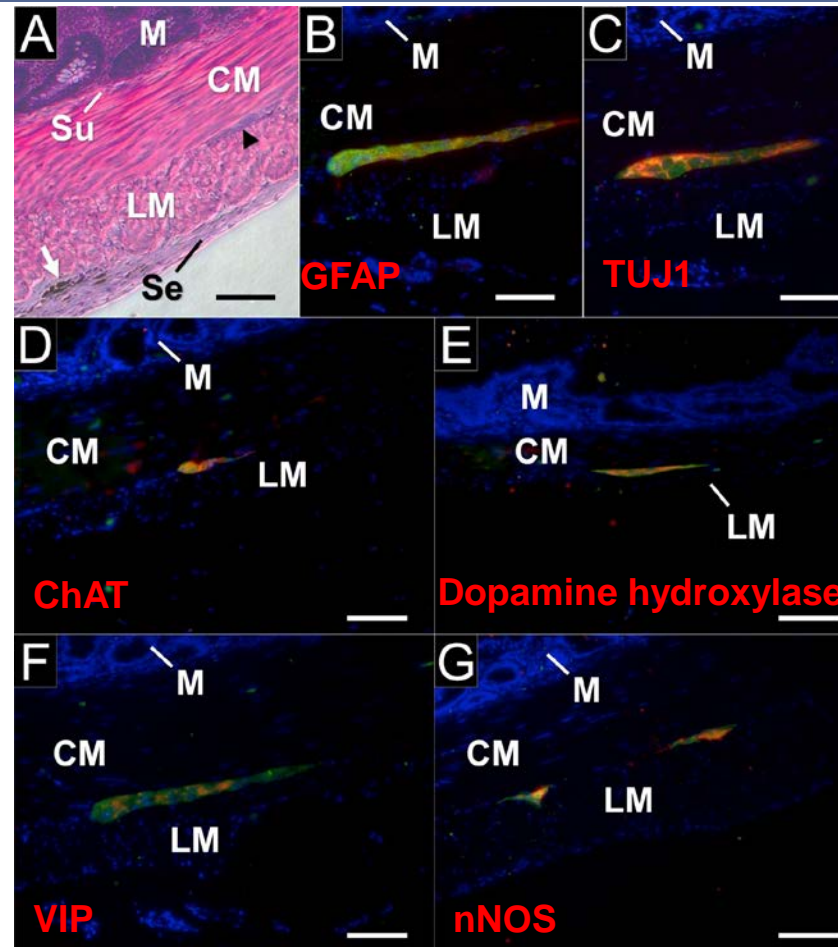
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GANGLIA FORMATION



GFP

DAPI



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SUMMARY

- Intestinal tissue regeneration is possible.
- More components are needed.
- Integrate with recipient's circulation.



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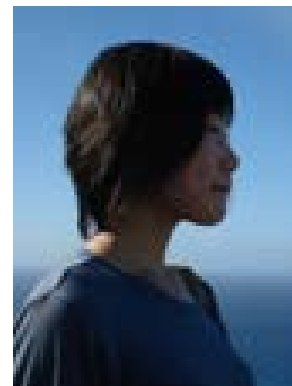
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