Short-term and long-term human or mouse organoid units generate tissue-engineered small intestine without added signalling molecules.

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Public Summary:
NEW FINDINGS: What is the central question of this study? Tissue-engineered small intestine was previously generated in vivo by immediate implantation of organoid units derived from both mouse and human donor intestine. Although immediate transplantation of organoid units into patients shows promise as a potential future therapy, some critically ill patients might require delayed transplantation. What is the main finding and its importance? Unlike enteroids, which consist of isolated intestinal crypts, short- and long-term cultured organoid units are composed of epithelial and mesenchymal cells derived from mouse or human intestine. Organoid units do not require added signalling molecules and can generate tissue-engineered intestine in vivo. ABSTRACT: Mouse and human postnatal and fetal organoid units (OUs) maintained in either short-term culture (2 weeks) or long-term culture (from 4 weeks up to 3 months) without adding exogenous growth factors were implanted in immunocompromised mice to form tissue-engineered small intestine (TESI) in vivo. Intestinal epithelial stem and neuronal progenitor cells were maintained in long-term OU cultures from both humans and mice without exogenous growth factors, and these cultures were successfully used to form TESI. This was enhanced with OUs derived from human fetal tissues. Organoid unit culture is different from enteroid culture, which is limited to epithelial cell growth and requires supplementation with R-Spondin, noggin and epidermal growth factor. Organoid units contain multiple cell types, including epithelial, mesenchymal and enteric nervous system cells. Short- and long-term cultured OUs derived from mouse and human intestine develop into TESI in vivo, which contains key components of the small intestine similar to native intestine.

Scientific Abstract:
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