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## **GlutN: GlutN: A translational approach from plant to patient to improve knowledge on non-coeliac gluten/wheat sensitivity**

Emmanuelle Bancel, Mélanie Lavoignat, Marie-Agnès Peyron, Bruno Novales, Brigitte Chanteranne, Emmanuelle Kesse-Guyot, Véronique Santé-Lhoutellier, Catherine Ravel, Angéline D'orlando, Corinne Bouteloup-Demange

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## ➤ **GlutN: A translational approach from plant to patient to improve knowledge on non-coeliac gluten/wheat sensitivity**

E. Bancel, V. Santé-Lhoutellier, M.A. Peyron, E. Kesse-Guyot, B. Novales, A. D'orlando, M. Lavoignat, B. Chanteranne, C. Bouteloup, L. Halupka, L. Martin, H. Zhour, E. Pujos-Guillot, C. Ravel

# ➤ The two faces of wheat gluten proteins

## Wheat, an important staple crop

- It contributes more than 20% of the energy and protein intake of human
- Gluten proteins (gliadins and glutenins) represent about 80% of the total grain proteins
- The unique properties of the gluten protein fraction allow the processing of wheat



A source of plant proteins (S-AA rich, Lysine poor) knowing that revegetation of the protein diet has to be achieved for a sustainability



Wheat proteins, especially gluten proteins, which have an unusual AA sequence, can trigger health problems due their resistance to digestion



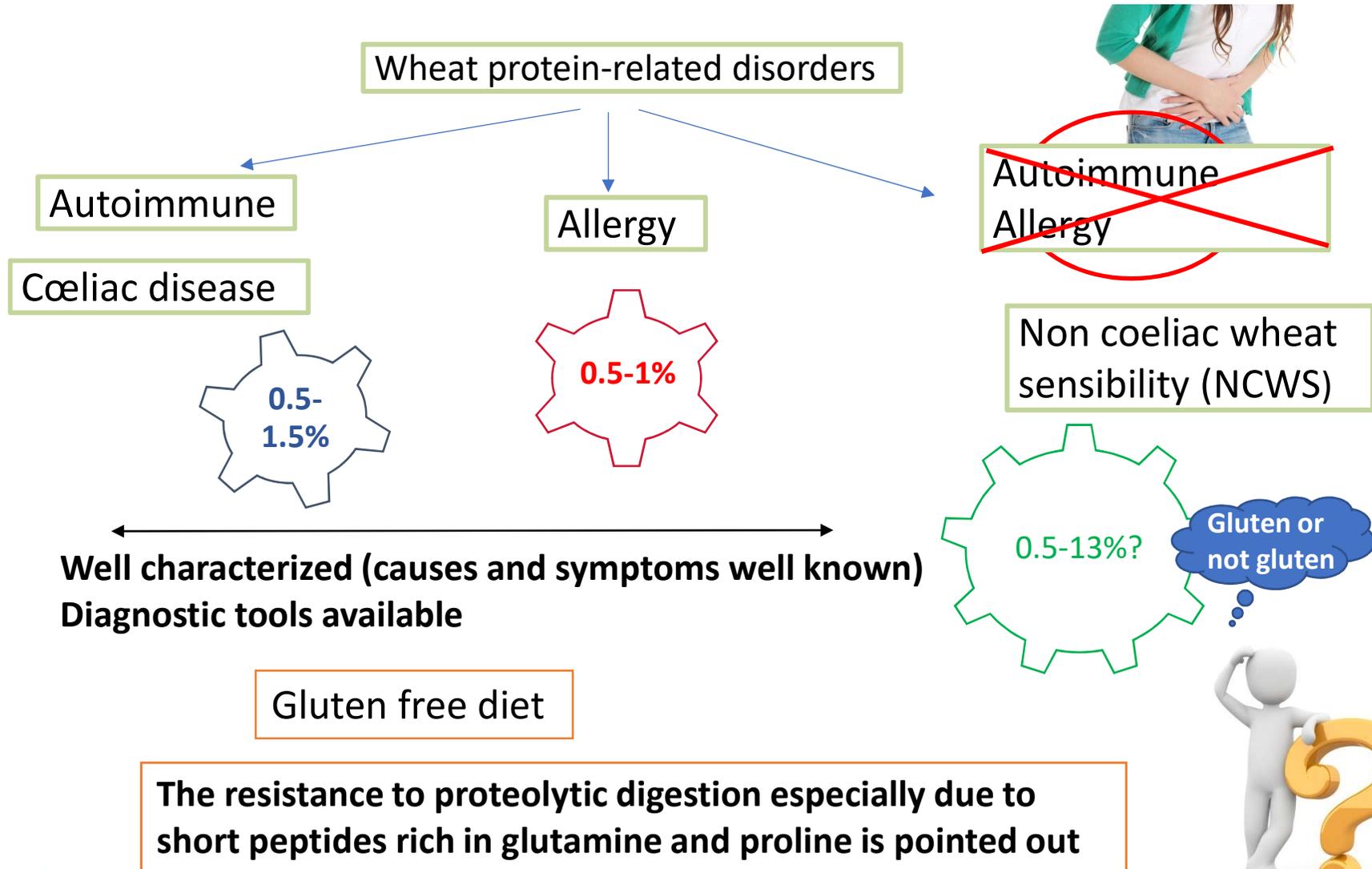
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# ➤ Wheat protein-related disorders

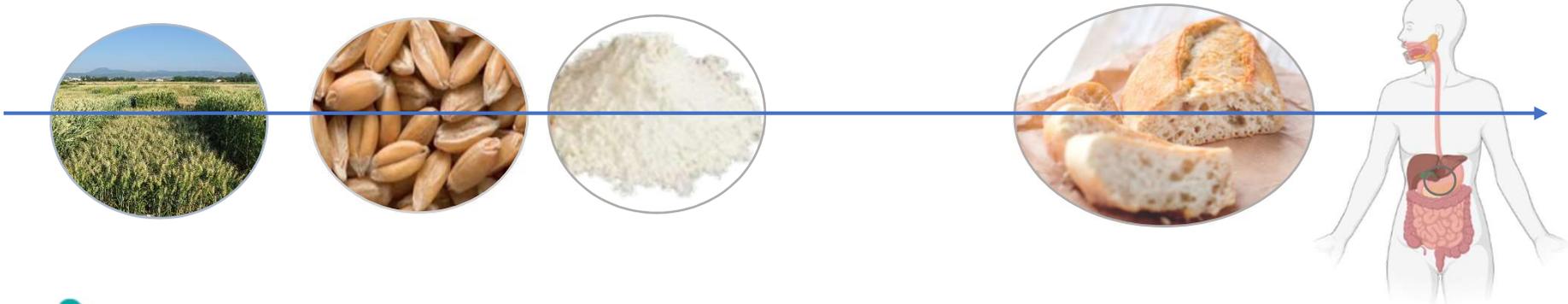
Reviewed by Sapone A, et al. 2012



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# ➤ GlutN, a project dedicated to NCWS

A translational multidisciplinary projet, from field to fork  
2018-2023



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## ➤ GlutN: Wheat and specific breads to solve gluten sensitivity

### Objectives for the « field »

- Identification of plant characteristics, which influence bread proteins *in vitro* digestibility, and could be used for indirect selection
- Setting lines or processes for producing specific and more easy-to-digest breads for NCWS patients

### Objectives for the «fork »

- Etiology: Is gluten the causal element of NCWS (and more)?
- Developing biomarkers to objectively diagnose the NCWS
- Assessing occurrence

What are the tasks and the main results of GlutN to reach these objectives?



# ➤ GlutN: Wheat and specific breads to solve gluten sensitivity



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**Epidemiology** : NCWS occurrence



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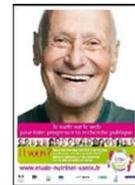
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## > Epidemiology



[www.etude-nutrinet-sante.fr](http://www.etude-nutrinet-sante.fr)

**160,000 « nutrinautes » well described**



**33 647 members** responded to specific survey about gluten exclusion

**20,456 non coeliac non allergic members were included.  
What is their profile?**



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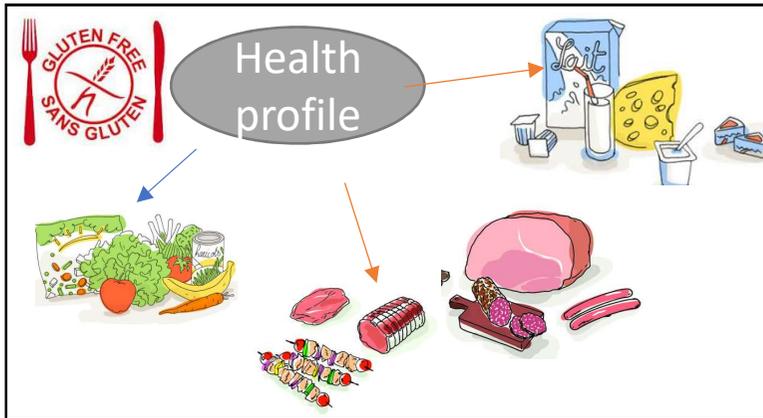
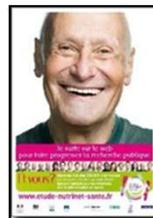
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XIV International

1

# Epidemiology

20,456 « nutrinautes » included.



- Individuals excluding gluten have a healthier profile

After adjustment to fit to the French population

Gluten exclusion	10.31 – 11.22%
Complete exclusion	1.65 - 2.01%
NCWS	2.63 - 3.06%

- The occurrence of NCWS is about 3%



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Perrin L et al. 2019. DOI: <https://doi.org/10.1017/S0007114519001053>

➤ **GlutN: Wheat and specific breads to solve gluten sensitivity** **From field to fork**



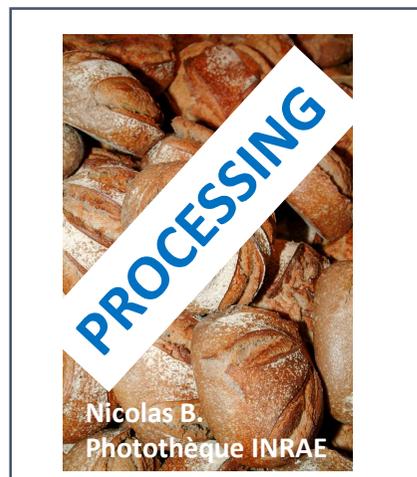
**DIJON CÉRÉALES**  
ACTIFS, POSITIFS, COOPÉRATIFS



ANR-INBS11-0010



2



3



4



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## ➤ The partial bread protein digestibility (PPD)



**75 cultivars** comprising **old** (<1960) and **recent** cultivars (>1960) phenotyped and genotyped

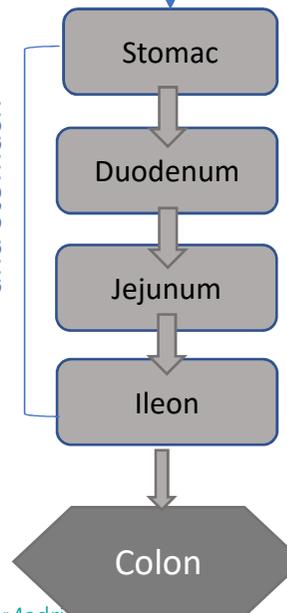
17 (8 old + 9 modern cultivars) illustrating the phenotypic diversity

Bread making with each cultivar and a standard yeast process



Partial *in vitro* digestion (2 hours)  
N quantification

N in small intestine and stomach



Partial Protein Digestibility

**PPD =**

$$\frac{\text{Assimilated N}}{\text{Total N}}$$

Non assimilated N

Assimilated N

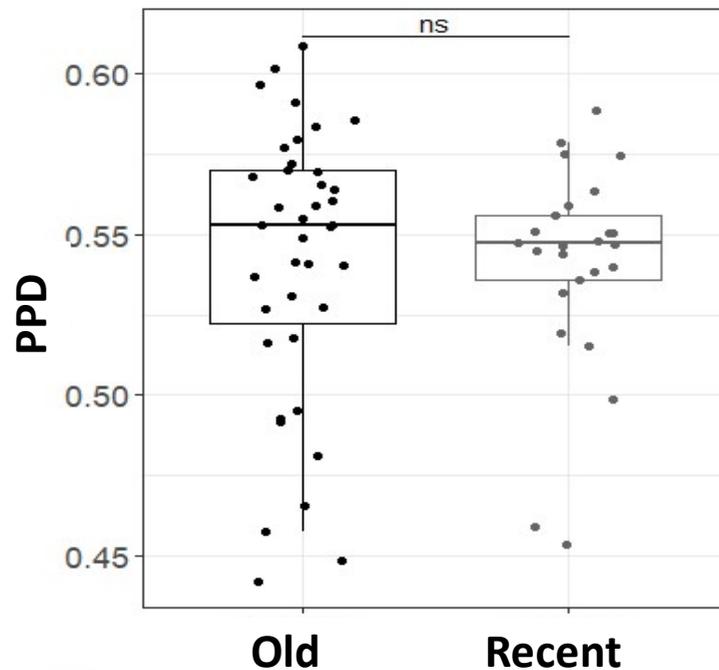


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## ➤ What does reveal the PPD?

	P value	% Variance explained by the genotype
<b>PPD</b>	<b>0.013</b>	<b>42.65 %</b>

A genetic variability for PPD (0.44-0.61), significantly influenced by the genotype



PPD is not influenced by the age of the cultivar



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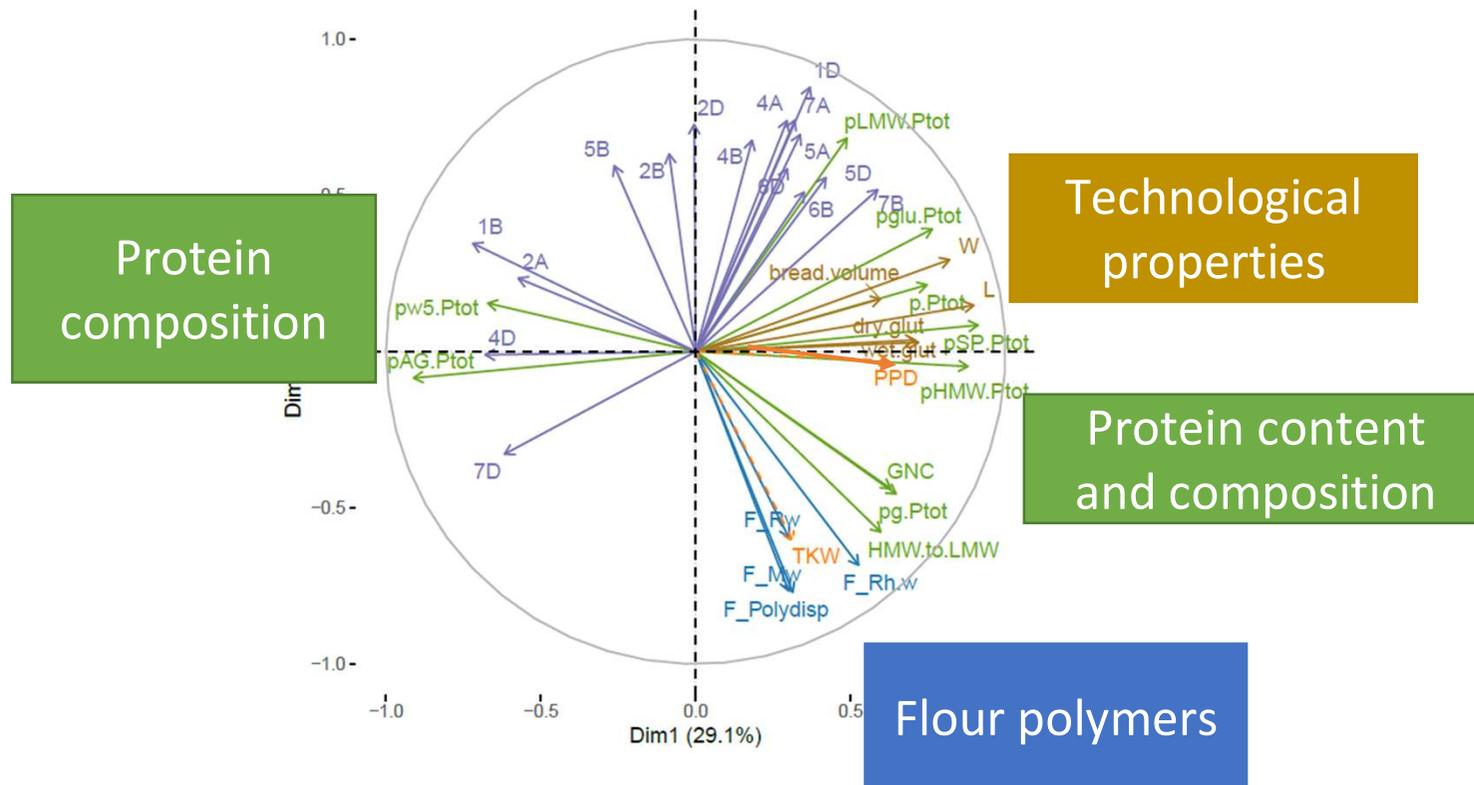
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Lavoignat et al. 2022. DOI: <https://doi.org/10.1016/j.jcs.2022.103533>

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## ➤ What does reveal the PPD?



- The PPD for high yielding lines could be indirectly improved



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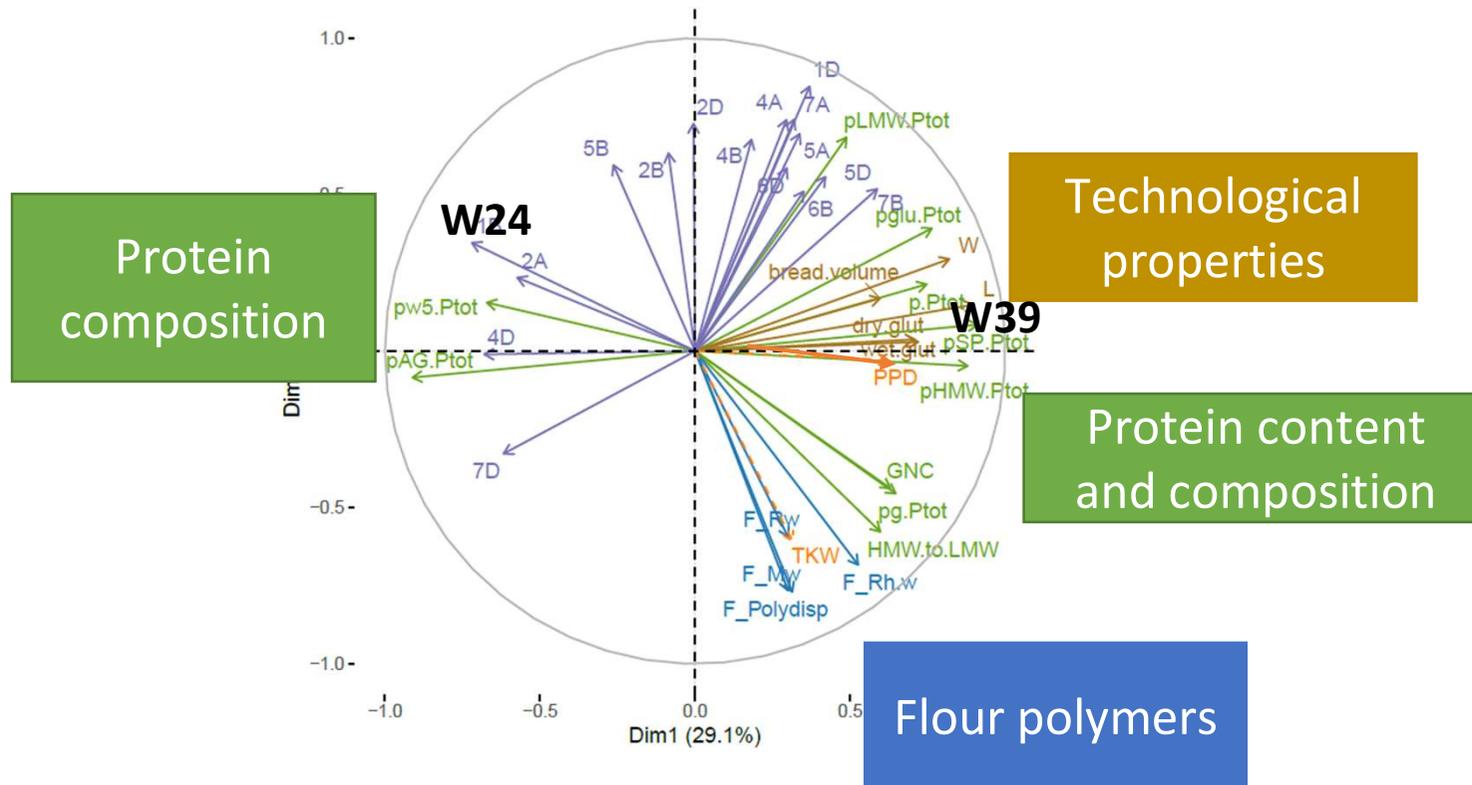
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## ➤ What does reveal the PPD?

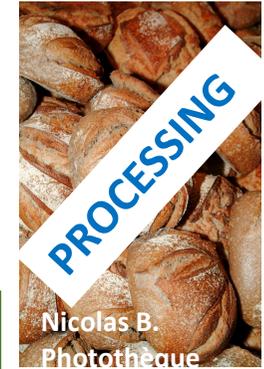


- Contrasted lines for PPD can be identified
- Sourdough breads were also made

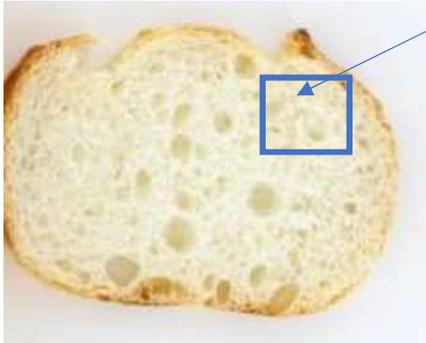


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# Differences between baking processes observed by ESEM

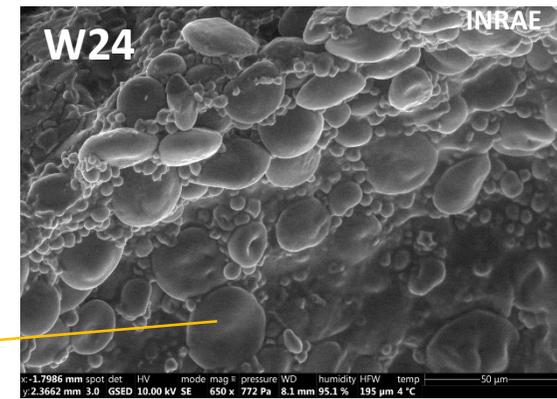
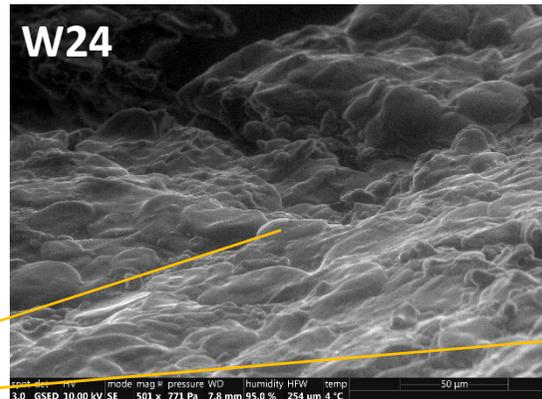


Peripheral sample

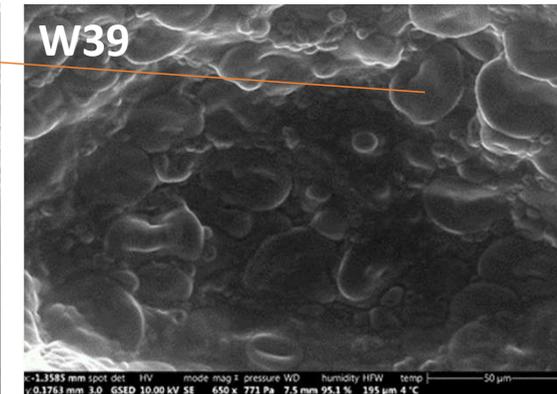
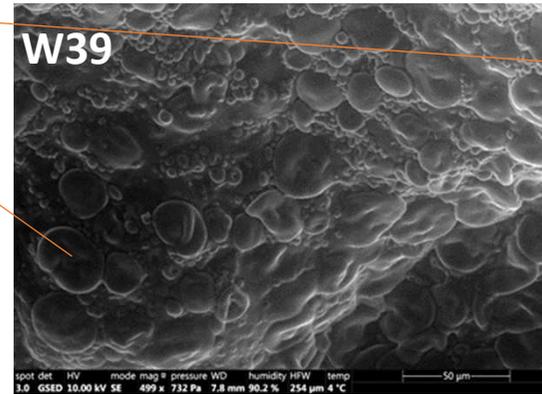


YEAST

SOURDOUGH



Starch Granules



- A strong influence of the process (more intact starch granules in the sourdough breads). A influence of the cultivars
- Protein digestion depends on the digestion of the gluten-starch matrix

4

# > From field to fork



  
4 genotypes

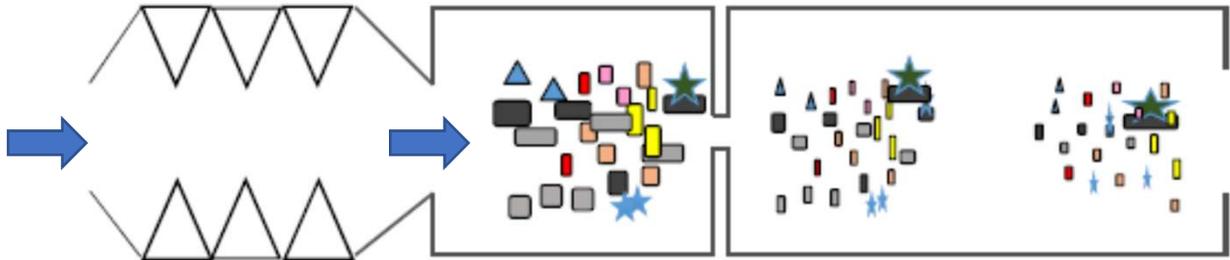
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2 processes



*In vitro*  
Mastication /  
digestion

Digestion (4h)  
Stomac      Small intestin



***In vitro* masticator (AM2)**



Action of salivary amylase

***In vitro* Dynamic digestor (DIDGI)**



Gastric and intestinal samples produced at different times

• Production and analysis of bolus

• Digestate analysis



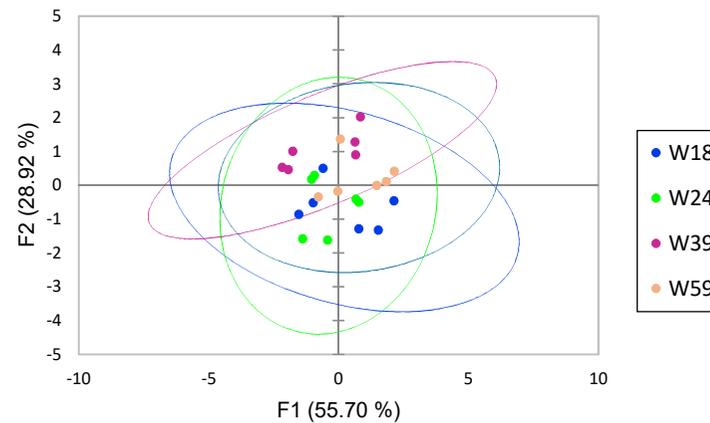
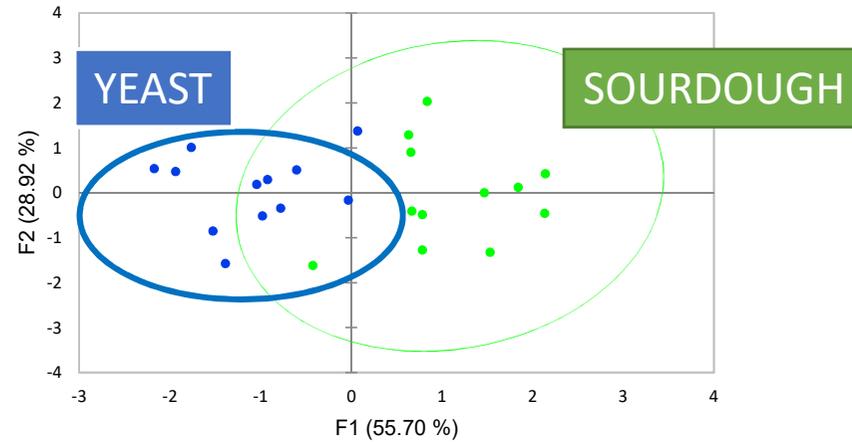
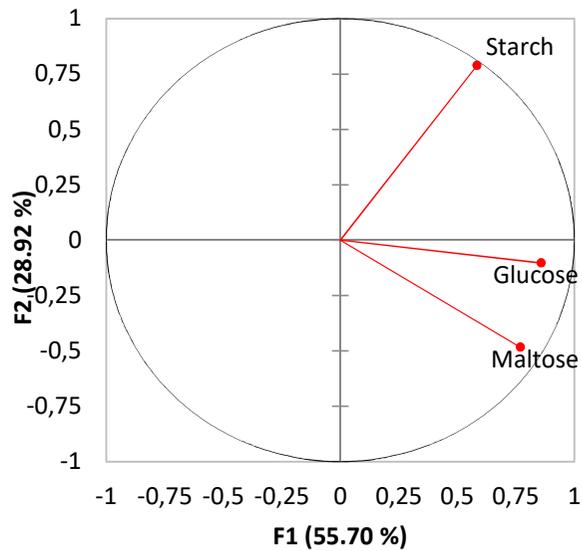
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## ➤ Profiling carbohydrates of breads after oral digestion

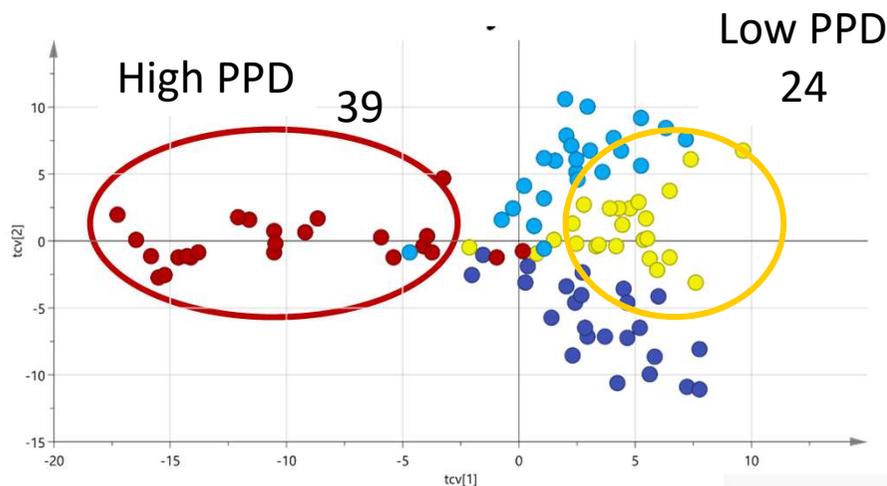


Difference for starch, glucose and maltose composition related to the process

# ➤ Metabolomics from bread gastric digestates

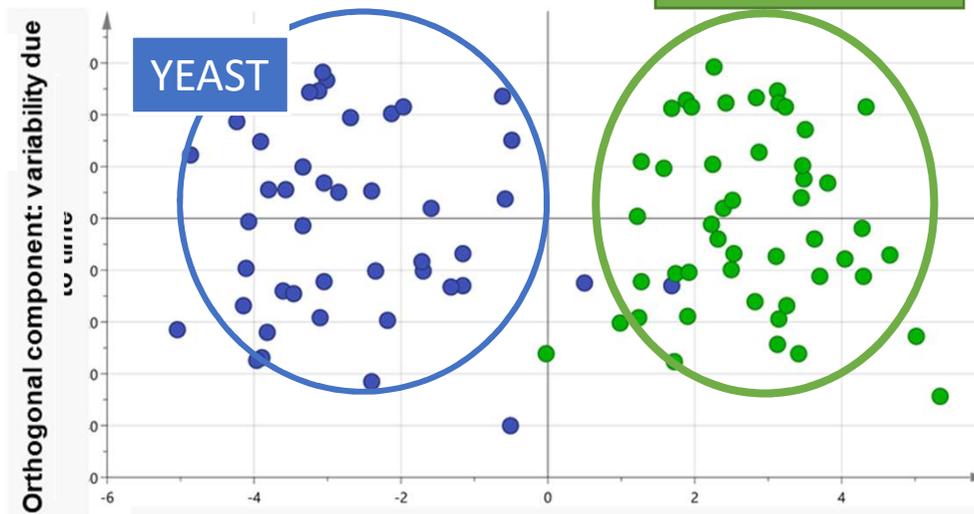


Cultivars



Cultivar 39 differs from the others

Process



Differences related to the process



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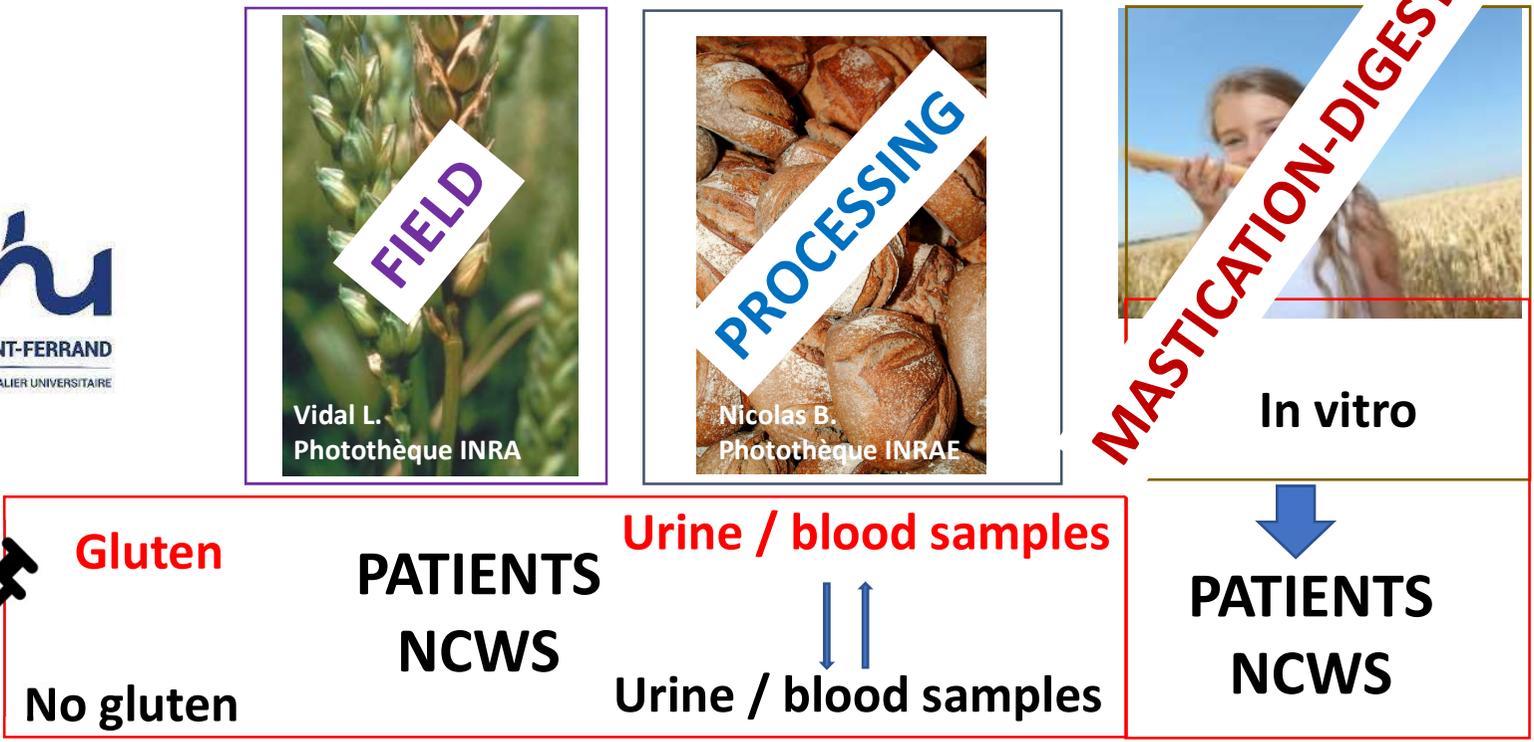
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➤ **GlutN: Wheat and specific breads to solve gluten sensitivity**

**From field to fork**



5



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## ➤ A Clinical trial in two steps

For both steps, the necessary condition is the cohort recruitment  
The objective is to recruit well-characterized patients

**125 candidates**

45 patients screened by Dr BOUTELOUP and followed by a nutritionist

**28/45 patients may be included**

**20 inclusions**



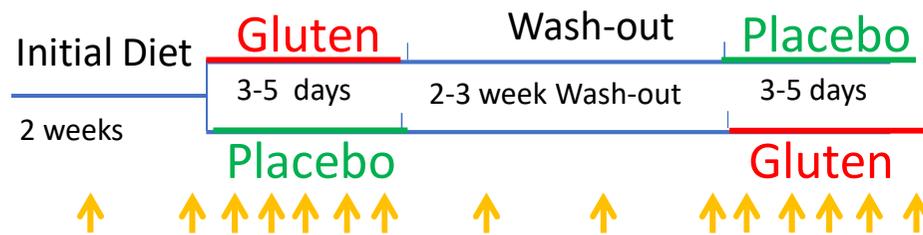
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# > A Clinical trial in two steps 1. Is gluten guilty?

## Gluten vs placebo double-blind cross-over test



**GSRs (symptom evaluation)**

**Urine and blood samples**

→ **Untargeted metabolomics**

**What kind of food**  
Gluten = 8g/day  
Gluten/placebo: identical food as far as possible  
Initial diet, Wash-out: gluten free diet  
Fructanes are controlled

**20 patients have completed the trial**



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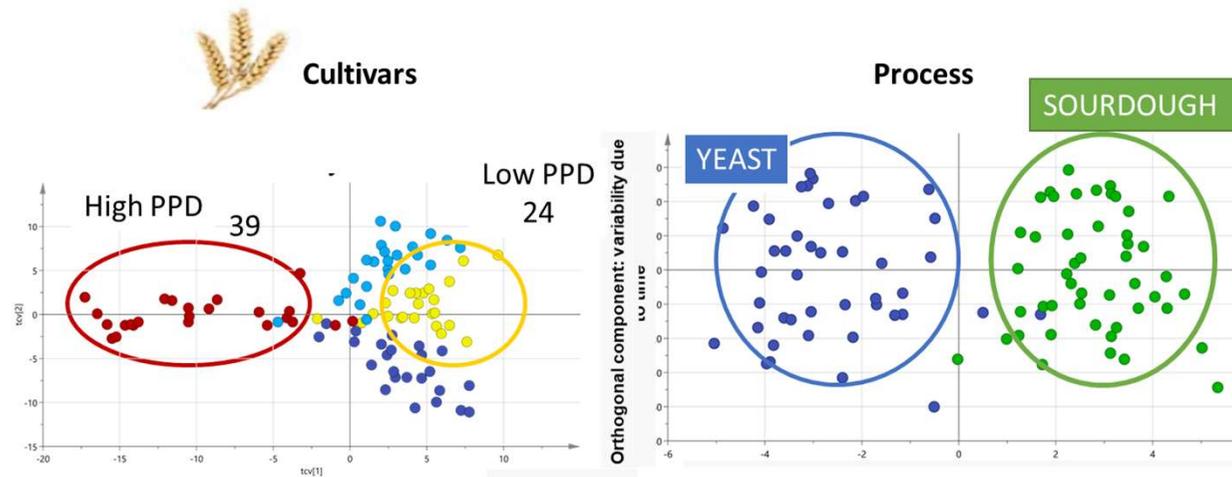
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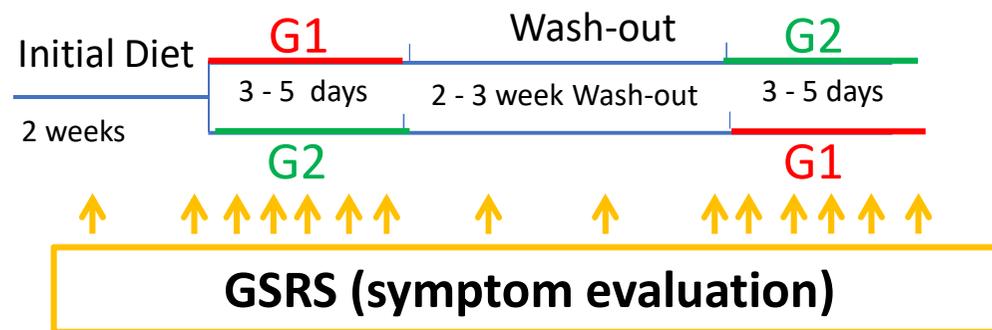
# ➤ A Clinical trial in two steps: the second step (in progress)

## 2. Could specific bread be developed for NSWS patients?

A specific bread is a combination between a wheat genotype and a process



sourdough breads made with genotype 39 vs genotype 24 cross over test



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## ➤ Take home message

**It is possible to improve PPD**

**Differences are highlighted related to the cultivar and the baking process**

**The clinical study is in progress. The perspective is to integrate data from *in vitro* oral and gastro-intestinal digestion and clinical results to establish a link with NCWS**



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➤ Thank you for your attention  
Thank you to all the partners

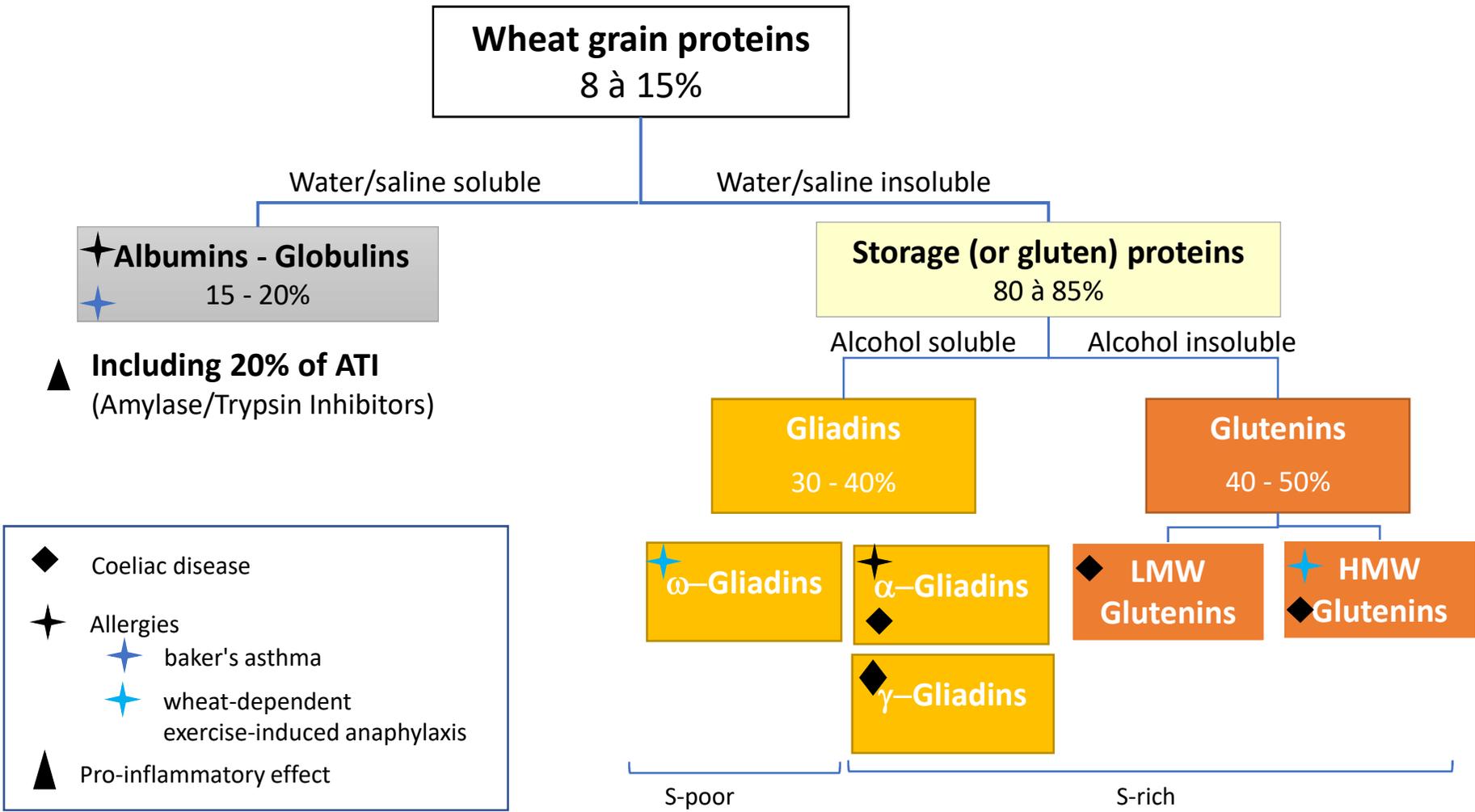


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# ➤ Wheat protein-related disorders



## ➤ What does reveal the bread protein digestibility

E. Bancel  
C. Ravel



2



A set of **75 cultivars** comprising **old** (<1960) and **recent** cultivars (>1960) was cultivated at two locations

They were genotyped and phenotyped



**8 old + 9 modern cultivars illustrating the global phenotypic diversity were selected**



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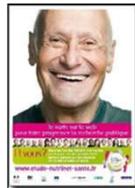
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# Epidemiology



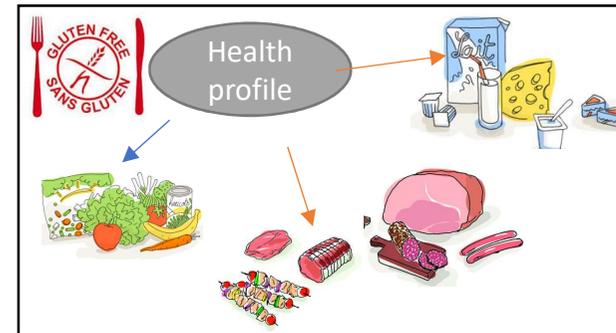
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After adjustment to fit to the French population

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Complete exclusion	1.65 - 2.01%
NCWS	2.63 - 3.06%

• The occurrence of NCWS is about 3% biblio de 0,5 à13%