From: [redacted]
Sent: Friday, July 18, 2014 2:42 AM
To: Jeffrey Epstein
Subject: interesting study - microbiome

Sean Davies, Ph.D., =enter, Zhongyi Chen, M.D., Ph.D., left, and Lilu Guo, Ph.D., are =tudying using bacteria as a therapeutic compound in the gut to =ounteract the effects of a high-fat diet. (photo by Joe =owell)

Regulatory issues must be addressed before moving to =uman studies, Davies said, but the findings published in the August =ssue of theJournal of Clinical =nvestigation <http://www.jci.org/articles/view/72517> suggest that it may be possible to =anipulate the bacterial residents of the gut – the gut microbiota — =o treat obesity and other chronic diseases.

Davies has a =ong-standing interest in using probiotic bacteria — "friendly" =acteria like those in yogurt — to deliver drugs to the gut in a =ustained manner, in order to eliminate the daily drug regimens =ssociated with chronic diseases.

In 2007, he received a National =nstitutes of Health Director's New Innovator Award to develop and =est the idea.

"The NIH basically said, 'we like this idea, =ow make it work,'" Davies said. "The New Innovator Award was =ritical to our success."

Other studies have demonstrated that =he natural gut microbiota plays a role in obesity, diabetes and =ardiovascular disease.

"The types of bacteria you have in your =ut influence your risk for chronic diseases," Davies said. "We =ondered if we could manipulate the gut microbiota in a way that would =romote health."

To start, the team needed a safe bacterial =train that colonizes the human gut. They selected E. =oli Nissle 1917, which has been used as a probiotic treatment =or diarrhea since its discovery nearly 100 years ago.

They genetically =odified the E. coliThe investigators added the NAPE-producing bacteria to the drinking =ater of mice eating a high-fat diet for eight weeks. Mice that received =he modified bacteria had dramatically lower food intake, body fat, =nsulin resistance and fatty liver compared to mice receiving control =acteria.

They found that these protective effects persisted for =t least four weeks after the NAPE-producing bacteria were removed from =he drinking water. And even 12 weeks after the modified bacteria were =emoved, the treated mice still had much lower body weight and body fat =ompared to the control mice. Active bacteria no longer persisted after =bout six weeks.

"We still haven't achieved our ultimate goal, =hich would be to do one treatment and then never have to administer the =acteria again," Davies said. "Six weeks is pretty long to have =ctive bacteria, and the animals are still less obese 12 weeks =ut.

"This paper provides a proof of concept," he said. =93Clearly, we can get enough bacteria to persist in the gut and have a =ustained effect. We would like for that effect to last =onger."

Davies noted that the researchers also observed effects =f the compounds in the liver, suggesting that it may be possible to use =odified bacteria to deliver therapeutics beyond the gut.

The =nvestigators are currently working on strategies to address regulatory =ssues related to containing the bacteria, for example by knocking out =enes required for the bacteria to live outside the treated =ost.

Zhongyi Chen, M.D., Ph.D., and Lilu Guo, Ph.D., are co-first =uthors of the JCI paper. This research was supported =y the New Innovator Award (OD003137) and by other grants from the =ational Institutes of Health (AT007830, DK059637, DK020593, RR024975, =K092993).

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