Public Abstract

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Title:COMPLEX MICROBIOTA TARGETED REDERIVATION (CMTR) AS AN ALTERNATIVE METHOD TO STUDY EFFECT OF GUT MICROBIOTA ON HOST PHYSIOLOGY

Rodent models are invaluable tools to study the effects of differing gut bacteria (microbiota) on health and disease. To assess the role of gut microbiota (GM) on mouse model disease outcome, a process known as complex microbiota targeted rederivation (CMTR) can be used. With CMTR, embryos from mice of the desired model are surgically transferred into surrogate dams with GM that differs in composition. Unfortunately, differing GM are often present in inbred strains of mice complicating CMTR as these mice frequently have small litter sizes and variations in maternal care which can add unwanted experimental variables. To overcome this, we exploited the benefits of outbred mice as surrogates by establishing colonies of outbred CD1 mice with differing GM profiles. CD1 embryos were transferred into CD1 or C57BL/6 surrogate dams that varied by GM composition and complexity to establish three separate mouse colonies. Using targeted next generation sequencing, female offspring were shown to have similar GM profiles to surrogate dams. Breeding colonies of CD1 mice with distinct GM profiles were maintained for four generations, demonstrating stability of GM profiles within these colonies. We then compared changes in disease outcome of B6 IL-10-/- and C3H IL-10-/- mouse models of inflammatory bowel disease by using either CD1 colonies or the inbred strains from which the colonies were derived. Disease pathology of the cecum and colon were assessed and found to be significantly different between groups depending on GM profile, but no differences were seen when surrogate source of GM (CD1 vs inbred strain) was compared. These findings underscore that CMTR using outbred CD1 colonies will be an invaluable experimental resource for experiments desiring to assess the role of complex microbiota on model phenotypes.