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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



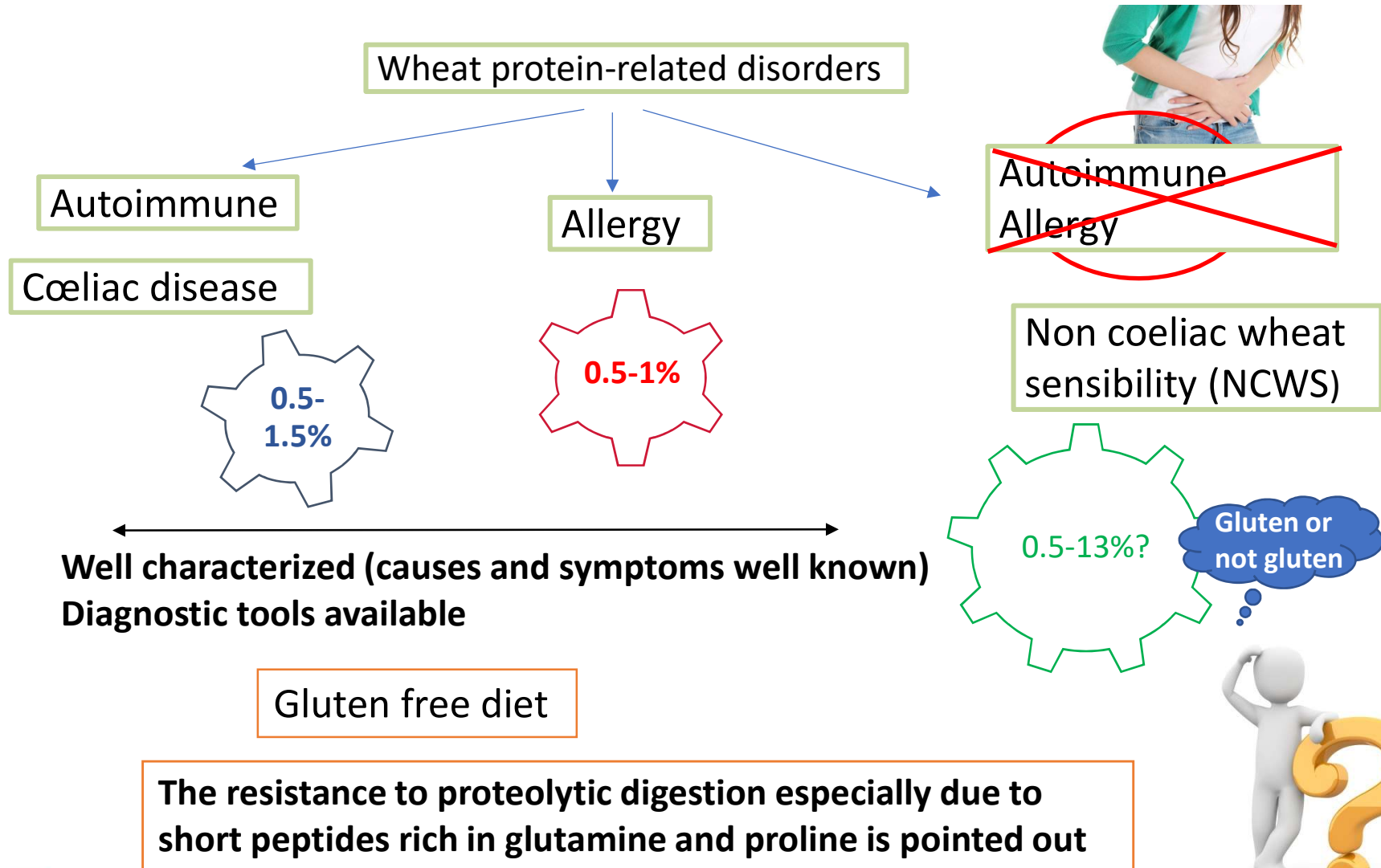
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➤ Wheat protein-related disorders

Reviewed by Sapone A, et al. 2012

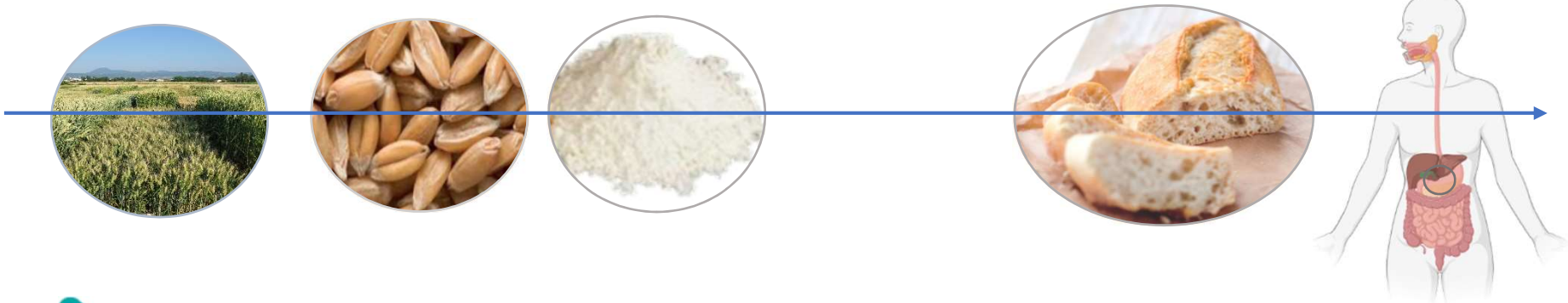


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➤ GlutN, a project dedicated to NCWS

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**



1



Epidemiology : NCWS occurrence



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1

> Epidemiology



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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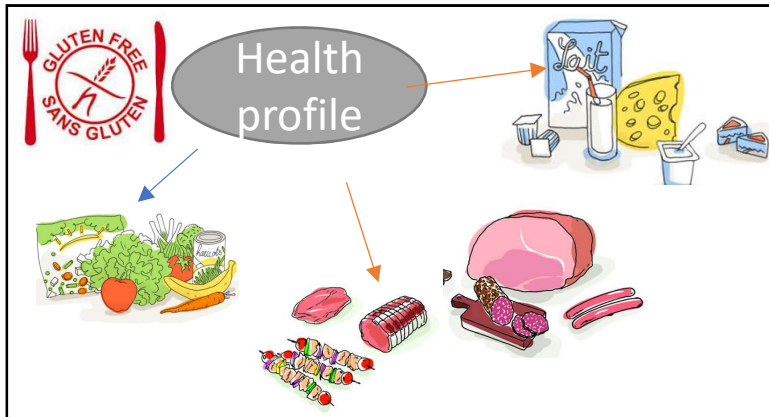
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XIV International

1

Epidemiology

20,456 « nutrinautes » included.

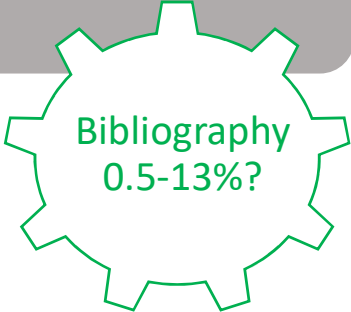


- Individuals excluding gluten have a healthier profile

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>

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

From field to fork



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2

➤ The partial bread protein digestibility (PPD)



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

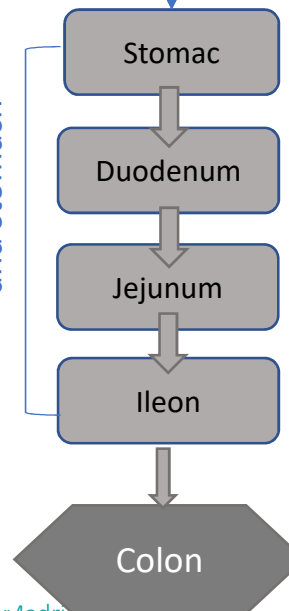
17 (8 old + 9 modern cultivars) illustrating the phenotypic diversity

Bread making with each cultivar and a standard yeast process



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

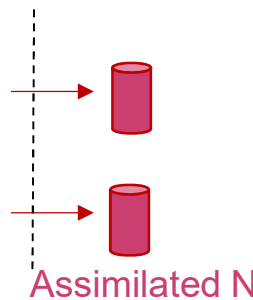
N in small intestine and stomach



Partial Protein Digestibility

PPD =

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



Non assimilated N

Colon

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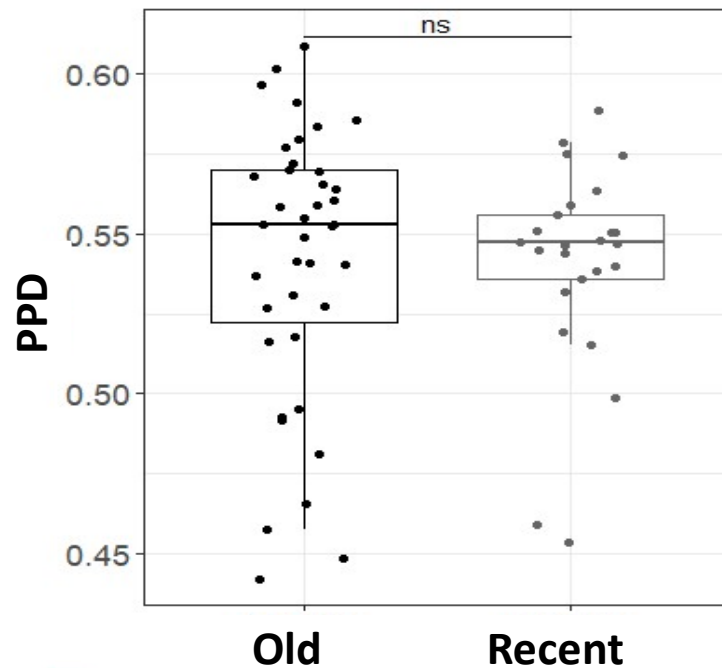


2

➤ What does reveal the PPD?

	P value	% Variance explained by the genotype
PPD	0.013	42.65 %

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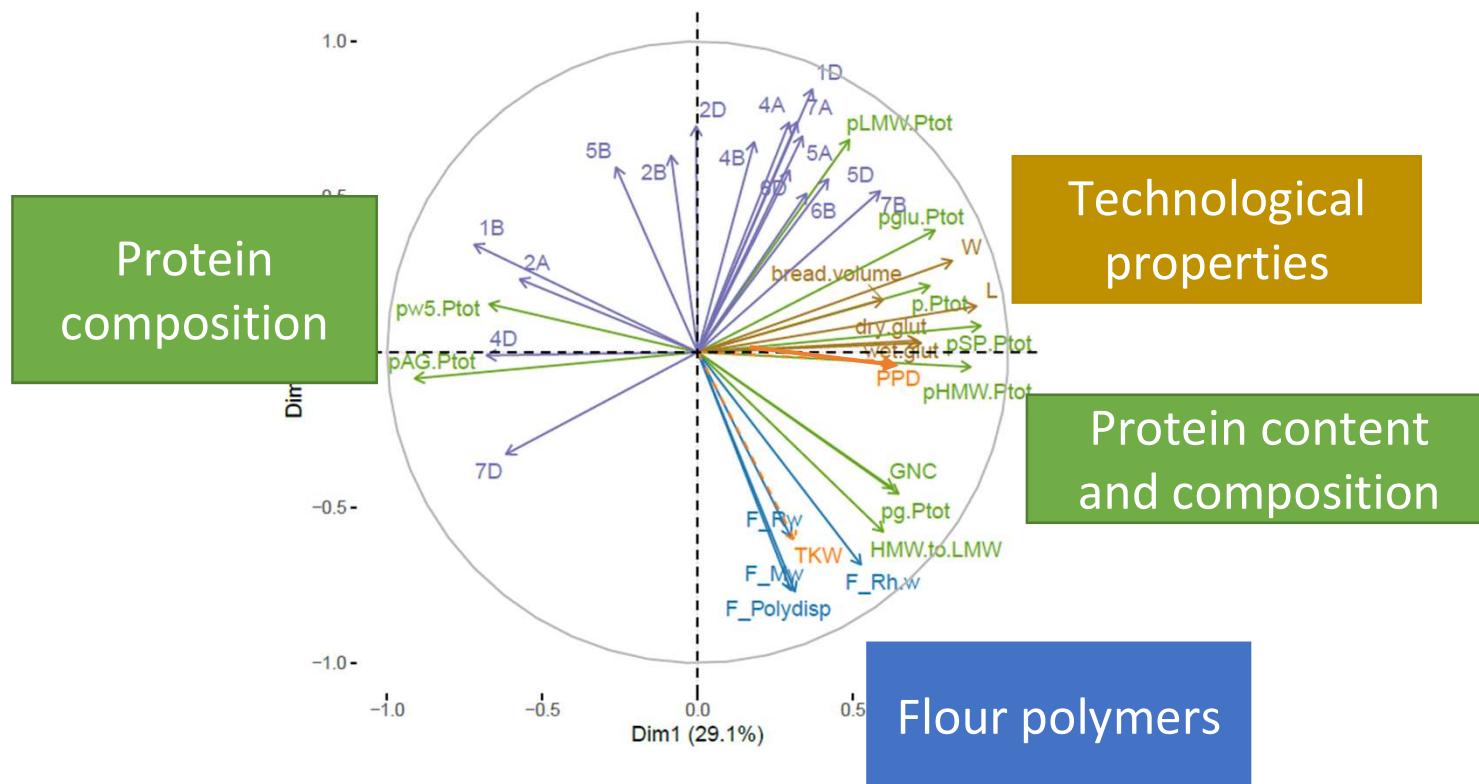
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Lavoignat et al. 2022. DOI: <https://doi.org/10.1016/j.jcs.2022.103533>

2

➤ What does reveal the PPD?



- The PPD for high yielding lines could be indirectly improved



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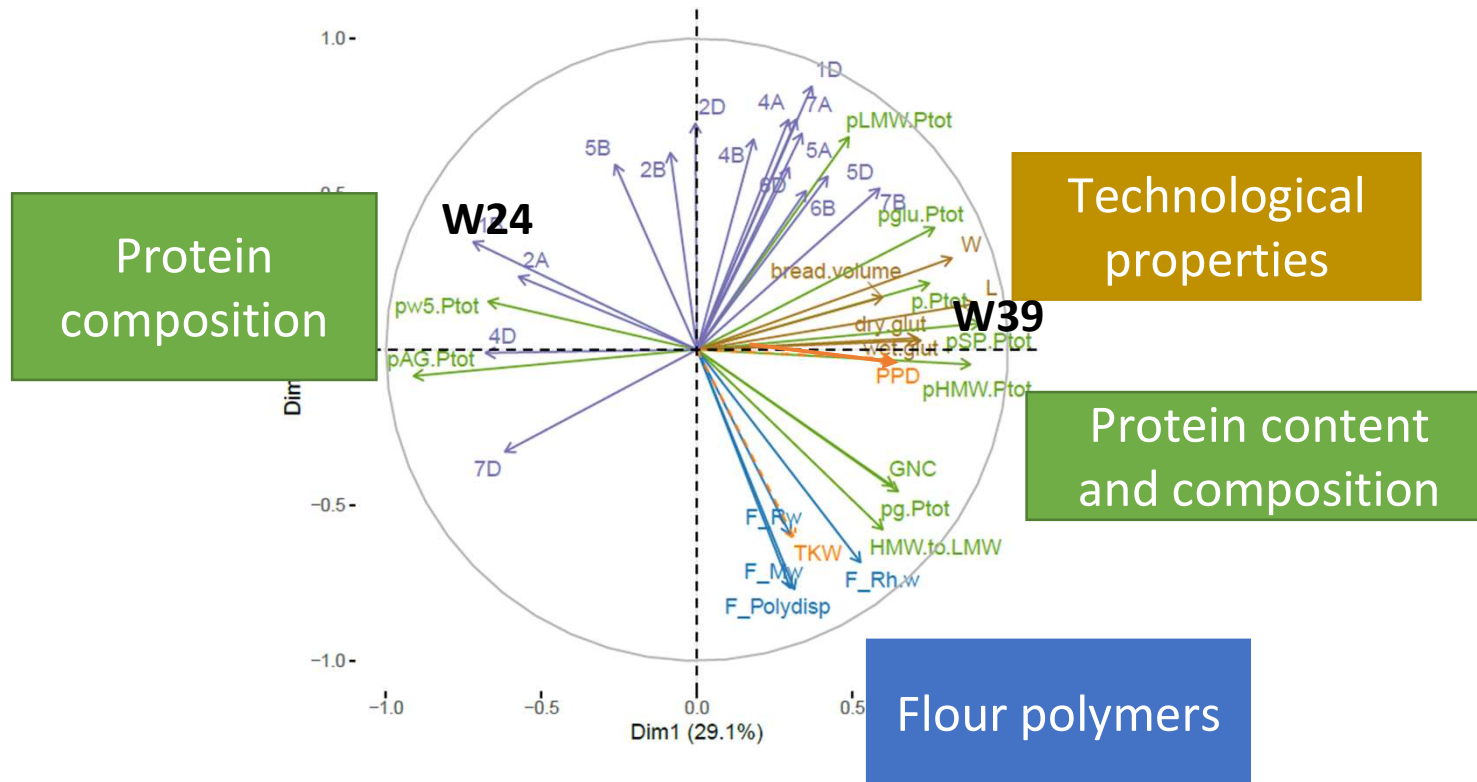
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12

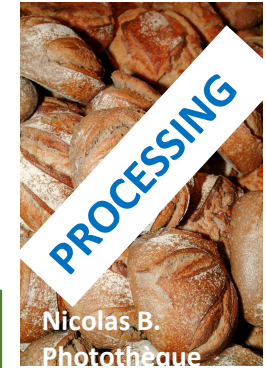
➤ What does reveal the PPD?



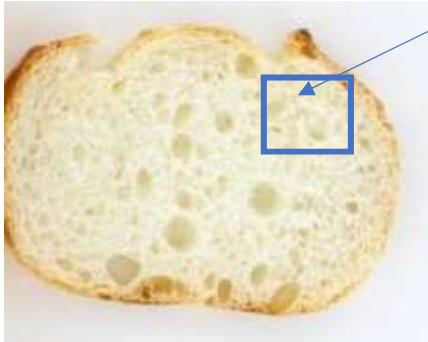
- Contrasted lines for PPD can be identified
- Sourdough breads were also made

3

Differences between baking processes observed by ESEM

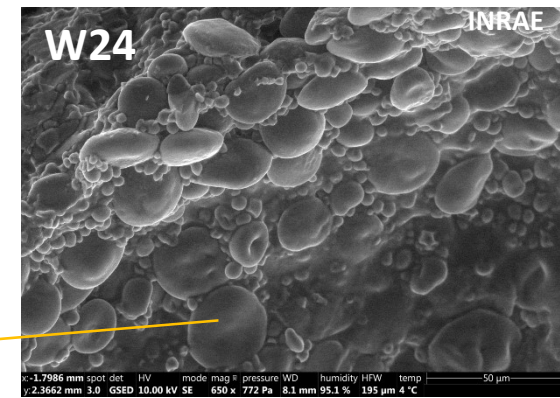
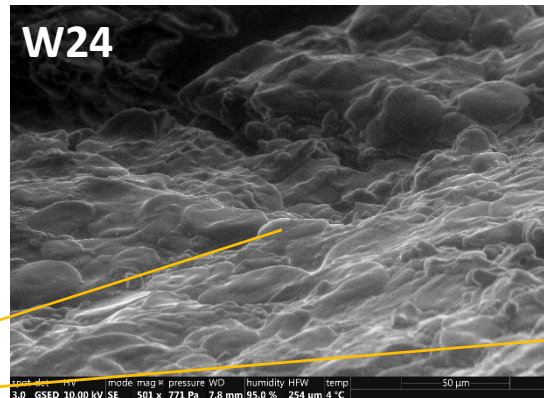


Peripheric sample

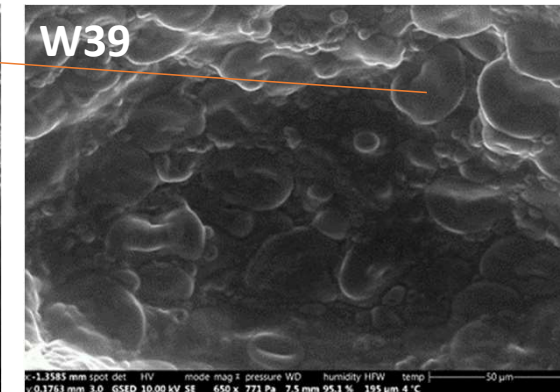
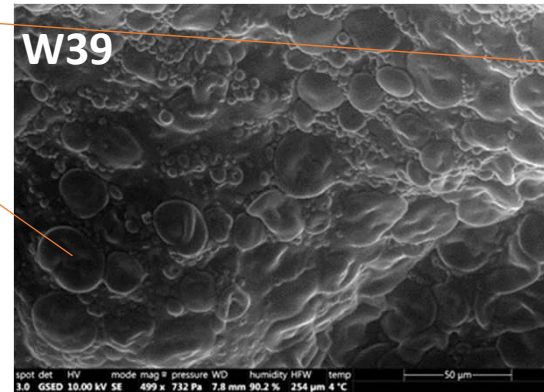


YEAST

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

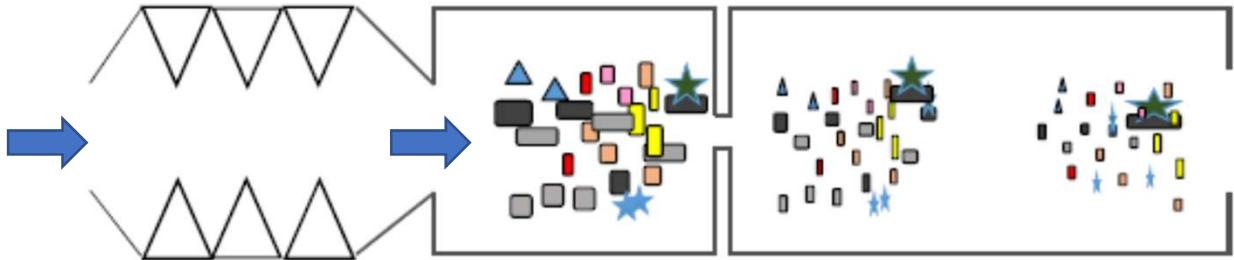
X

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



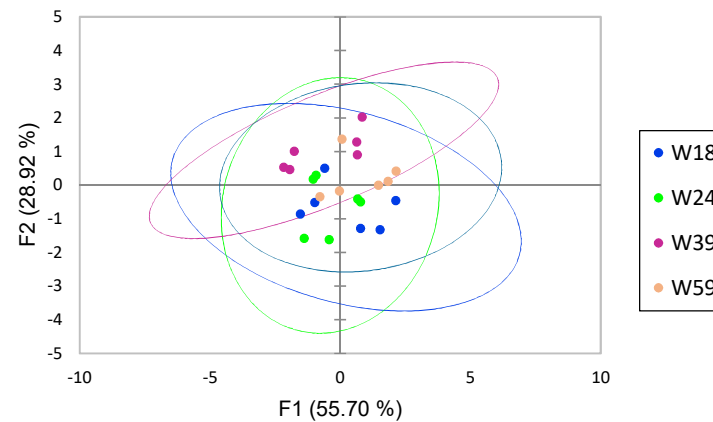
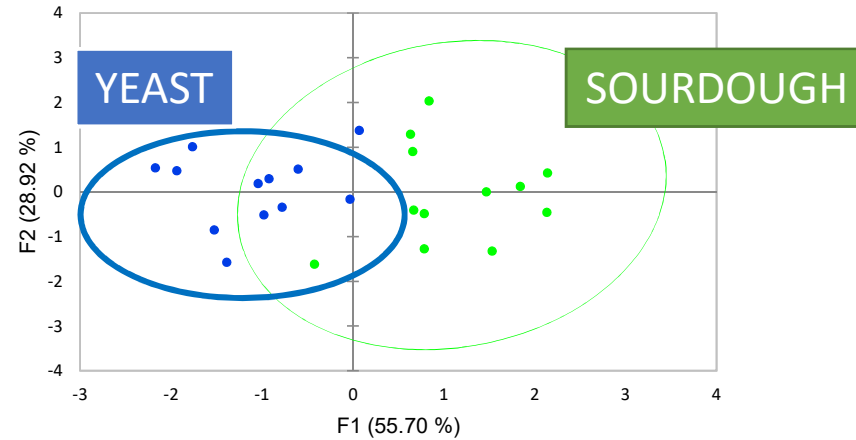
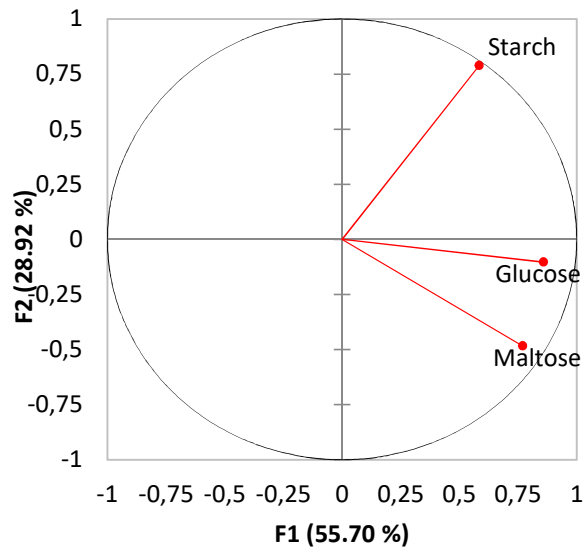
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➤ Profiling carbohydrates of breads after oral digestion

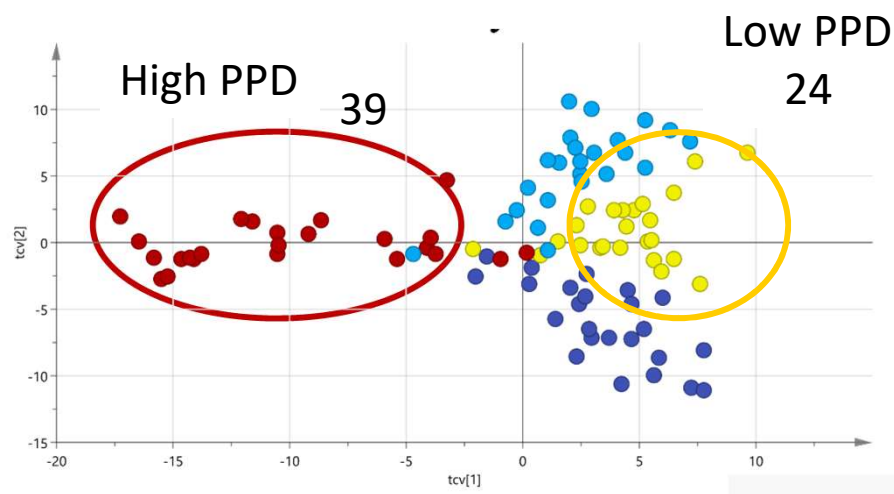


Difference for starch, glucose and maltose composition related to the process

➤ Metabolomics from bread gastric digestates

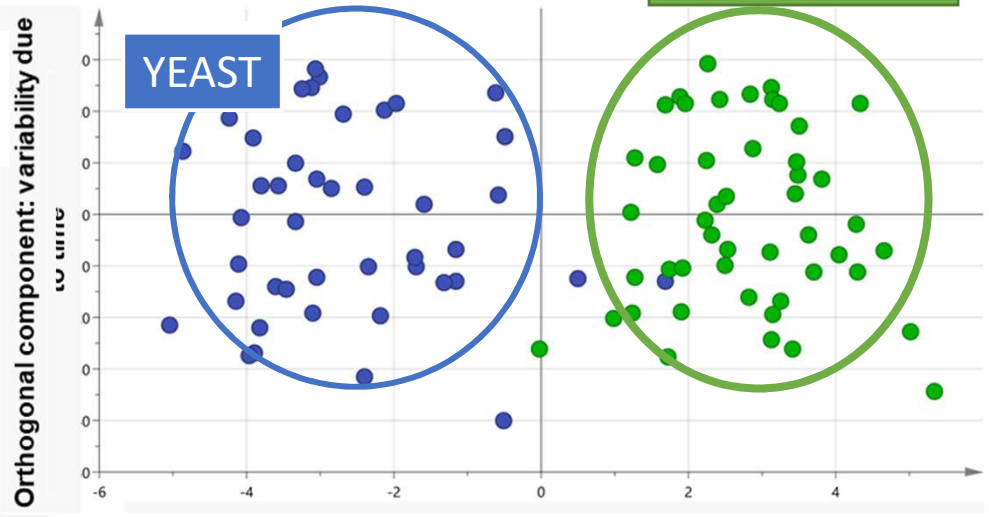


Cultivars



Cultivar 39 differs from the others

Process



Differences related to the process



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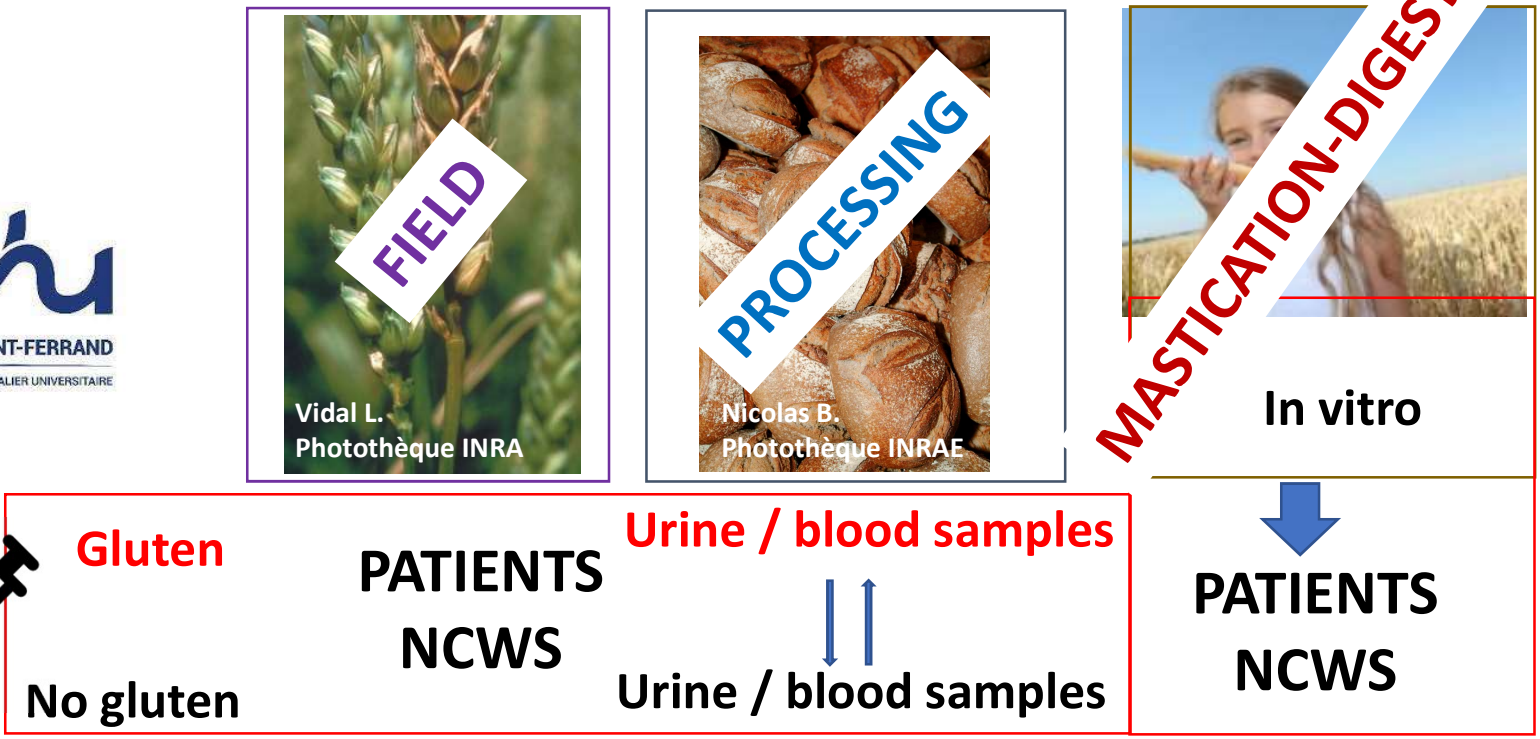
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➤ **GlutN: Wheat and specific breads to solve gluten sensitivity**

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



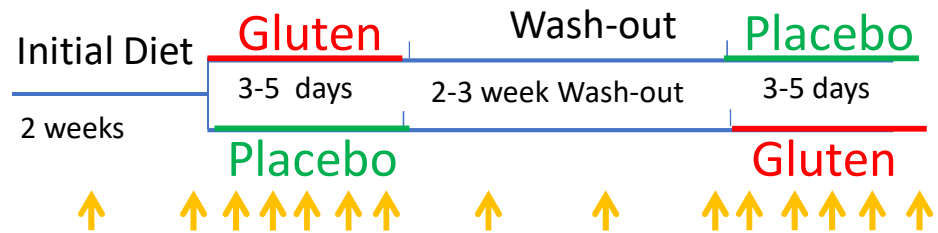
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➤ A Clinical trial in two steps 1. Is gluten guilty?

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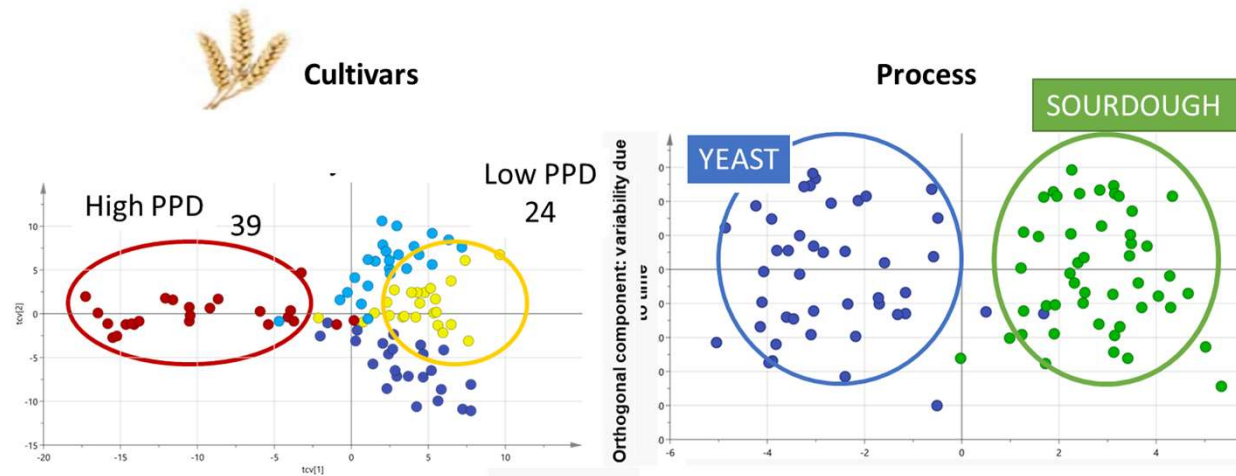
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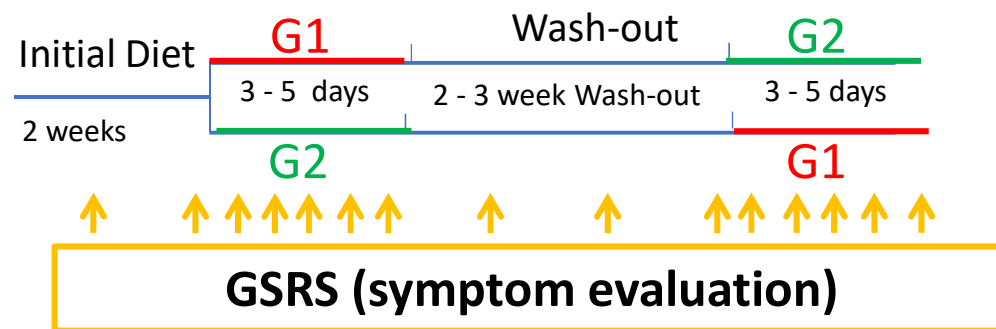
➤ A Clinical trial in two steps: the second step (in progress)

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



ANR-INBS11-0010



DIJON CÉRÉALES
ACTIFS, POSITIFS, COOPÉRATIFS

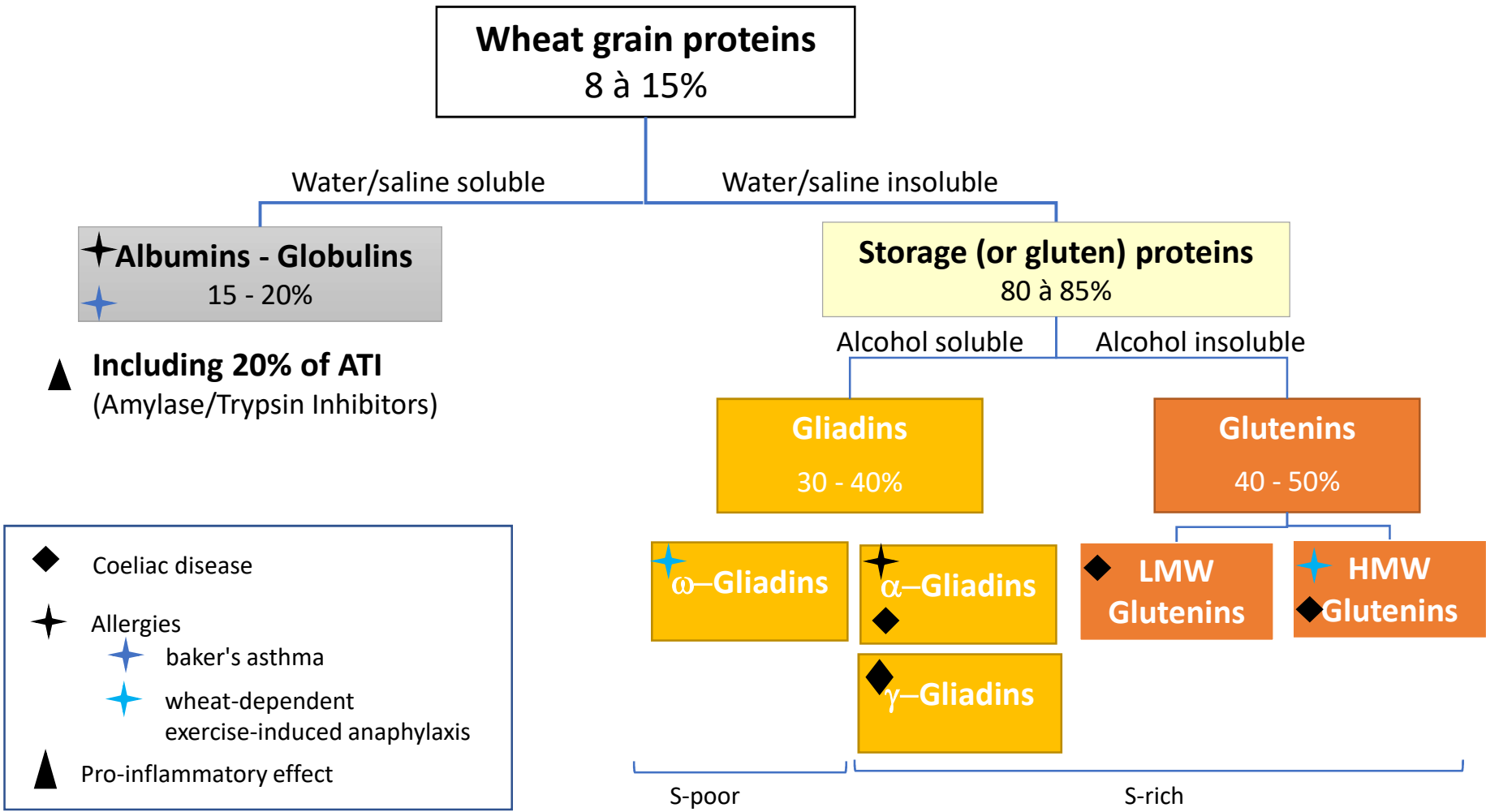


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➤ Wheat protein-related disorders



➤ 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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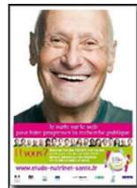
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Epidemiology

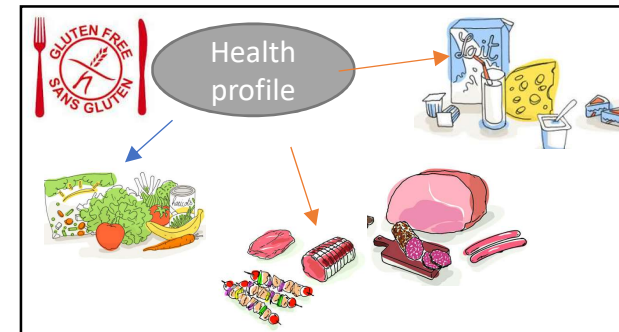


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- Individuals excluding gluten have a healthier profile

After adjustment to fit to the French population

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NCWS	2.63 - 3.06%

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