Remote control of intestinal tumorigenesis by the microbiota

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Crohn’s Disease (CD) and Colorectal cancer microbiomes

General dysbiosis in CD with lower *Firmicutes* and higher *Bacteroidetes*

Scanlan et al J Clin Microbiol

Subclinical dysbiosis in asymptomatic relatives of patients with CD

Joossens et al Gut. 2011 60(5):631-7

Microbial dysbiosis in colorectal cancer patients


Merieux Foundation, June, 11th 2013
**Working hypothesis**

Intestinal mucosa

Homeostasis

Barrier function

Microbiota

Dysbiosis

Inflammation

Intestinal mucosa

Barrier function
The microbiota of Nod2\(^{-/-}\) mice intrinsically drives disease risk.

Reciprocal microbiota transplantation experiments:
- Host safe
- Host at-risk

Graph showing body weight loss over days of treatment with DSS 2%.

Histological score comparisons:
- Nod2\(^{+/+}\) -> GF-Nod2\(^{+/+}\)
- Nod2\(^{-/-}\) -> GF-Nod2\(^{+/+}\)

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*J Clin Invest 2013 108(23):9601-6*
Microbiota transplantation rescued Nod2⁻/⁻ mice from disease risk

Reciprocal microbiota transplantation experiments

Host at-risk ⇔ Host safe
Dysbiotic microbial ecology of Nod2−/− mice is linked to risk for colitis

J Clin Invest 2013 108(23):9601-6
Bacteroides, Butyrivibro & Lachnobacterium are linked to disease risk

![Graph showing the percent abundance of various bacteria](image-url)
Bacterial commensals of Nod2<sup>-/-</sup> mice are involved in disease risk
The enhanced risk for colitis in Rip2\(^{-/-}\) mice is maternally transmissible
Absence of NOD2/RIP2 engenders a transmissible risk for colitis
Risk of carcinorogenesis is communicable to immunocompetent hosts
Neutralizing IL-6 reduces tumor progression in Nod2−/− and Rip2−/− mice
NOD2 keeps bad bacteria at bay through IL-6
Take-home messages

• Correcting dysbiosis by fecal transplantation: from folk medicine to science

• Towards a better understanding of missing heritability
Acknowledgments

Thanks for your attention