Docket #: S06-394

Ex vivo expansion and culture of intestinal epithelium

Stem cells are generally influenced by a microenvironmental niche, typically comprised of epithelial and mesenchymal cells and extracellular substrates. Many attempts have been made to produce culture systems that mimic normal intestinal epithelial growth and differentiation. The tissue is largely inaccessible for experimental manipulation and time-series observation; thus, a long-term methodology will future investigations of intestinal biology.

The Kuo lab at Stanford have developed the first robust method for the culture, proliferation and expansion of intestinal epithelium for greater than 140 days. The technique faithfully recapitulates numerous features of intestinal growth *in vivo*, including cellular ultrastructure, presence of enterocytes, goblet and enteroendocrine cells, and Wnt-dependent proliferation. The technology could be used for autologous transplant, cell therapy, and tissue engineering to treat patients with intestinal failure. In addition, the invention could be applied to drug development - for developing either a culture system to conduct ADME (Absorption, Distribution, Metabolism and Excretion) studies on new drug candidates or an *in vitro* model for testing therapeutic agents against intestinal pathogens.

Applications

- **Intestinal transplantation** - grow tissue from autologous cultures or ES cells for treatment of intestinal failure
- **ADME studies** - culture system for absorption, distribution, metabolism and excretion studies of new drug candidates
- **Gene therapy delivery system**
- **Anti-infective drug screening** - cultured epithelium could be used to create an *in vitro* model to test therapeutic agents against intestinal pathogens

Advantages

- **Long term culture** - epithelium can be grown for over 140 days, previously primary intestinal epithelium has only been able to be cultured for 1-2 days.
- **Recapitulates features of *in vivo* tissue:**
  - cellular ultrastructure
  - enterocytes
  - goblet and enteroendocrine cells
  - Wnt-dependent proliferation

Publications

- Ootani A, Li X, Sangiorgi E, Ho QT, Ueno H, Toda S, Sugihara H, Fujimoto K, Weissman IL, Capecchi MR, Kuo CJ. Sustained in vitro intestinal epithelial culture within a Wnt-dependent stem cell niche. Nat Med. 2009 Apr 27.

Patents

- Published Application: 20100047853
- Published Application: 20150344849
- Issued: 9,464,275 (USA)
- Issued: 10,704,026 (USA)

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