

Necator americanus Infection in Celiac Disease

Can a neo-helminth infection inhibit
gluten sensitivity
- a model for autoimmune diseases

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***Necator americanus*-hookworm: pathogen or commensal?**



- 500×10^6 still infected
- Anemia (1.4×10^6 L blood loss per day)
- Context:
 - Marginal society?
 - Transitional society?
 - Modern society?

Necator americanus

intimately adapted to humans

- **NA has adapted**
 - zone of immune privilege.
- **IL-10 and TGF- β**
 - enhanced
- **TNF- α and IFN- γ**
 - suppressed

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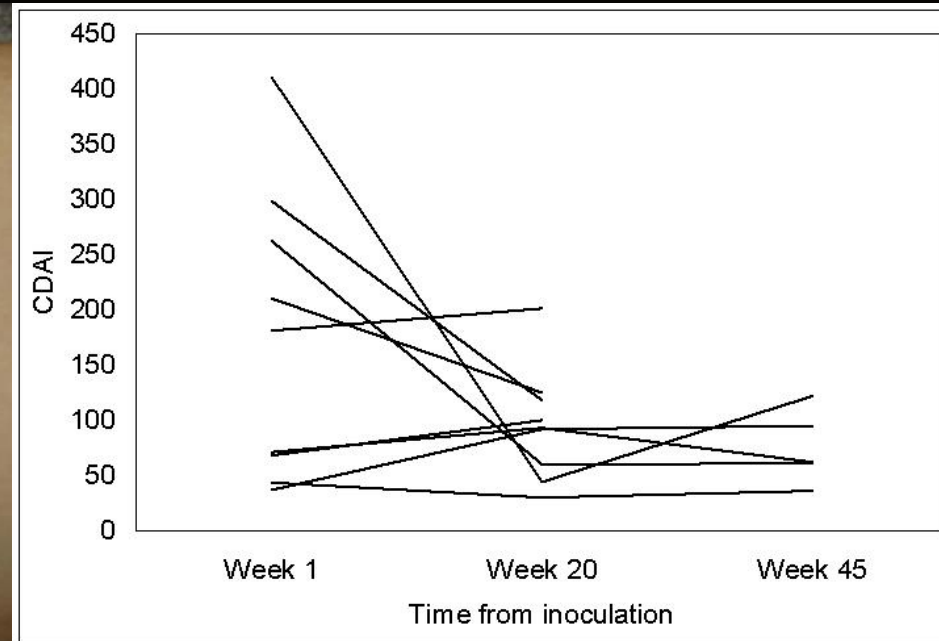
JHC

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Given®

NA in Crohn's disease



- Most subjects were immune suppressed and remained reliant on immunosuppressants
- Unsuppressed subjects did better

Celiac: A model for IBD?

	IBD	Celiac
Genetic (Innate and adaptive immunity)		
Environmental (including hygiene)		
Stochastic (including infectious events)		
Reactive to lumen content		
Associated with autoimmune diseases		

Celiac is not IBD

Just as *NA* is not generic for helminth

	IBD	Celiac
Inflammatory pathways	Th-1/Th-2, IL-17, IL-23 IL-18, Th-17, IFN- γ	IL-15, IL-21, IFN- α IL-18, Th-17, IFN- γ
Antigenic stimulus	Endogenous-flora Pro- and antibiotics	Exogenous-gluten Easily manipulated Multilayered
Therapy	Immune suppressive	Gluten restriction
In vitro/ex vivo opportunities	+	++++

NA in Celiac: Methods

($n = 20$; HLA DQ2 – Gluten Free Diet)

- Double-blind, placebo controlled
 - 10 inoculated (10 iL3 at week-0 and 5 more at week-12)
 - 10 sham inoculated
 - detailed assessments week-20 (5-days gluten) -21
- Primary end-points
 - IFN- γ ELISPOT (α -gliadin/Q65E and PT-digest)
 - mucosal IEL, villous:crypt and Marsh grade
- Secondary end-points
 - comfort diary, blood indices, mucosal health (CE)
 - collect and archive sera, PBMC, mucosa
(ex vivo immunological profiling and in vitro stimulation testing)

Conclusions (with caveats)

- Experimental *Necator americanus* infection is easily achieved, well-tolerated and safe.
- In healthy people with celiac disease, *NA* appears to disrupt inflammatory and immunological responsiveness to gluten
- Celiac disease is an excellent model to test the relationship between helminths and autoimmunity.