

# Researchers study pre- and probiotic use in premature infants for a deadly intestinal disease

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Scientists at UC Davis will launch a groundbreaking study to determine the best cocktail of pre- and probiotic supplements to give to premature infants to prevent a deadly intestinal disease. Probiotics are live, beneficial microorganisms that confer health benefits, like the live bacteria in yogurt. Prebiotics are sugars that stimulate the growth of these bacteria.

The study is a novel approach to the primary prevention of necrotizing enterocolitis (NEC), the third-leading cause of death among preemies.

"It would be wonderful to be able to find a way to prevent this debilitating disease in infants and we believe that probiotics are a safe and effective way to do that," said study co-principal investigator Mark Underwood, an assistant clinical professor of neonatology at UC Davis Children's Hospital.

The study is unique because it will combine the expertise of neonatologists at UC Davis Children's Hospital with the expertise of researchers on the UC Davis campus in the departments of chemistry and viticulture and enology who specialize in research on the bacteria enriched by human milk.

The babies in the study will receive doses of both pre- and probiotic supplements identified by UC Davis milk researcher Carlito Lebrilla, a

professor of chemistry, and David Mills, a microbiologist and professor of viticulture and enology.

Lebrilla, a chemist, identified the prebiotics in human milk, called oligosaccharides, and described their structure.

Microbiologist Mills has found that these sugars stimulate the growth of healthy bacteria, called bifidobacteria, in the intestine. Bifidobacteria normally flourish in gastrointestinal tract of healthy breast-fed infants.

"Certain bifidobacteria are amazingly adept at breaking down and consuming these complex oligosaccharides from milk," Mills said.

Lebrilla and a group of scientists at UC Davis have been examining the components of human milk that previously had no known nutritional value to the infant. It now appears that the purpose of these milk components is to nourish healthy bacteria in the intestine.

"That seems to one of their main functions," Lebrilla said. "If you feed the prebiotics, or oligosaccharides, to unhealthy bacteria they won't eat it."

Lebrilla said that the purpose of the healthy bacteria in the intestine is not known. But one idea is that they simply block the proliferation of unhealthy bacteria, he said.

"The beauty of this collaboration is that we can go from fundamental research to clinical trials quickly because we have all the expertise at UC Davis," Lebrilla said.

In the study, preemies in the UC Davis Children's Hospital Neonatal Intensive Care Unit will receive the oligosaccharides and two different types of bifidobacteria twice a day from birth until their discharge from

the hospital. Researchers will examine saliva and other specimens to see what dose, type and combination of the pre- and probiotics work best to grow healthy bacteria.

"I don't think you could have put together a research group like this together anywhere else in the country," Underwood said. "This could only happen at UC Davis."

The cause of NEC is unknown. The disease doesn't occur often in healthy full-term infants and is seen less in premature babies who receive breast milk. However, 10 percent of preemies get NEC and of those, 40 percent die.

Scientists think NEC may be caused by exposure to disease-causing bacteria rather than healthy bacteria.

"Healthy babies are held, kissed, breast-fed and get good bacteria from their mothers and fathers. Preemies live in hospitals and can't be held because they're too fragile. They get colonized with unhealthy bacteria. We think that makes them sick," Underwood said.

Infants born at between 24 to 33 weeks gestation and weighing less than 1,500 grams — under three pounds — are considered premature and spend months in the hospital. About 13 percent of U.S. infants were born prematurely in 2006.

The NEC study is funded by a five-year, \$3 million grant from the Eunice Kennedy Shriver National Institute of Child Health and Human Development and the National Institute of Allergy and Infectious Disease.

The grant will also fund research to identify the role that "defensins," protein-like molecules that act as natural antibiotics in the body, play in

NEC. Defensins are found in every species of plant and animal and, in humans, on the skin, in white blood cells, and the linings of the surfaces of the eyes, ears, mouth, nose, intestines, lungs and urinary tract.

Charles Bevins, a professor in the Department of Medical Microbiology and Immunology, has found that premature infants have low levels of defensins in the intestinal tract. Bevins will research whether premature infants with the lowest levels of defensins are at greatest risk of getting NEC.

Source: University of California - Davis

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