

Resource Summary Report

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An organotypic slice model for ex vivo study of neural, immune, and microbial interactions of mouse intestine

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Protocol Information

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Summary: Organotypic tissue slices provide seminatural, three-dimensional microenvironments for use in ex vivo study of specific organs and have advanced investigative capabilities compared with isolated cell cultures. Several characteristics of the gastrointestinal tract have made in vitro models for studying the intestine challenging, such as maintaining the intricate structure of microvilli, the intrinsic enteric nervous system, Peyer's patches, the microbiome, and the active contraction of gut muscles. In the present study, an organotypic intestinal slice model was developed that allows for functional investigation across regions of the intestine. Intestinal tissue slices were maintained ex vivo for several days in a physiologically relevant environment that preserved normal enterocyte structure, intact and proliferating crypt cells, submucosal organization, and muscle wall composition. Cell death was measured by a membrane-impermeable DNA binding indicator, ethidium homodimer, and less than 5% of cells were labeled in all regions of the villi and crypt epithelia at 24 h ex vivo. This tissue slice model demonstrated intact myenteric and submucosal neuronal plexuses and functional interstitial cells of Cajal to the extent that nonstimulated, segmental contractions occurred for up to 48 h ex vivo. To detect changes in physiological responses, slices were also assessed for segmental contractions in the presence and absence of antibiotic treatment, which resulted in slices with lesser or greater amounts of commensal bacteria, respectively. Segmental contractions were significantly greater in slices without antibiotics and increased native microbiota. This model renders mechanisms of neuroimmune-microbiome interactions in a complex gut environment available to direct observation and controlled perturbation.

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