

Oats in coeliac disease - do we have the full picture?

Knut E. A. Lundin

Professor, Consultant gastroenterologist

Endoscopy Unit, Dept of Transplantation medicine

Centre for Immune Regulation

Oslo University Hospital, Rikshospitalet

Medical Faculty, University of Oslo



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Disclosures

None relevant for this presentation

FAQs

- Does oats contain “gluten”?
- Is it safe for me?
- Is it safe for my child?
- Is there any benefit?
- What should I do if I “feel something”?
- Should I go to my doctor? My gastroenterologist? Does he/she know what to do?

Topics

- Immunology of coeliac disease – basic aspects
- Oats as member of grass family
- History of oats and coeliac disease
- Clinical trials on oats
- Oats specific T cells
- Recent development on this topic
- Conclusions

Willem K. Dicke defined celiac disease a lifelong and gluten induced disease



- Dutch pediatrician
- On track of gluten since 1934, concluded during WWII and soon thereafter
- Challenge experiments
- Resistance from catholic church
- Wheat, rye and barley (and oats) responsible

TABLE 1. Gluten-free regimes throughout the U.K. and Ireland

Centre	Advised to exclude			
	Wheat	Rye	Barley	Oats
Birmingham	Yes	Yes	No*	No*
Leicester	Yes	Yes	No*	No*
Cardiff	Yes	Yes	No*	No*
Ipswich	Yes	Yes	Yes	No
Leeds	Yes	Yes	No	No
London				
Gt Ormond St	Yes	Yes	No*	No*
St Bartholomew's	Yes	Yes	Yes	Yes
Guy's	Yes	Yes	Yes	No
Wexham	Yes	Yes	No*	No*
Scotland				
Aberdeen	Yes	Yes	No*	No*
Edinburgh	Yes	Yes	Yes	Yes
Glasgow	Yes	Yes	Yes†	Yes†
Ireland				
Dublin	Yes	Yes	Yes	Yes
Coeliac Society	Yes	Yes	Yes	No

* Exclusion advised if poor response to wheat and rye exclusion.

† Allowed when patients asymptomatic, and if remain so.
(Information obtained from hospital dietetics departments and the Coeliac Society.)

As noted by Watson, in Scotland “it would have been obvious many years ago if coeliac children and adults who are taking porridge relapse”

Schmitz J
Editorial in BMJ on
oats toxicity 1997

Challenge studies

Vol. 333 No. 16

DIETS WITH AND WITHOUT OATS IN ADULTS WITH CELIAC DISEASE

1033

A COMPARISON OF DIETS WITH AND WITHOUT OATS IN ADULTS WITH CELIAC DISEASE

ESKO K. JANATUINEN, M.D., PEKKA H. PIKKARAINEN, M.D., TARJA A. KEMPPAINEN, M.Sc.,
VELI-MATTI KOSMA, M.D., RITVA M.K. JÄRVINEN, M.Sc., MATTI I.J. UUSITUPA, M.D.,
AND RISTO J.K. JULKUNEN, M.D.

ABSENCE OF TOXICITY OF OATS IN PATIENTS WITH DERMATITIS HERPETIFORMIS

CATHERINE M. HARDMAN, M.R.C.P., JENNIFER J. GARIOCH, M.R.C.P., JONATHAN N. LEONARD, M.D.,
HUGH I.W. THOMAS, F.R.C.P., MARJORIE M. WALKER, F.R.C.PATH., JENNIFER E. LORTAN, F.R.C.PATH.,

European Journal of Clinical Nutrition (2003) 57, 163–169

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www.nature.com/ejcn

ORIGINAL COMMUNICATION

Adult coeliac patients do tolerate large amounts of oats

S Størsrud^{1*}, M Olsson², R Arvidsson Lenner¹, LÅ Nilsson³, O Nilsson⁴ and A Kilander²

¹Department of Clinical Nutrition, Sahlgrenska University Hospital, Gothenburg, Sweden; ²Department of Medicine, Sahlgrenska University Hospital, Gothenburg, Sweden; ³Department of Medical Microbiology and Immunology, Sahlgrenska University Hospital, Gothenburg, Sweden; and ⁴Department of Pathology, Sahlgrenska University Hospital, Gothenburg, Sweden

to
versitetssykehus



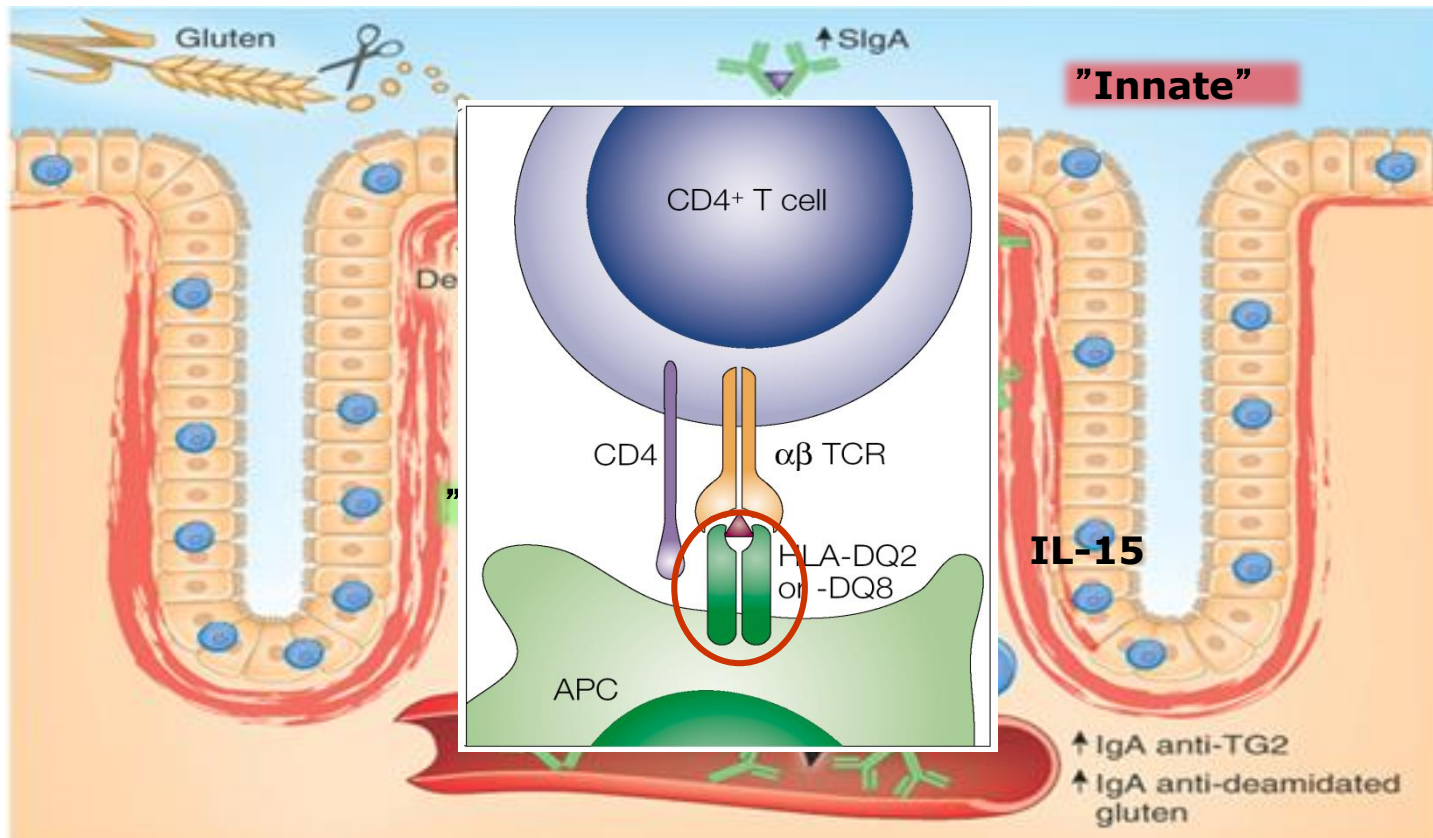
And systematic reviews

- Coeliac disease and oats: A systematic review
 - Haboubi et al, Postgrad Med J 2006
- Can oats be taken in a gluten free diet? A systematic review
 - Garsed and Scott, Scand J Gastro 2007
- Introduction of oats in the diet of individuals with celiac disease: A systematic review
 - Pulido et al. Adv Food Nutr Res 2009

Concerns

- Small studies
 - Garside and Scott found 10 studies with 165 patients
- Several cases of with-drawals
 - Usually without further investigations
 - Often due to symptoms compatible with active CD
- Follow-up, cross-sectional studies usually performed on those who continue with oats

The Immune reaction in CD



Sollid, LM & Lundin KE,
Mucosal Immunology 2009, modified

The grass family (Gramineae)

Bambusoideae	Pooideae		Panicoideae	Cloorhoideae
Oryzeae	Triticeae	Aveneae	Paniceae	Coonyconotese
Oryza (rice)	Triticum (wheat)	Avena (oats)	Perlascatum (pearl millett)	Sorghum (sorghum)
	Secale (rye)		Panicum (progo millett)	Zein (maize)
	Hordeum (barley)		Zetaris (foxtorn millett)	Coixx (Job's tears)

CASE REPORT

Oats induced villous atrophy in coeliac disease

K E A Lundin, E M Nilsen, H G Scott, E M Løberg, A Gjøen, J Bratlie, V Skar, E Mendez, A Løvik, K Kett

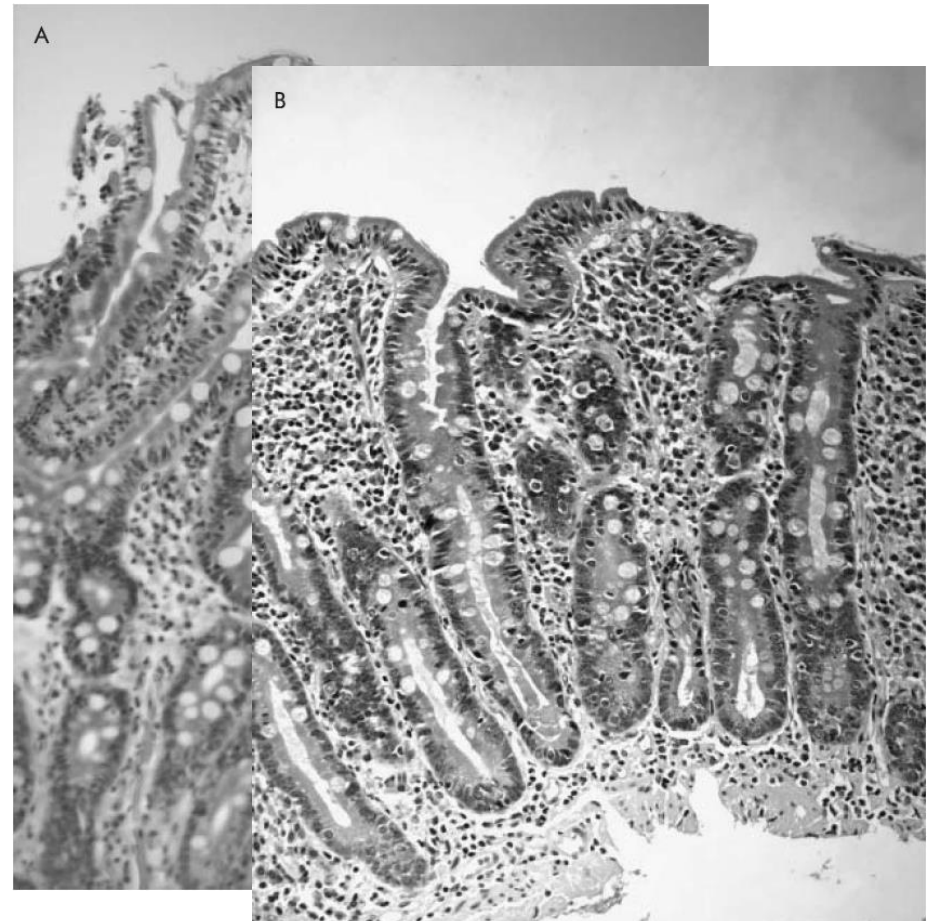
Gut 2003;**52**:1649–1652

Table 1 Six samples analysed for gluten content

Sample	Gluten level (ppm) by WB, MS, ELISA*	Ridascreen
1	18.0–23.0	Negative
2	13.0–17.0	Negative
3	1.6–<1.5	Negative
4	>>400	Positive (0.03%)
5	<1.5	Negative
6	<1.5	Negative

*Level of gluten as determined by a combination of western blot (WB), mass spectrometry (MS), and enzyme linked immunoassay (ELISA) using a cocktail of antibodies. The Ridascreen test has a limit of 5 ppm (0.001%). We tested 25 other samples and the Veterinary Institute, Oslo, tested 120 samples from this manufacturer without finding any positive results.

- 19 adult coeliac disease patients
- Challenged with pure oats for 8 weeks
- One developed villous atrophy and dermatitis





Contents lists available at ScienceDirect

e-SPEN, the European e-Journal of Clinical Nutrition and Metabolism

journal homepage: <http://www.elsevier.com/locate/clnu>

Original Article

Oats in a strictly gluten-free diet is associated with decreased gluten intake and increased serum bilirubin[☆]

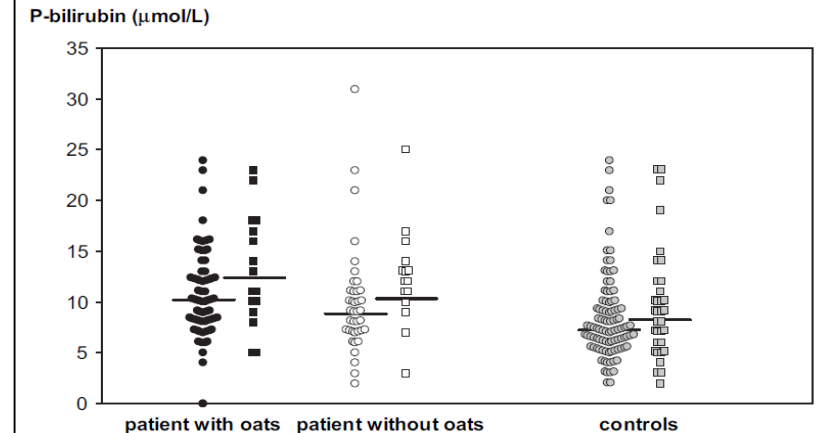
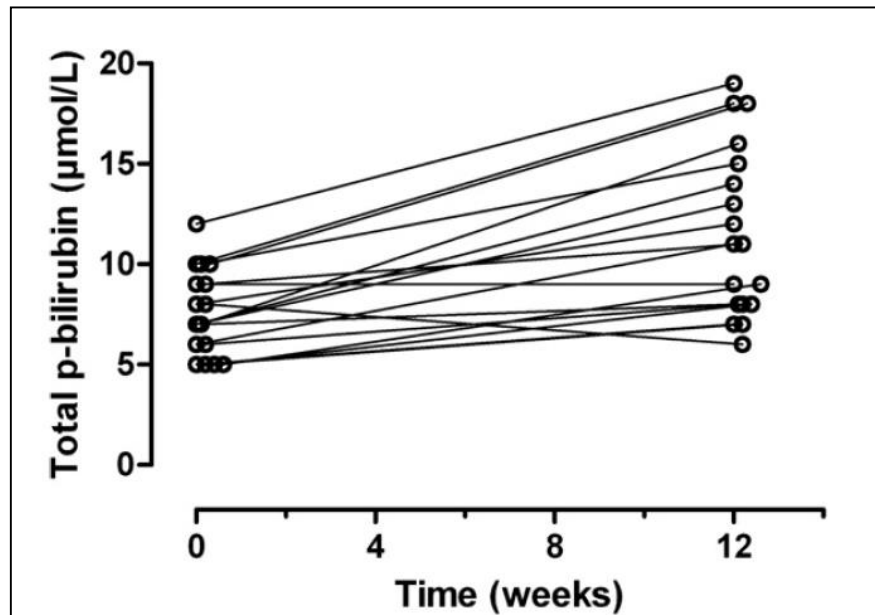
Astrid Løvik^{a,*}, Anne Ulla Gjøen^b, Lars Mørkrid^c, Vigdis Guttormsen^d, Thor Ueland^e, Knut E.A. Lundin^{a,f}

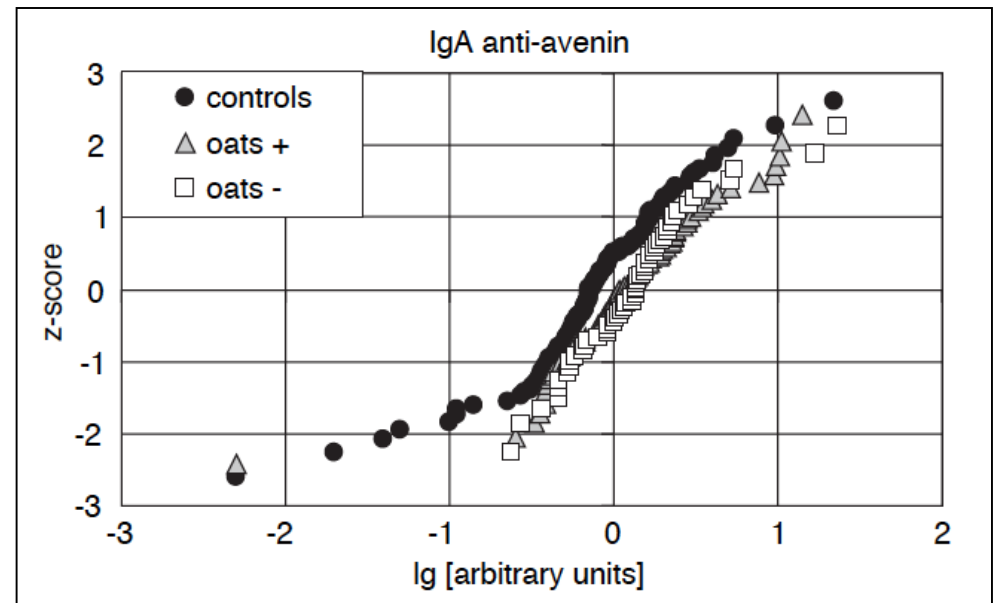
Fig. 2. P-bilirubin among CD patients (population II) and healthy controls (individual P-bilirubin levels and retransformed group medians from Ig values). Estimates: median values (Q1, Q3) were 10 (8,13) $\mu\text{mol/L}$ in female patients with oats (●), 9 (6,12) $\mu\text{mol/L}$ in female patients without oats (○), 13 (9,18) $\mu\text{mol/L}$ in male patients with oats (■) and 11 (8,16) $\mu\text{mol/L}$ in male patients without oats (□). The values among female controls (●) were 7 (5,10) $\mu\text{mol/L}$ and in male controls (■) values were 8 (6,12). There was no statistically significant difference in bilirubin values between patients with oats vs patients without oats ($p = 0.133$, ANOVA & post-hoc LSD). However, when corrections were made for gender and age (multiple regression analysis) there was a tendency for higher bilirubin values among patients with oats ($p = 0.08$).

ORIGINAL ARTICLE

No induction of anti-avenin IgA by oats in adult, diet-treated coeliac disease

VIGDIS GUTTORMSEN¹, ASTRID LØVIK², ASTA BYE¹, JORUNN BRATLIE³,
LARS MØRKRID⁴ & KNUT E. A. LUNDIN^{2,5}

- 136 adult coeliacs
 - 82 exposed to oats for > 6 months
- 139 controls



The Molecular Basis for Oat Intolerance in Patients with Celiac Disease

2004

Helene Arentz-Hansen¹, Burkhard Fleckenstein^{1,2}, Øyvind Molberg¹, Helge Scott³, Frits Koning⁴, Günther Jung⁵, Peter Roepstorff², Knut E. A. Lundin^{1,6}, Ludvig M. Sollid^{1*}

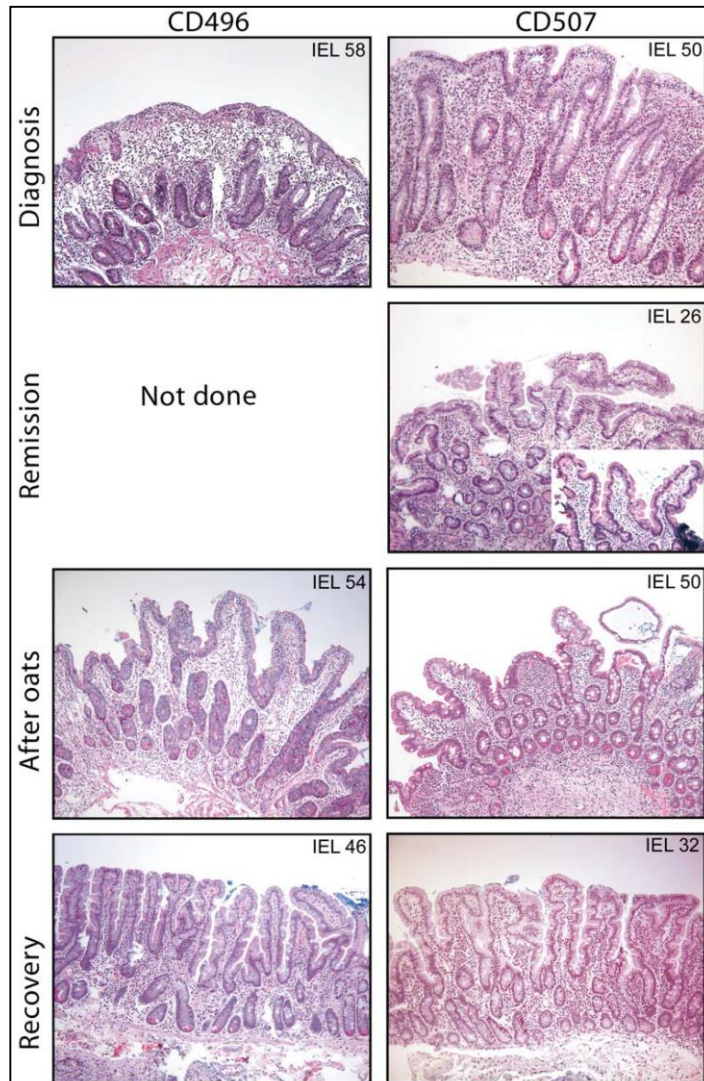


Figure 1. Histology of Intestinal Mucosa of Two of the Oat-Intolerant Patients

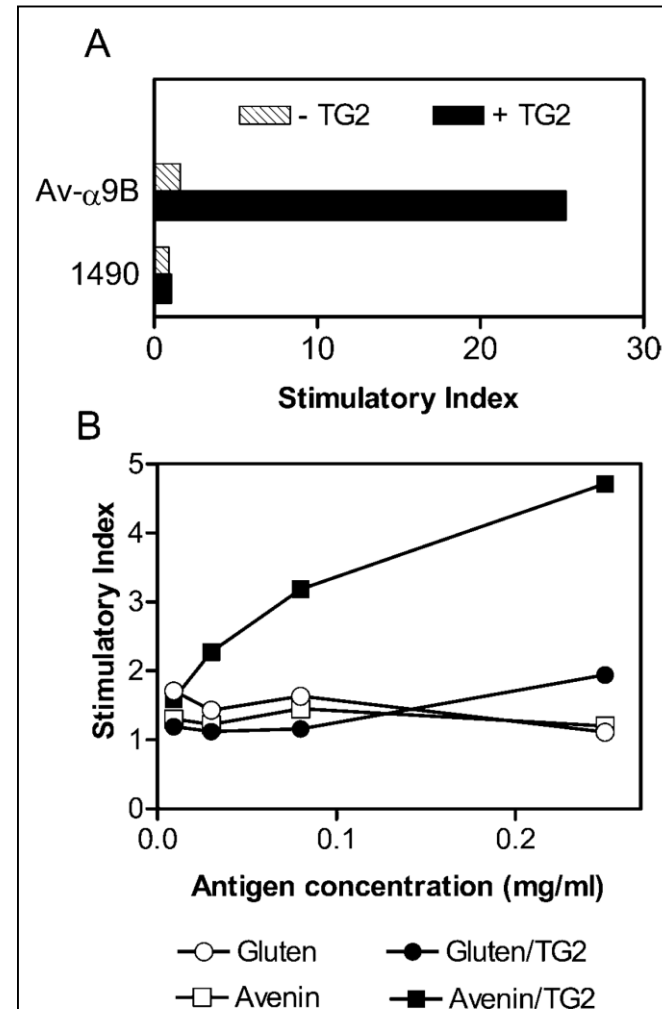


Figure 4. Reactivity of an HLA-DQ2-Restricted T-Cell Clone Derived from a T-Cell Line (CD496.2.3) Established by Avenin Stimulation of an Intestinal Biopsy of Patient CD496



Avenin T cell activating epitopes

Epitope	Previous names	Peptide-binding register, P1								
DQ2.5 restricted epitopes		1	2	3	4	5	6	7	8	9
DQ2.5-glia- α 1a	DQ2- α -I, α 9	P	F	P	Q	P	E	L	P	Y
DQ2.5-glia- α 1b	DQ2- α -III	P	Y	P	Q	P	E	L	P	Y
DQ2.5-glia- α 2	DQ2- α -II, α 2	P	Q	P	E	L	P	Y	P	Q
DQ2.5-glia- α 3	glia- α 20	F	R	P	E	Q	P	Y	P	Q
DQ2.5-glia- γ 1	DQ2- γ -I	P	Q	Q	S	F	P	E	Q	Q
DQ2.5-glia- γ 2	DQ2- γ -II, γ 30	I	Q	P	E	Q	P	A	Q	L
DQ2.5-glia- γ 3	DQ2- γ -III	Q	Q	P	E	Q	P	Y	P	Q
DQ2.5-glia- γ 4a	DQ2- γ -IV	S	Q	P	E	Q	E	F	P	Q
DQ2.5-glia- γ 4b	DQ2- γ -VIIc	P	Q	P	E	Q	E	F	P	Q
DQ2.5-glia- γ 4c	DQ2- γ -VIIa	Q	Q	P	E	Q	P	F	P	Q
DQ2.5-glia- γ 4d	DQ2- γ -VIIb	P	Q	P	E	Q	P	F	C	Q
DQ2.5-glia- γ 5	DQ2- γ -VI	Q	Q	P	F	P	E	Q	P	Q
DQ2.5-glia- ω 1	DQ2- ω -I	P	F	P	Q	P	E	Q	P	F
DQ2.5-glia- ω 2	DQ2- ω -II	P	Q	P	E	Q	P	F	P	W
DQ2.5-glut-L1	glutenin-17	P	F	S	E	Q	E	Q	P	V
DQ2.5-glut-L2	glutenin-156	F	S	Q	Q	Q	E	S	P	F
DQ2.5-hor-1	Hor- α 9, H α 9	P	F	P	Q	P	E	Q	P	F
DQ2.5-hor-2	Hor- α 2, H α 2	P	Q	P	E	Q	P	F	P	Q
DQ2.5-hor-3	hor-I-DQ2	P	I	P	E	Q	P	Q	P	Y
DQ2.5-sec-1	Sec- α 9, S α 9	P	F	P	Q	P	E	Q	P	F
DQ2.5-sec-2	Sec- α 2, S α 2	P	Q	P	E	Q	P	F	P	Q
DQ2.5-ave-1a	Av- α 9A	P	Y	P	E	Q	E	E	P	F
DQ2.5-ave-1b	Av- α 9B, 1490	P	Y	P	E	Q	E	Q	P	F

- Reviewed by Sollid et al, *Immunogenetics* 2012
- Data from groups of
 - Koning, NL
 - Anderson/Tye-Din, AUS
 - Sollid, NO



Oats maybe not complete harmless?

- Children on GFD-oats more Short chain fatty acids in stool compared to GFD-regular
 - Tjellström et al. 2014 *Alimentary Pharm Ther*
- Persistent duodenal intraepithelial lymphocytosis associated with oats intake
 - Tuire et al., 2012 *Am J Gastro*
- Increased mRNA for IL-10, TGF- β , NK receptor, TNF- α , IFN- γ in some pts on GFD-oats
 - Sjöberg et al. 2014 *Clin Transl Gastroenterol*

Why only some coeliacs intolerant?

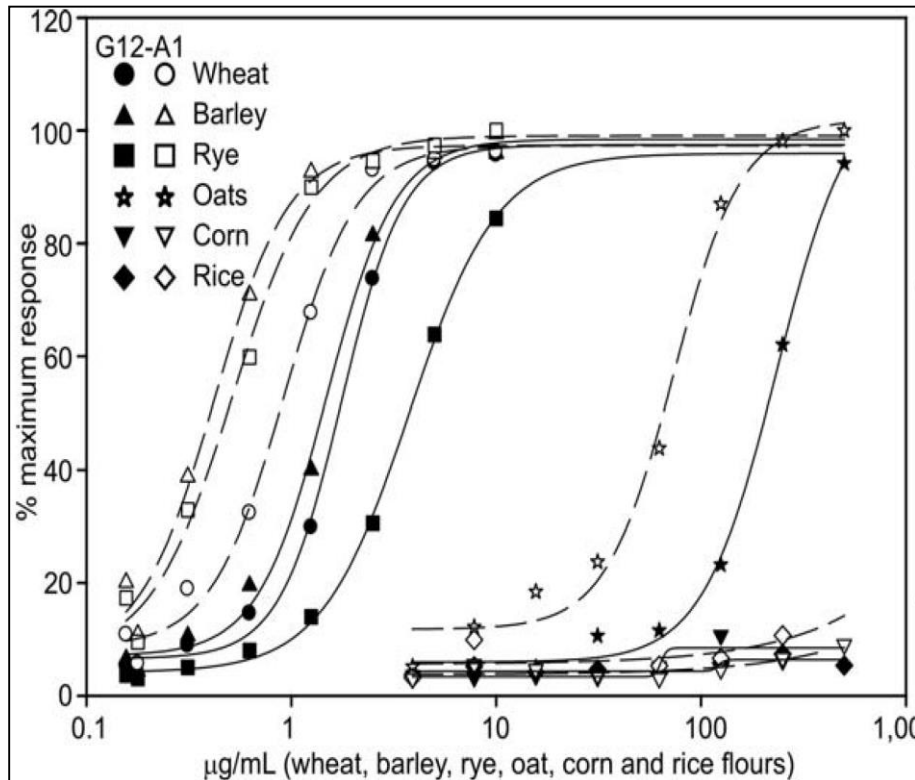


Figure 2. Comparative reactivity of prolamins from wheat, barley, rye, oats, (black) and A1 (white). Each point of the curve shows the mean of n = 3 assays. IC50

Less amount of “toxic epitopes” in oats

• Moron et al 2008 *PLoS One*

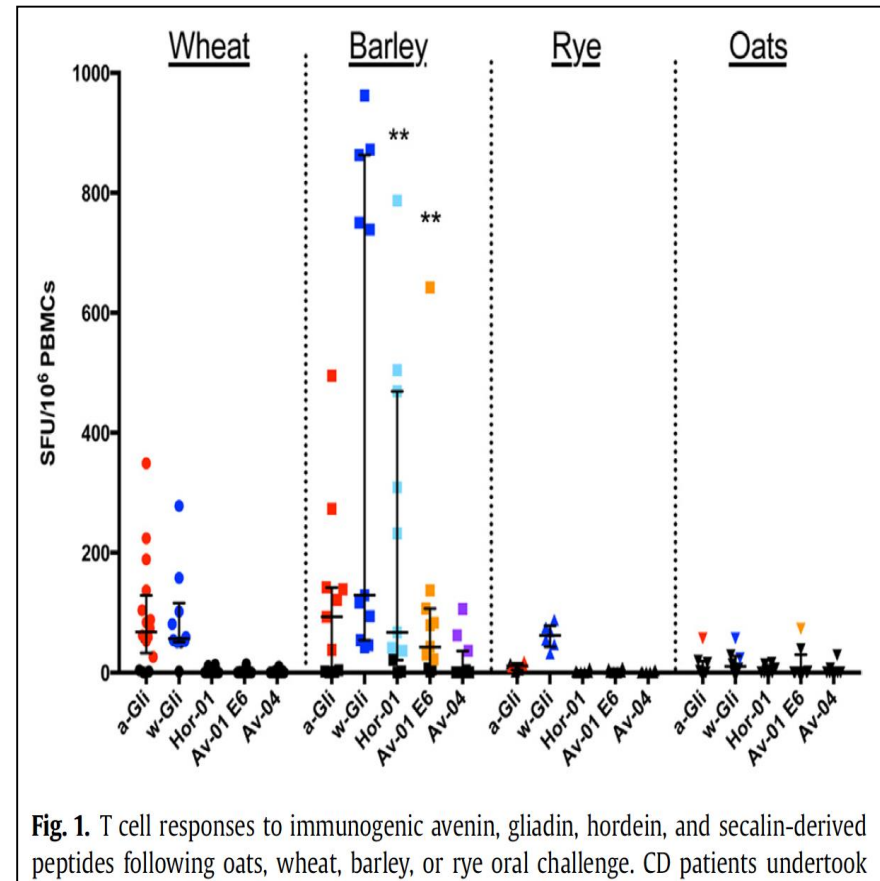


Fig. 1. T cell responses to immunogenic avenin, gliadin, hordein, and secalin-derived peptides following oats, wheat, barley, or rye oral challenge. CD patients undertook

Crossreactivity between barley and oats

• Hardy et al. 2014 *J Autoimmun*

Diversity in oat potential immunogenicity: basis for the selection of oat varieties with no toxicity in coeliac disease

Gut 2011

Isabel Comino,¹ Ana Real,¹ Laura de Lorenzo,^{1,2} Hugh Cornell,³ Miguel Ángel López-Casado,⁴ Francisco Barro,⁵ Pedro Lorite,⁶ M^a Isabel Torres,⁶ Ángel Cebolla,⁷ Carolina Sousa¹

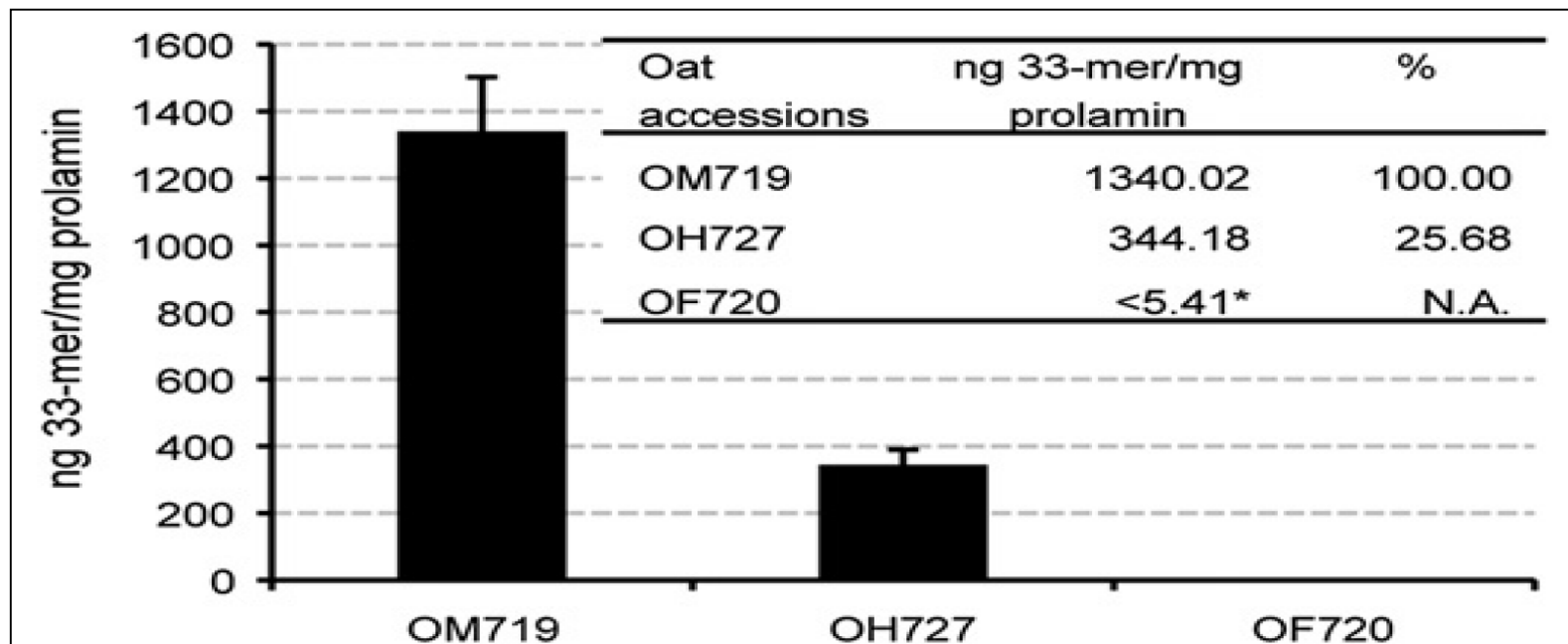


Figure 4 Detection of the concentration of the 33-mer peptide in different oat varieties. The concentration of 33-mer was determined by competitive ELISA using the monoclonal antibody (moAb) G12



Conclusions

- Oats to coeliacs still debated - but less so
- Vast majority of coeliacs tolerate gluten-free oats
 - NICE guidelines!
- Oats desired by most coeliacs
- Molecular basis of oats intolerance
- No hard end-points – no proven benefit
- Coeliacs should enjoy their gluten-free oats – clinicians must be aware of intolerance