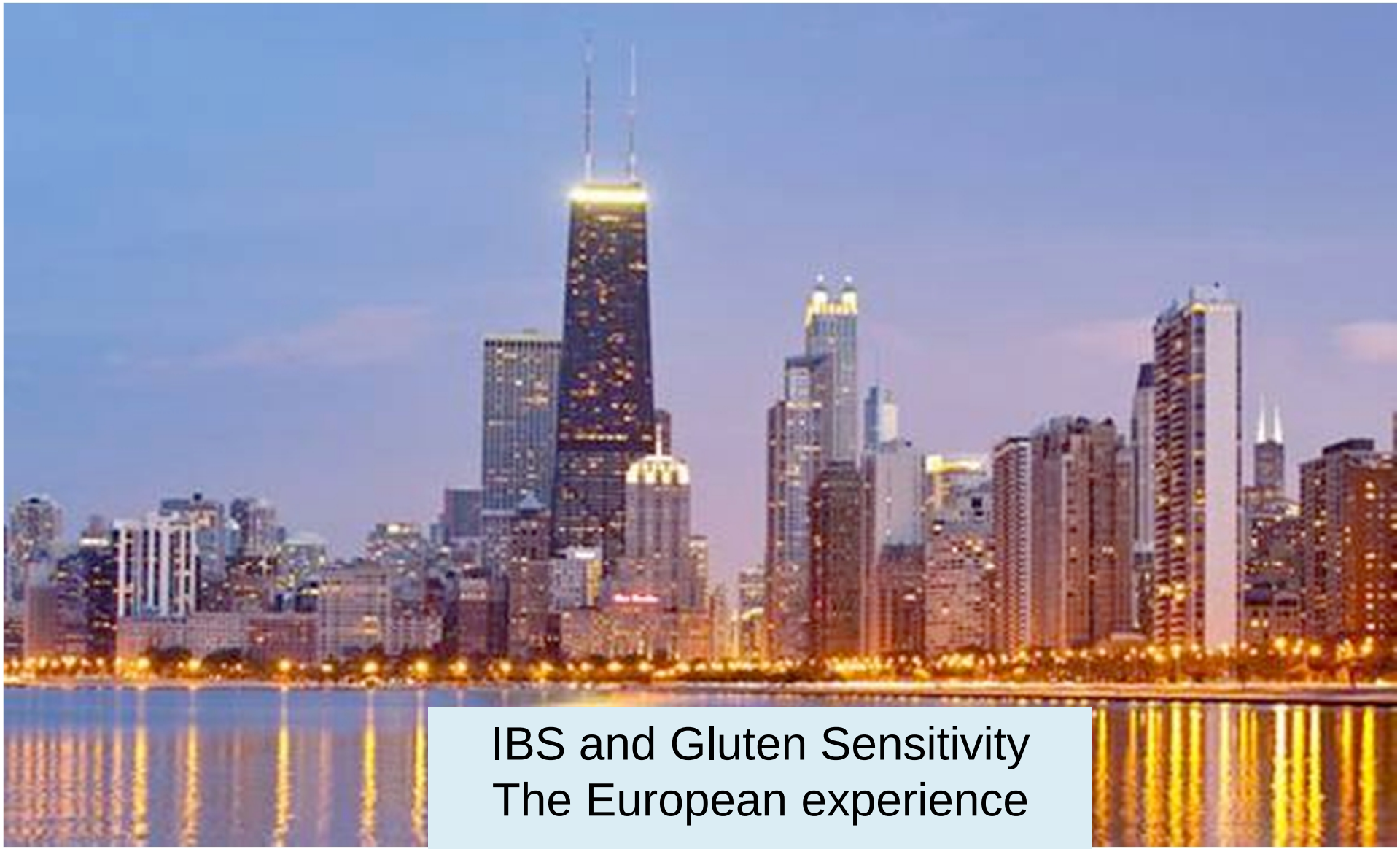
UNIVERSITÀ DEGLI STUDI DI PALERMO

ASP AGRIGENTO



IBS and Gluten Sensitivity
The European experience

Antonio Carroccio

Gluten-Sensitive Diarrhea Without Evidence of Celiac Disease

B. T. COOPER, G. K. T. HOLMES, R. FERGUSON, R. A. THOMPSON, R. N. ALLAN, and W. T. COOKE
The Nutritional and Intestinal Unit, The General Hospital, Birmingham and The Regional Immunology Laboratory, East Birmingham Hospital, Birmingham, England

Small-bowel mucosal inflammation in reticulin or gliadin antibody-positive patients without villous atrophy. *Scandinavian Journal of Gastroenterology, 33*, 944–949. Kaukinen, K., et al. (1998).

Intolerance to cereals is not specific for coeliac disease.
Scand J Gastroenterol. 2000 Sep;35(9):942-6.
Kaukinen K, et al.

CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2007;5:844–850

Predictors of Clinical Response to Gluten-Free Diet in Patients Diagnosed With Diarrhea-Predominant Irritable Bowel Syndrome

ULRICH WAHNSCHAFFE,* JÖRG–DIETER SCHULZKE,‡ MARTIN ZEITZ,‡ and REINER ULLRICH‡

What we learned from the European studies at the Oslo ICDS

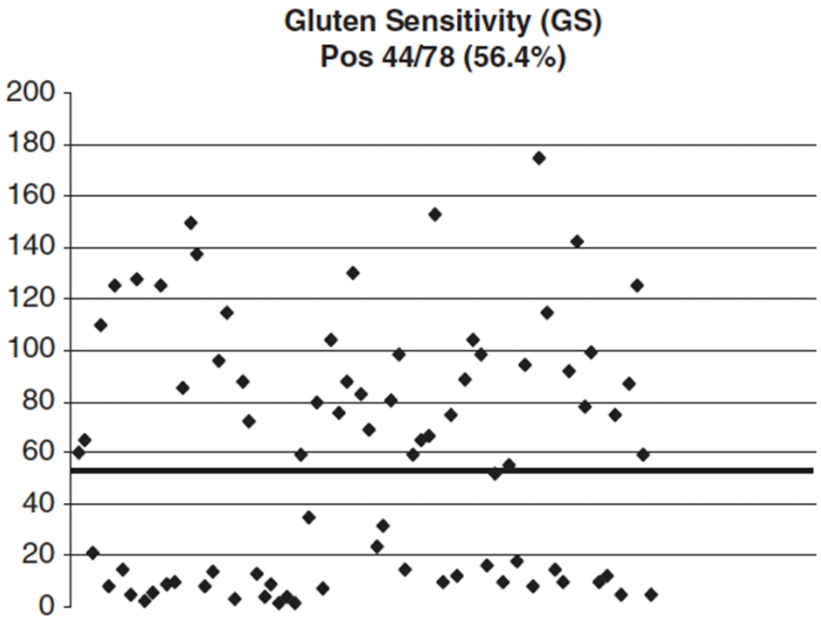
ORIGINAL ARTICLE

Serological Tests in Gluten Sensitivity (Nonceliac Gluten Intolerance)

Umberto Volta, MD, Francesco Tovoli, MD, Ronny Cicola, MD, Claudia Parisi, Angela Fabbri, MD, Maria Piscaglia, MD, Erica Fiorini, MD, and Giacomo Caio,

TABLE 1. Clinical Features of Gluten Sensitivity in Patients on a Gluten-containing Diet

	No. (%)
Gluten sensitivity patients	78
Intestinal Symptoms	75 (96%)
(at least 1 intestinal symptom)	
Abdominal pain	60 (77%)
Bloating	56 (72%)
Diarrhea	31 (40%)
Constipation	14 (18%)
Extraintestinal Symptoms	76 (97%)
(at least 1 extraintestinal symptom)	
Foggy mind	33 (42%)
Tiredness	28 (36%)
Eczema and skin rash	26 (33%)
Headache	25 (32%)
Joint/muscle pain	22 (28%)
Leg/arm numbness	13 (17%)
Depression	12 (15%)
Anemia	12 (15%)



Sapone *et al. BMC Medicine* 2011, **9**:23
http://www.biomedcentral.com/1741-7015/9/23

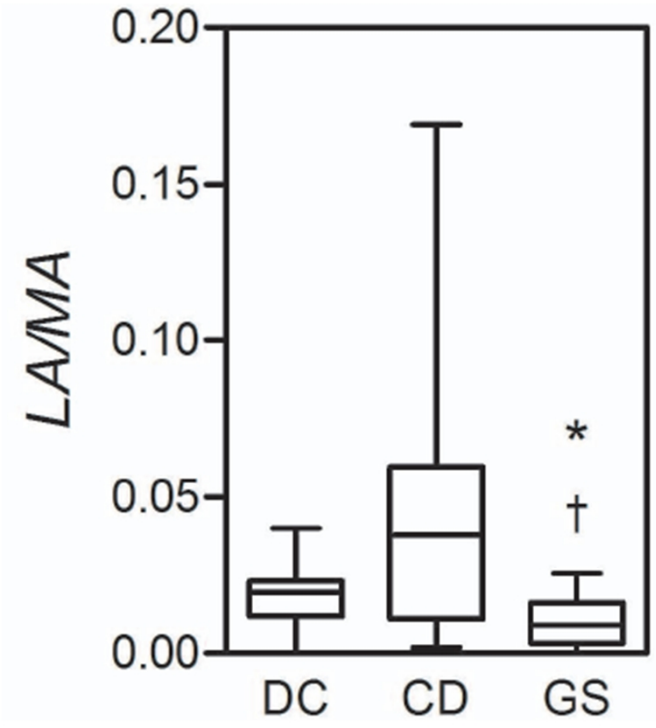
BMC Medicine

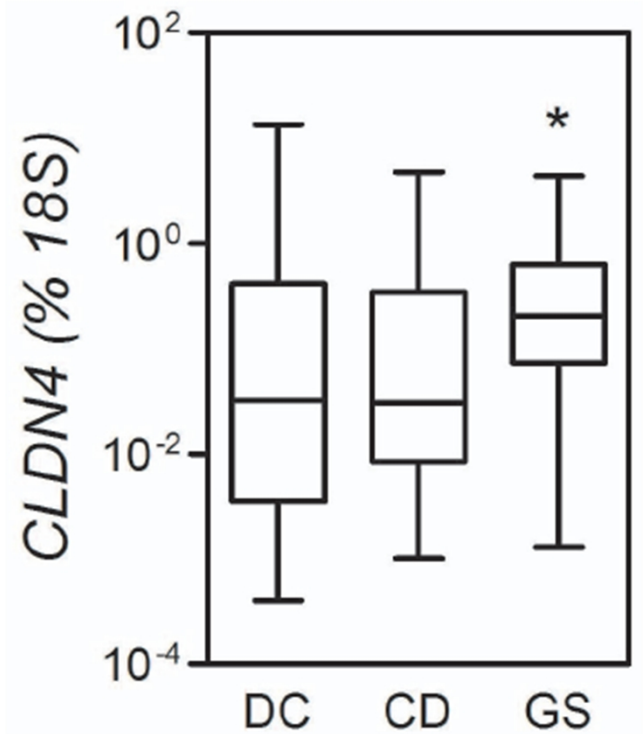
RESEARCH ARTICLE Open Access

Divergence of gut permeability and mucosal immune gene expression in two gluten-associated conditions: celiac disease and gluten sensitivity

Anna Sapone[1,2], Karen M Lammers[2], Vincenzo Casolaro[2,3], Marcella Cammarota[4], Maria Teresa Giuliano[4], Mario De Rosa[4], Rosita Stefanile[5], Giuseppe Mazzarella[5], Carlo Tolone[6], Maria Itria Russo[7], Pasquale Esposito[7], Franca Ferraraccio[8], Maria Carteni[4], Gabriele Riegler[1], Laura de Magistris[1], Alessio Fasano[2*]

GS
26
30.73 ± 12.19
17/9
Diarrhea
Abdominal pain
Weight loss
Gas
Bone or joint pain
Osteoporosis
Leg numbness
Muscle cramps
Unexplained anemia
Glossitis





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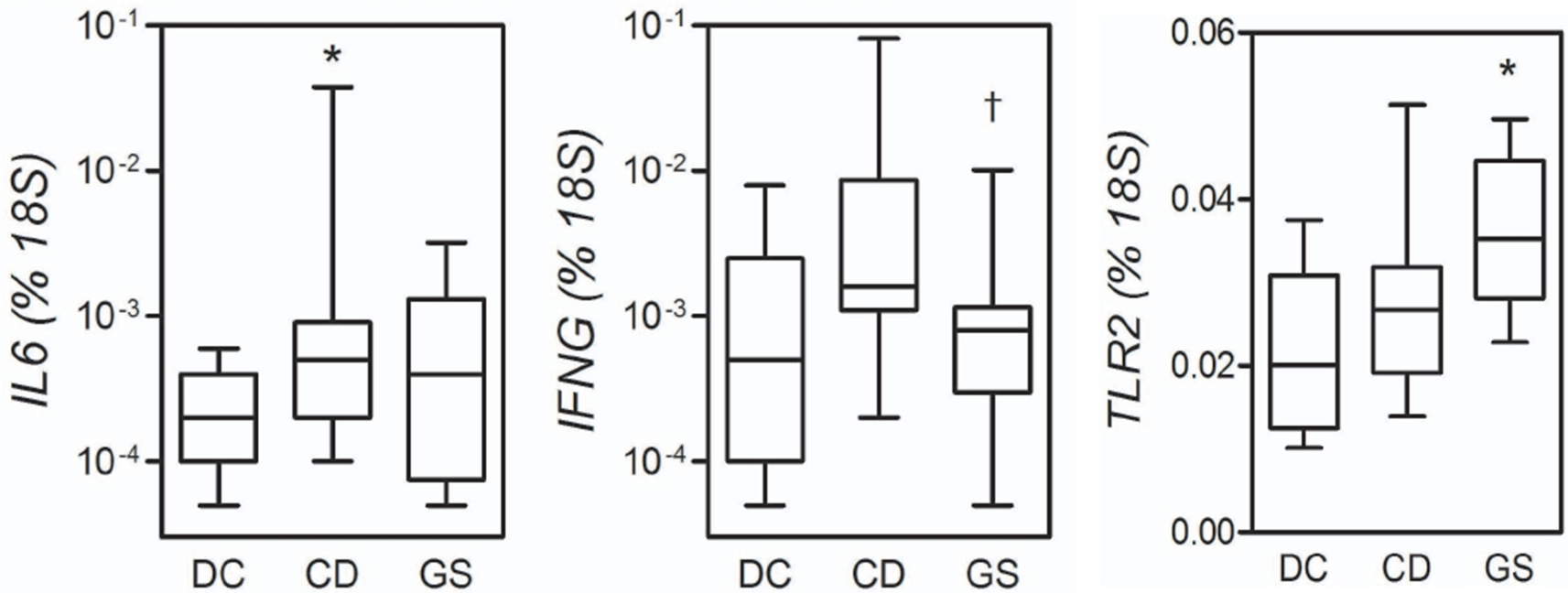

Non-Celiac Wheat Sensitivity Diagnosed by Double-Blind Placebo-Controlled Challenge: Exploring a New Clinical Entity

Antonio Carroccio[1], Pasquale Mansueto[2], Giuseppe Iacono[3], Maurizio Soresi[2], Alberto D'Alcamo[2], Francesca Cavataio[3], Ignazio Brusca[4], Ada M. Florena[5], Giuseppe Ambrosiano[2], Aurelio Seidita[2], Giuseppe Pirrone[2] and Giovanni Battista Rini[2]

Subjects with IBS-like symptoms according to the Rome II criteria and fulfilling the criteria for "gluten-sensitivity"

920 Patients elegible patient

Four weeks period of elimination diet and successive DBPC wheat challenge:

276 Suffered from wheat sensitivity or multiple food hypersensitivity, including wheat sensitivity

644 Not suffered from wheat sensitivity → Excluded

Four weeks period of elimination diet and successive DBPC cow's milk protein challenge:

Group 1: 70 patients suffering from wheat sensitivity alone

Group 2: 206 patients suffering from multiple food hypersesitivity, including wheat sensitivity

Control groups: 50 irritable bowel syndrome patients, and 100 celiac disease patients

Am J Gastroenterol advance online publication, 24 July 2012; doi:10.1038/ajg.2012.236

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Table 2. Clinical characteristics of the patients suffering from WS (*n*=276), CD (*n*=100), and IBS (*n*=50)

	WS	CD	IBS	*P* value
Anemia	67/276 (24%)	78/100 (78%)	4/50 (8%)	CD vs. WS 0.0001 WS vs. IBS 0.02 CD vs. IBS 0.0001
Weight loss	94/276 (35%)	52/100 (52%)	2/50 (4%)	CD vs. WS 0.002 WS vs. IBS 0.0001 CD vs. IBS 0.0001
Median (range) duration of symptoms (years)	7 (1–40)	4 (1–35)	7 (1–31)	WS and IBS vs. CD 0.002 WS vs. IBS NS
Median (range) number of previous endoscopies	3.5 (1–6)	1 (1–3)	0.5 (0–2)	WS vs. CD and IBS 0.001 CD vs. IBS NS
Self-reported wheat intolerance	137/276 (50%)	22/100 (22%)	7/50 (14%)	WS vs. CD and IBS 0.0001 CD vs. IBS NS
Family history of CD	14/276 (5%)	18/100 (18%)	0/50	CD vs. WS 0.01 CD vs. IBS 0.005 WS vs. IBS NS
History of food allergy in infancy	47/276 (18%)	6/100 (6%)	2/50 (4%)	WS vs. CD and IBS 0.01 CD vs. IBS NS
Coexistent atopic diseases	80/276 (29%)	8/100 (8%)	3/50 (6%)	WS vs. CD and IBS 0.0001 CD vs. IBS NS

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Table 3. Number and percentage of positive test results for: serum AGA IgA and IgG, HLA haplotype DQ2 and/or DQ8, serum anti-betalactoglobulin IgG, and flow cytometric basophil activation test in patients with WS and in the control groups (CD and IBS)

	WS (*n*=276)	CD (*n*=100)	IBS (*n*=50)	*P* value
AGA IgA	110/276 (40%)	72/100 (72%)	5/50 (10%)	WS vs. CD 0.001 WS vs. IBS 0.0001 CD vs. IBS 0.0001
AGA IgG	155/276 (55%)	78/100 (78%)	7/50 (14%)	WS vs. CD 0.01 WS vs. IBS 0.0001 CD vs. IBS 0.0001
DQ2 or DQ8 haplotype	146/276 (53%)	100/100 (100%)	14/50 (28%)	WS vs. CD 0.001 WS vs. IBS 0.0001 CD vs. IBS 0.0001
EmA in biopsy culture medium	22/276 (8%)	51/51 (100%)	0/9 (0%)	WS vs. CD 0.0001 WS vs. IBS, NS CD vs. IBS 0.0001
Anti-betalactoglobulin IgG	94/276 (35%)	Not performed	7/50 (14%)	<0.0005
Basophil activation	184/276 (66%)	Not performed	2/50 (4%)	<0.0001

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	WS (*n*=276)	CD (*n*=100)	IBS (*n*=50)	*P* value
Duodenal histology				
CD3+ >25/100 EC	248/276 (90%)	100/100 (100%)	0/9 (0%)	WS and CD vs. IBS 0.0001
CD3+ number/100 EC	43±9	68±8	15±5	CD vs. WS and IBS *P*<0.0001 WS vs. IBS *P*<0.0001
Eosinophil count per 10 HPF	63±20	38±16	31±12	WS vs. CD and IBS *P*<0.0005
Colon histology				
Presence of lymphoid nodules	84/276 (31%)	Not performed	0/35 (0%)	*P*<0.0001
IEL infiltration	68/276 (25%)	Not performed	8/35 (23%)	NS
Eosinophil infiltration in the lamina propria	165/276 (60%)	Not performed	1/35 (3%)	WS vs. IBS *P*<0.0002
Intra-epithelial eosinophil infiltration	174/276 (63%)	Not performed	0/35 (0%)	WS vs. IBS *P*<0.0001

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CLINICAL GASTROENTEROLOGY AND HEPATOLOGY 2013;■:1–6

Gliadin Does Not Induce Mucosal Inflammation or Basophil Activation in Patients With Nonceliac Gluten Sensitivity

CRISTINA BUCCI,* FABIANA ZINGONE,* ILARIA RUSSO,* IVONNE MORRA,* RAFFAELLA TORTORA,‡ NORBERTO POGNA,§ GIULIA SCALIA,‖ PAOLA IOVINO,* and CAROLINA CIACCI*

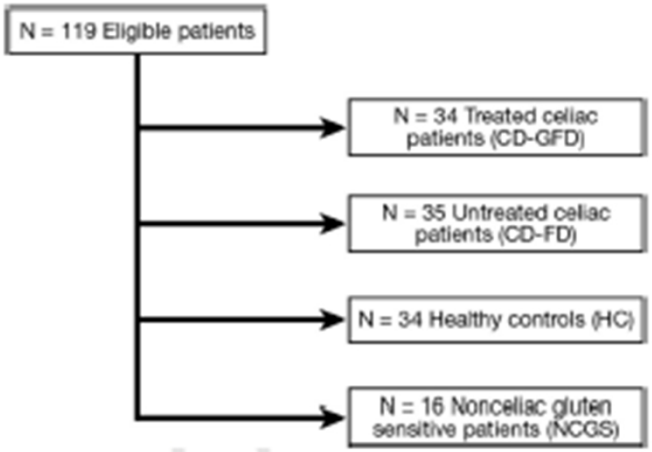
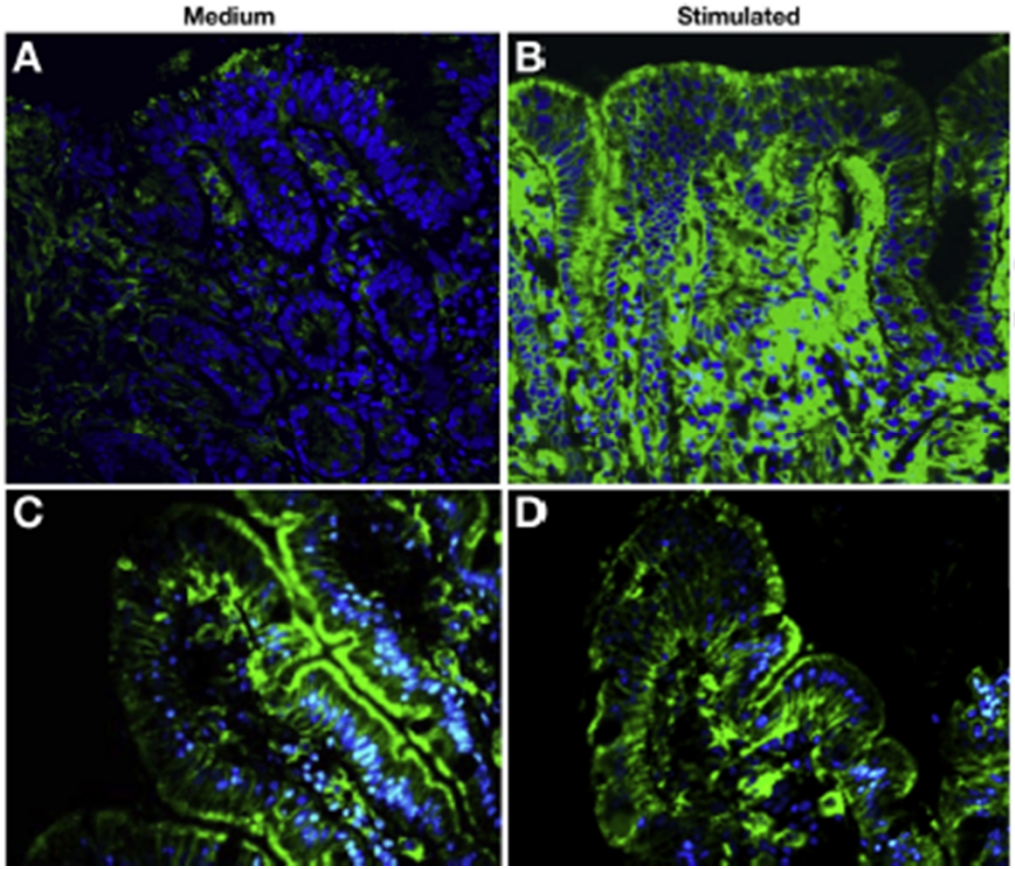


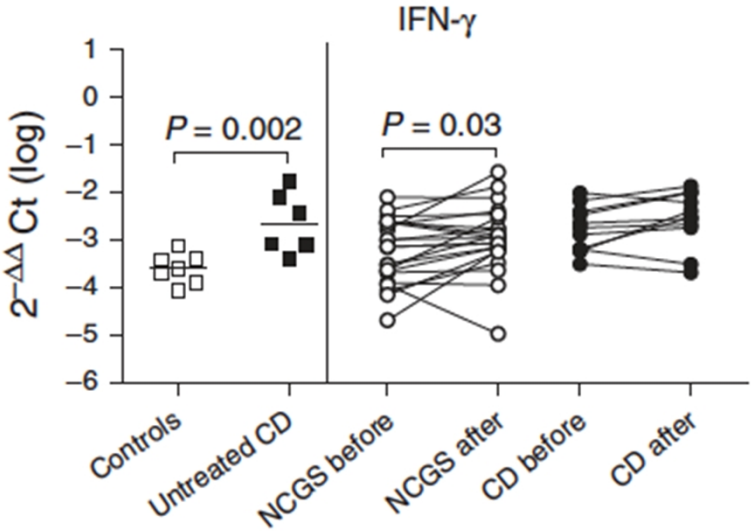
Table 2. Response to In Vitro Gliadin Challenge Among Groups

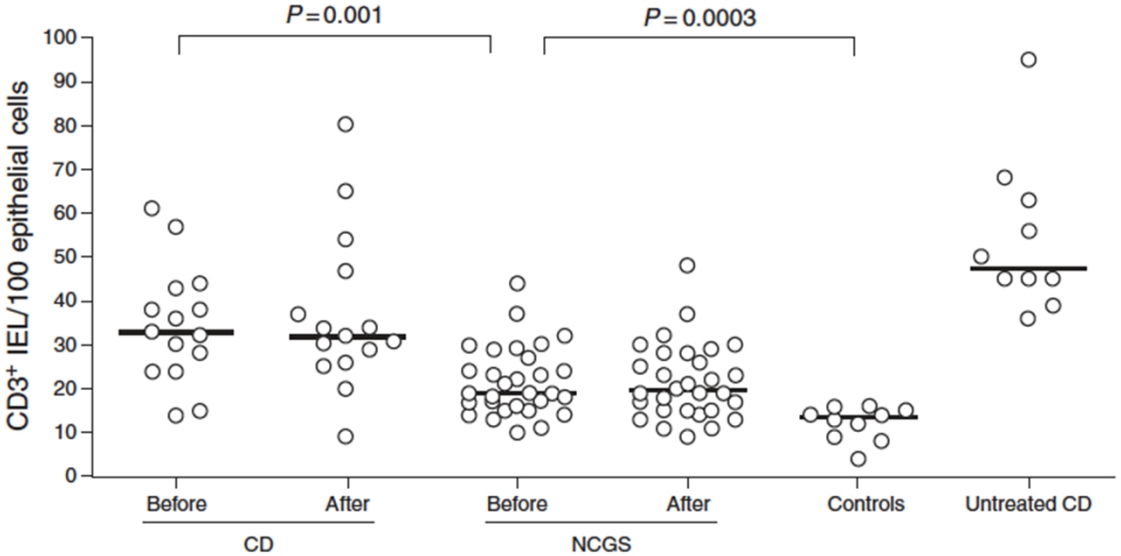
	CD-GFD (34)	CD-FD (35)	HC (34)	NCGS (16)	*P* value
Early markers of inflammation					
PY99	34 (100%)	33 (94%)	1 (2%)	1 (6.2%)	.00
HLA-DR (epithelial)	34 (100%)	34 (97%)	0	0	.00
ICAM-1	34 (100%)	34 (97%)	3 (11%)	3 (18.7%)	.00
Late markers of inflammation					
HLA-DR (crypt)	34 (100%)	34 (97%)	0	0	.00
CD3	32 (94%)	35 (100%)	3 (8%)	0	.00
CD25	28 (82%)	32 (91%)	2 (5%)	0	.00
CD69	34 (100%)	34 (97%)	3 (11%)	1 (6.2%)	.00



Mucosal Cytokine Response After Short-Term Gluten Challenge in Celiac Disease and Non-Celiac Gluten Sensitivity

Margit Brottveit, MD, PhD[1,7], Ann-Christin R. Beitnes, MD, PhD[2,7,8], Stig Tollefsen, MSc, PhD[2,9], Jorunn E. Bratlie, BLS[3], Frode L. Jahnsen, MD, PhD[4], Finn-Eirik Johansen, MSc, PhD[4], Ludvig M. Sollid, MD, PhD[5] and Knut E.A. Lundin, MD, PhD[2,6]





OTHER ??

CD-like

* HLA DQ2 +
* Increased CD3+
* Positive EmA in culture medium
* Family history of CD

Psychological factors

* Visceral hypersensitivity
* No mucosal inflammation
* Depression/anxiety

Dietary change

⇩

Change of microbioma

Allergy-like

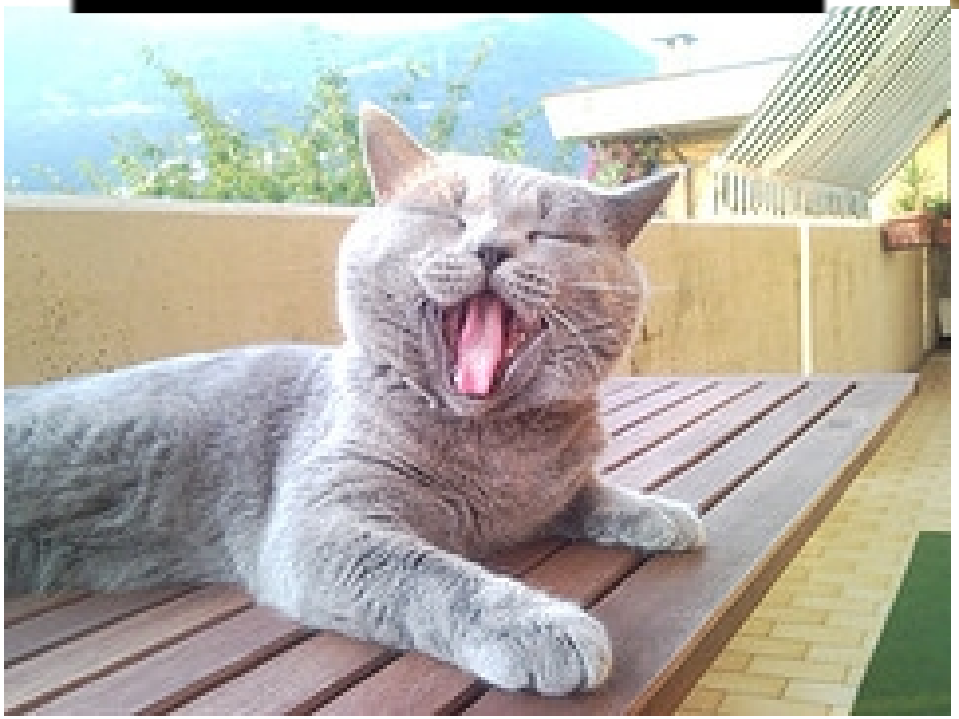
* Eos infiltrate
* AGA IgG +ve
* BAT positivity
* Coexistent atopy
* History of food allergy in infancy

ATIs–innate immunity

- Wheat A-T inhibitors
- TLR4 / CD 14 activation
- Innate immunity

FODMAP effect

- Normal histology
- Symptoms resolution on low FODMAP diet



Thank you for your attention