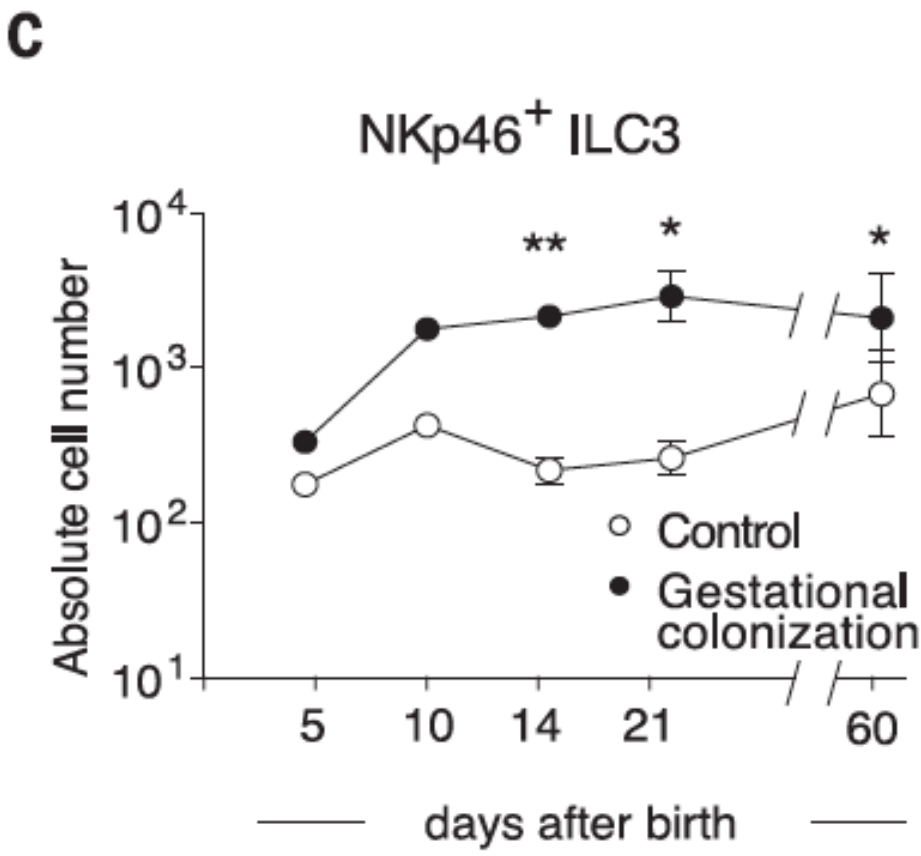

Caption: The numbers of an innate lymphoid cell, known as NKp46+ ILC3, found in the small intestines of recently born, germ-free mouse pups at various time points after birth. Shaded circles represent pups that gestated inside initially germ-free mothers whose intestines were temporarily exposed to a strain of E. coli during mid-pregnancy (=gestational colonization). Unshaded circles represent controls that gestated inside mothers that remained germ-free throughout pregnancy. Each point represents the mean cell number found in a group of 3-10 pups (+/- one standard deviation). A single star * indicates that the difference between the control and experimental groups has a p-value ≤ 0.05 and two stars ** represent a p-value ≤ 0.01.

BACKGROUND INFORMATION

In placental animals, a fetus develops in an almost sterile environment during gestation and typically remains separated from live microbes until birth. After birth, the intestines and other body surfaces become rapidly colonized with a community of largely benign microbes (the microbiota). It has therefore long been assumed that the influence of the microbiota on the development of the immune system does not begin until after birth when newborns come into contact with live microbes in the environment. Scientists challenged this idea by investigating whether microbial colonization of mothers during gestation influences the immune system development of their offspring. Their hypothesis is that bacterial-derived metabolites from the maternal microbiota reach the fetus (through the placenta) and the newborn (through the milk during lactation), impacting the immune system development of the offspring.

In this study, scientists compared the offspring of two groups of mice, one in which the mothers were kept germ-free throughout pregnancy, and the other in which the mother was germ-free before the pregnancy and was exposed to a strain of *E. coli*, called HA107, in the intestine during mid-pregnancy (gestational colonization). The HA107 strain is engineered to linger in the intestinal tract only temporarily. As a result, the mothers that were exposed to HA107 during pregnancy became germ-free again before their pups were born. To confirm that pups were not exposed to live HA107 or any other bacteria, the scientists tested the mothers' placentas and their newborn pups and found no live bacteria.

By analyzing different types of immune cells populating the intestines of the pups for 60 days after birth, the scientists hoped to discover whether the bacterial exposure of the mothers' intestines during pregnancy influences the development of the pups' immune systems. One of these immune white blood cell (leukocyte) types that they investigated is a subset of the innate lymphoid cell population known as NKp46+ ILC3 (hereafter ILC3). These cells produce and release cytokines, which are small proteins that regulate the function of other immune cells and play an important role in establishing and maintaining the intestinal homeostasis and its relationship with the microbiota. The pups were weaned from their mothers' milk at 25 days, so by sampling for 60 days, they were testing whether the effect on the immune system was persistent.