Cystic Fibrosis Research News

Title:
Immunotyping of clinically divergent p.Phe508del homozygous monozygous cystic fibrosis twins

Authors:
Esther Schamschula, Wolfgang Hagmann, Yassen Assenov, Silke Hedtfeld, Ahmed K. Farag, Lennart M. Rösner, Lutz Wiehlmann, Frauke Stanke, Sebastian Fischer, Angela Risch, Burkhard Tümmler

Affiliations:

aDepartment of Biosciences, Paris Lodron University of Salzburg, Salzburg, Austria
bDivision of Epigenomics, DKFZ - German Cancer Research Center, Heidelberg, Germany
cClinic for Pediatric Pneumology, Allergology and Neonatology, Hannover Medical School, Hannover, Germany
dDepartment of Dermatology and Allergy, Division of Immunodermatology and Allergy Research, Hannover Medical School, Hannover, Germany
eResearch Core Unit Genomics, Hannover Medical School, Hannover, Germany
fBiomedical Research in Endstage and Obstructive Lung Disease Hannover (BREATH), German Center for Lung Research Hannover Medical School, Hannover, Germany

What was your research question?
What makes monozygous cystic fibrosis twins, identical twins from the same egg, different in their host response during infections?

Why is this important?
Recurrent airway infections confound the daily life of all individuals with cystic fibrosis. Depending on an enormous number of inherited and environmental factors and the current state of health, the course of an infection may vary from a benign cold to a severe pneumonia. This number of factors is dramatically reduced if you compare monozygous twins who share an identical genomic blueprint and who always have been living together. However, because identical twins do not experience identical disease outcomes, they are ideal candidates to understand how the immune system determines outcomes.
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What did you do?
We examined twin pairs of the European CF Twin and Sibling Study. We compared twins with really similar outcomes to those with really diverse outcomes in their ability to generate the different cells of the immune system use to recognize things foreign to the body like germs, and methylation of the DNA which influence expression of genes.

What did you find?
Each twin was carrying his/her own individual repertoire of receptors to recognize parts of foreign germs but in contrast to unrelated people, each CF twin pair also shared a few dozen receptors with each other. The DNA methylation profile was very similar among monozygous twin pairs, but when twins were very different in their health, their DNA methylation profile at areas related to the immune system was also very different.

What does this mean and reasons for caution?
Humans are most diverse from each other in their repertoire to recognize microbes. However, the non-random sharing of sequence-identical receptors among monozygous twins indicates that even the response to microbial antigens is governed by genetic determinants. The DNA methylation pattern in peripheral blood differs at genes that modulate the host defense during infections.

What’s next?
Further studies on monozygous twins could help us understand how our genes determine the generation of the immune repertoire in cystic fibrosis.

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