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, Angélina D'orlando, Corinne Bouteloup-Demange

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PROJET FINANCÉ PAR L'ANR - PROJECT FUNDED BY THE ANR

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

TYFA

INRAE

GlutN

Wheat protein-related disorders

Reviewed by Sapone A, et al. 2012

Wheat protein-related disorders

Autoimmune

Cœliac disease

0.5-1.5%

Allergy

0.5-1%

~~Autoimmune~~
~~Allergy~~

Non coeliac wheat sensibility (NCWS)

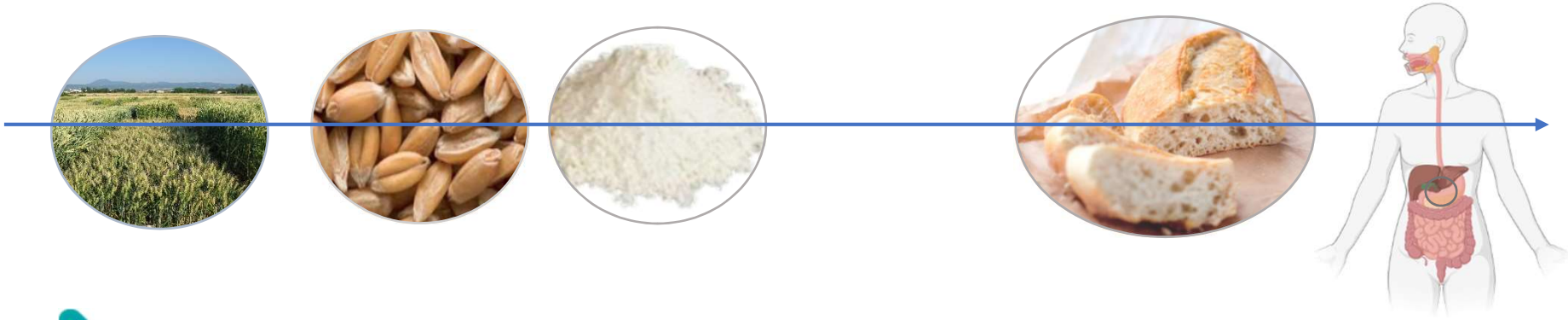
0.5-13%?

Gluten or not gluten

Well characterized (causes and symptoms well known)
Diagnostic tools available

Gluten free diet

The resistance to proteolytic digestion especially due to short peptides rich in glutamine and proline is pointed out



GlutN, a project dedicated to NCWS

A translational multidisciplinary projet, from field to fork

2018-2023

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)?
- ❑ Developping biomarkers to objectively diagnose the NCWS
- ❑ Assessing occurence

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

GlutN: Wheat and specific breads to solve gluten sensitivity

1

Équipe de Recherche en Épidémiologie Nutritionnelle

Epidemiology : NCWS occurrence

1

Epidemiology

www.etude-nutrinet-sante.fr

160,000 « nutrinautes » well described

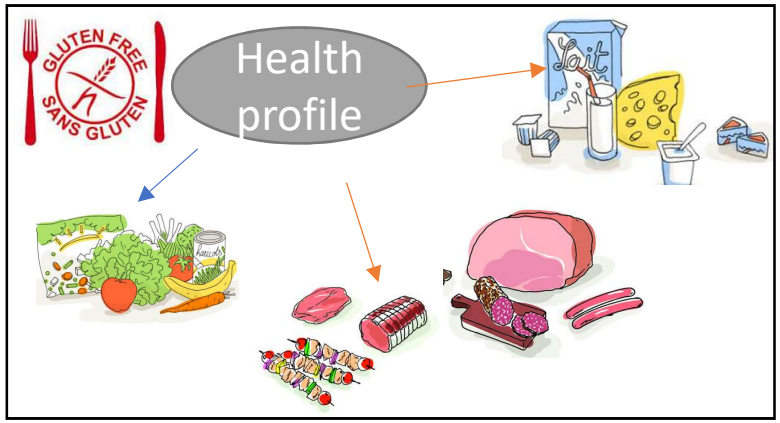
33 647 members responded to specific survey about gluten exclusion

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

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%**

Bibliography 0.5-13%?

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

CÉRÉLAB Centre de Recherche & d'Application

DIJON CÉRÉALES ACTIFS, POSITIFS, COOPÉRATIFS

QuaPA

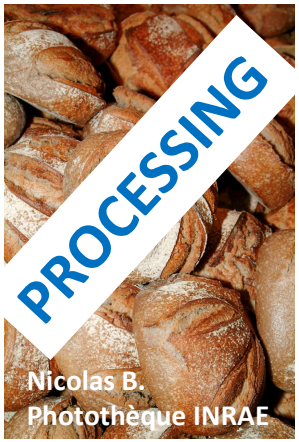
GDEC Génétique Diversité Écophysiologie des Céréales

UR 1268 bia Biopolymères Interactions Assemblages

UNH Unité de Nutrition Humaine

METABOHUB Plate-Forme EXPLORATION du METABOLISME

ANR-INBS11-0010



In vitro

2 3 4

The partial bread protein digestibility (PPD)

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

↓

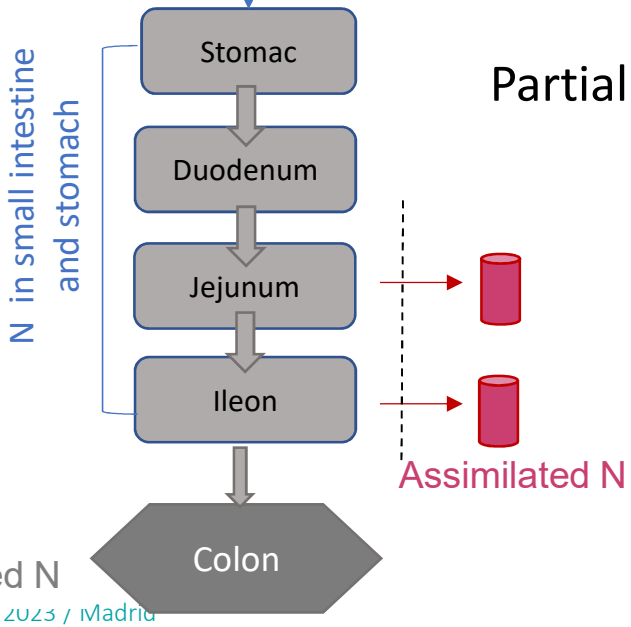
17 (8 old + 9 modern cultivars) illustrating the phenotypic diversity

↓

Bread making with each cultivar and a standard yeast process

GlutN

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



Partial Protein Digestibility

PPD =

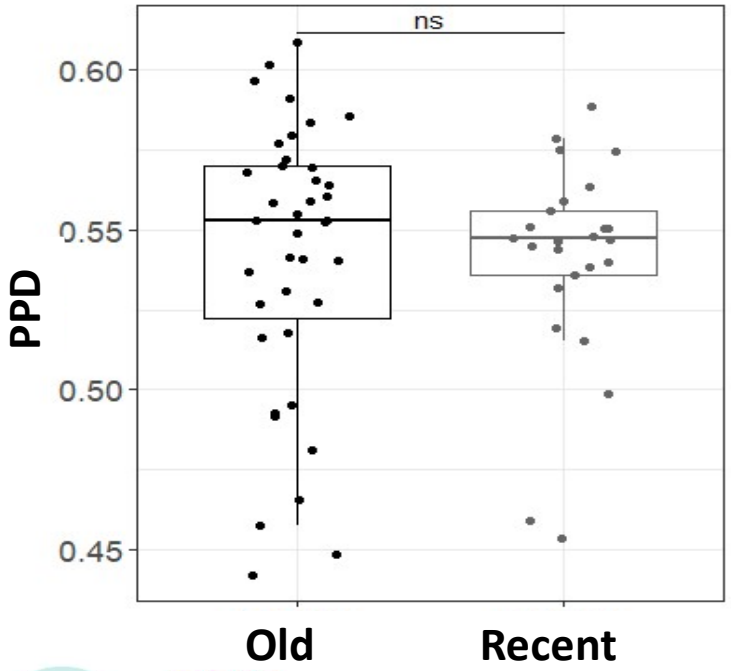
$$\frac{\text{Assimilated N}}{\text{Total N}}$$

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

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

What does reveal the PPD?

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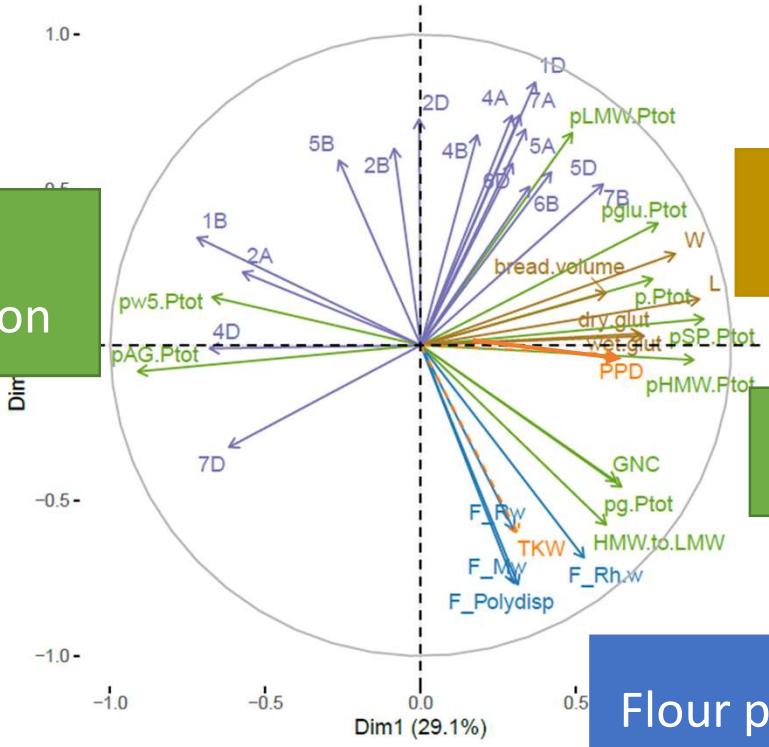

Protein composition

Technological properties

Protein content and composition

Flour polymers

- The PPD for high yielding lines could be indirectly improved

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

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What does reveal the PPD?

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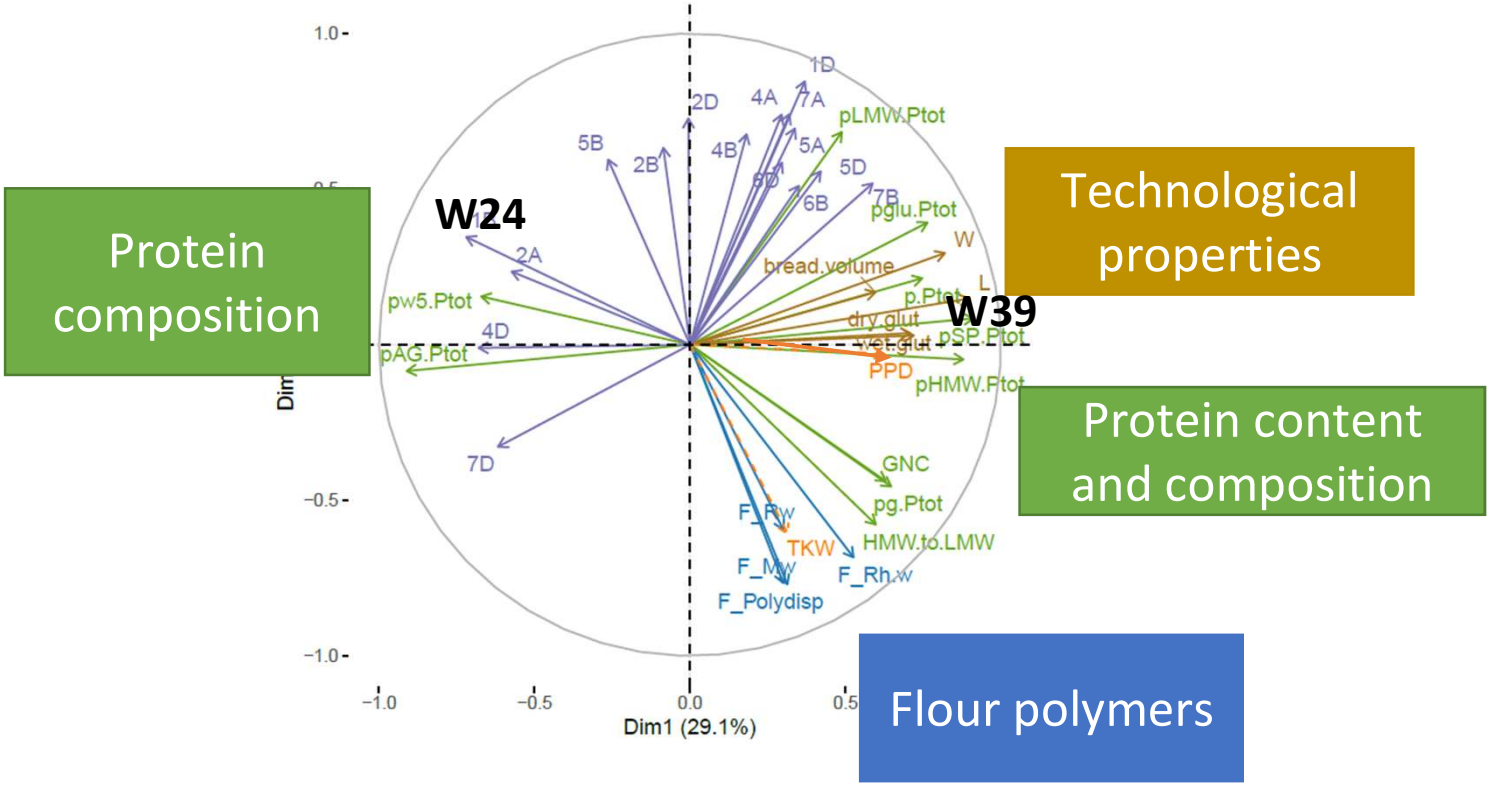
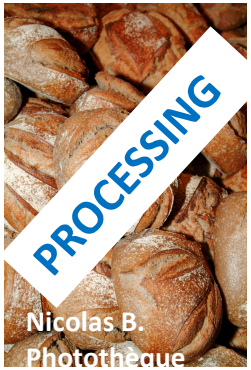


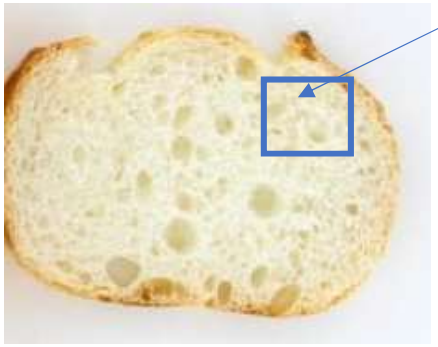
- Contrasted lines for PPD can be identified
- Sourdough breads were also made

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

3 Differences between baking processes observed by ESEM



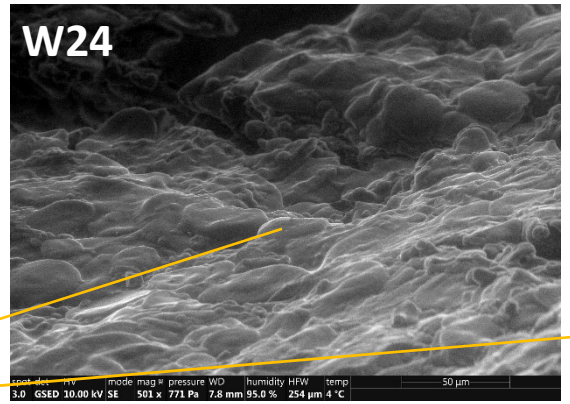
Peripheric sample

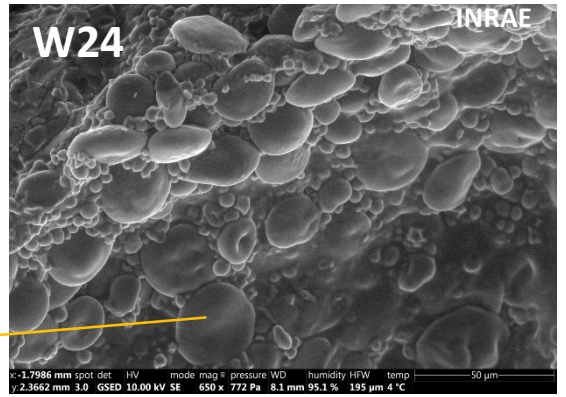


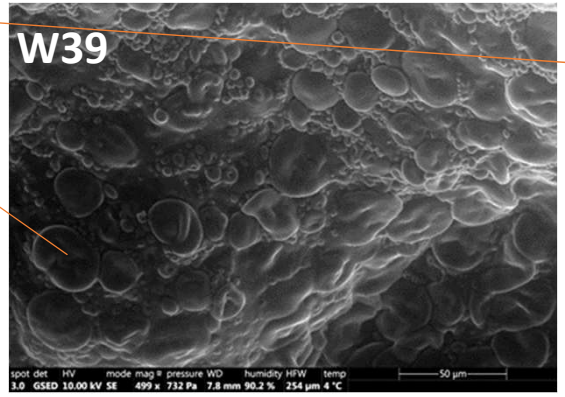
YEAST

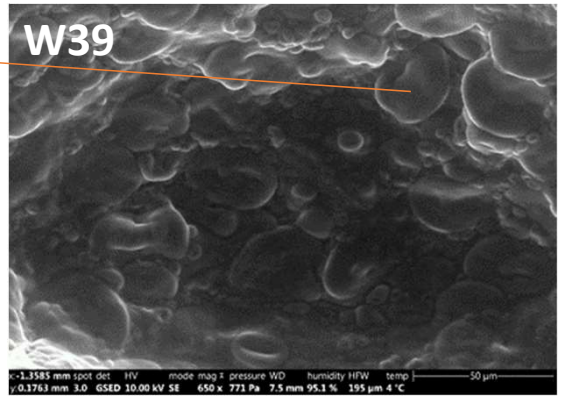
SOURDOUGH

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

From field to fork

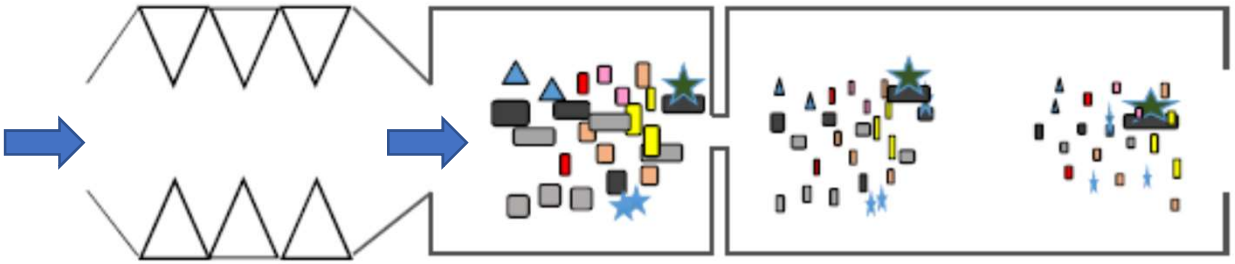
4 genotypes

X

2 processes

In vitro
Mastication / digestion

Digestion (4h)
Stomac Small intestin



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

Action of salivary amylase

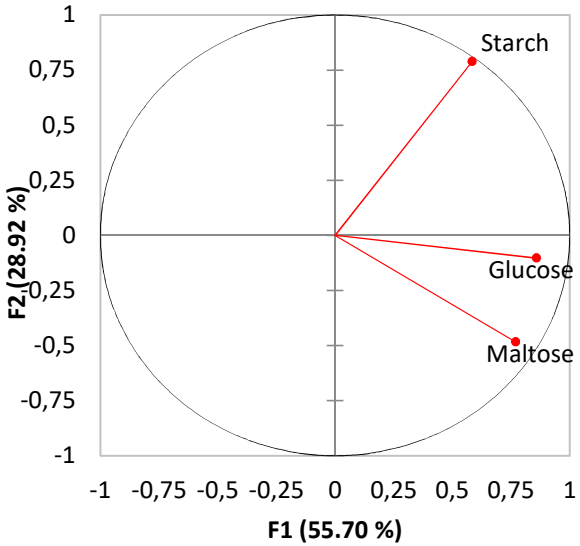
In vitro Dynamic digestor (DIDGI)

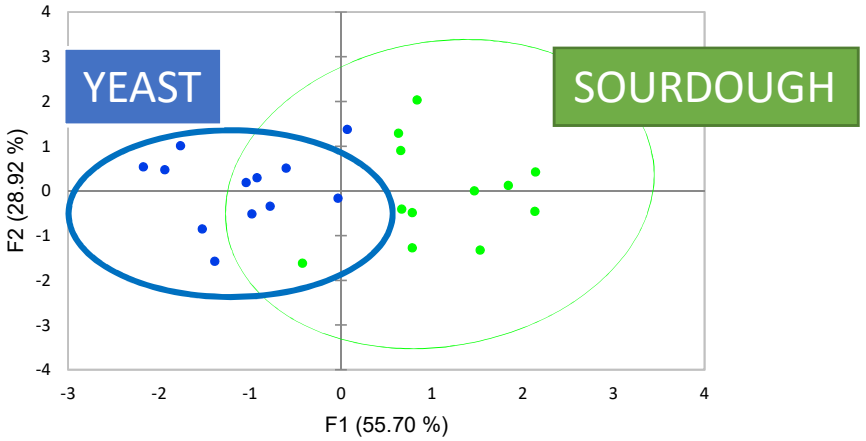
Gastric and intestinal samples produced at different times

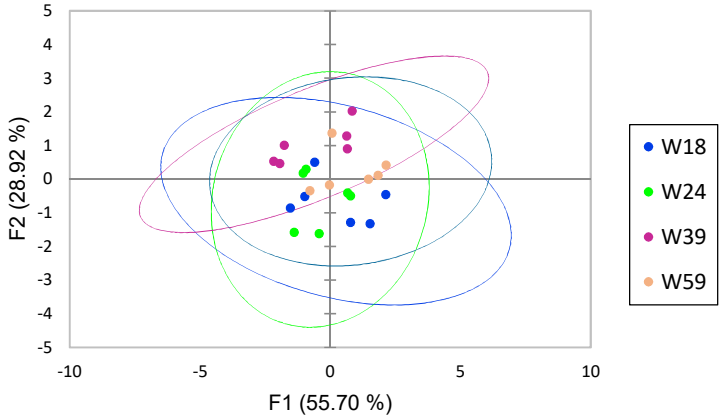
- Production and analysis of bolus

- Digestate analysis

4 Profiling carbohydrates of breads after oral digestion



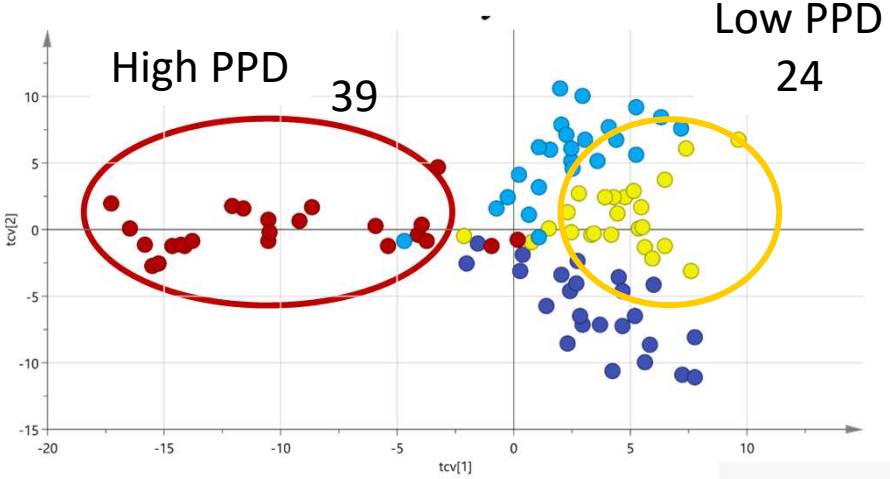




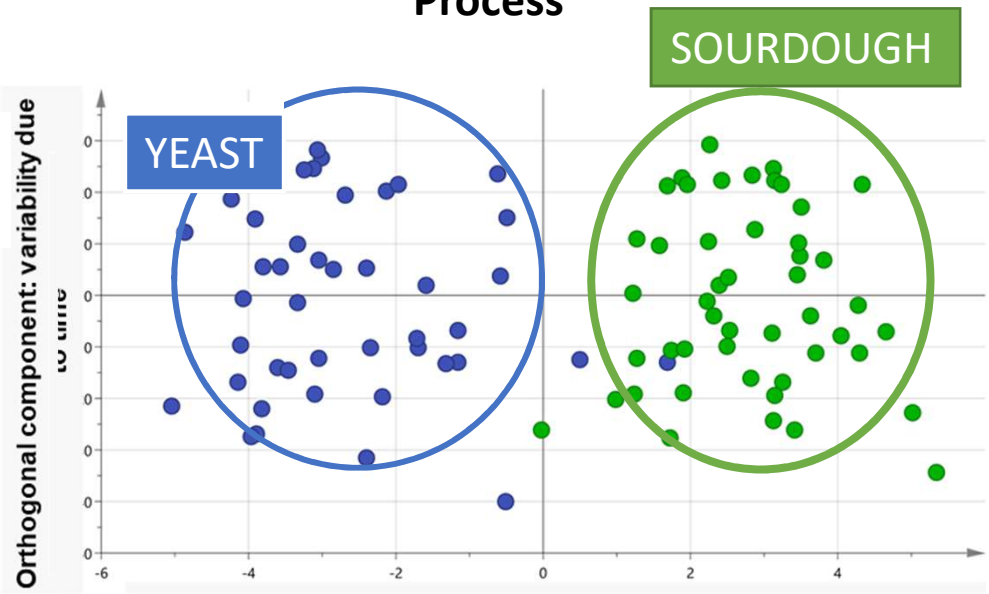
Difference for starch, glucose and maltose composition related to the process

Metabolomics from bread gastric digestates

Cultivars



Process

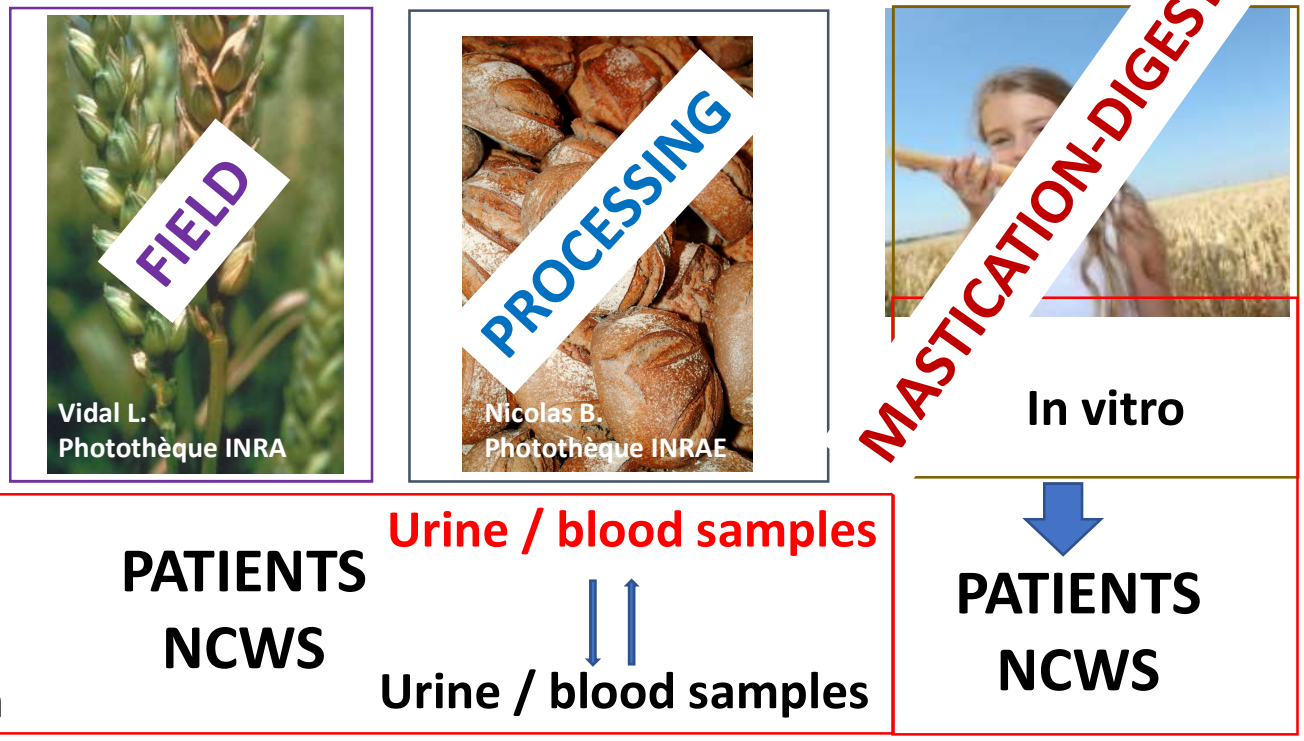


Cultivar 39 differs from the others

Differences related to the process

GlutN: Wheat and specific breads to solve gluten sensitivity

From field to fork



A Clinical trial in two steps

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

125 candidates

45 patients screened by Dr BOUTELOUP and followed by a nutritionist

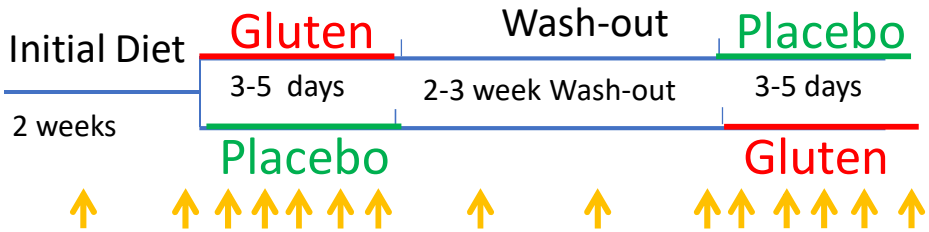
28/45 patients may be included

20 inclusions

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

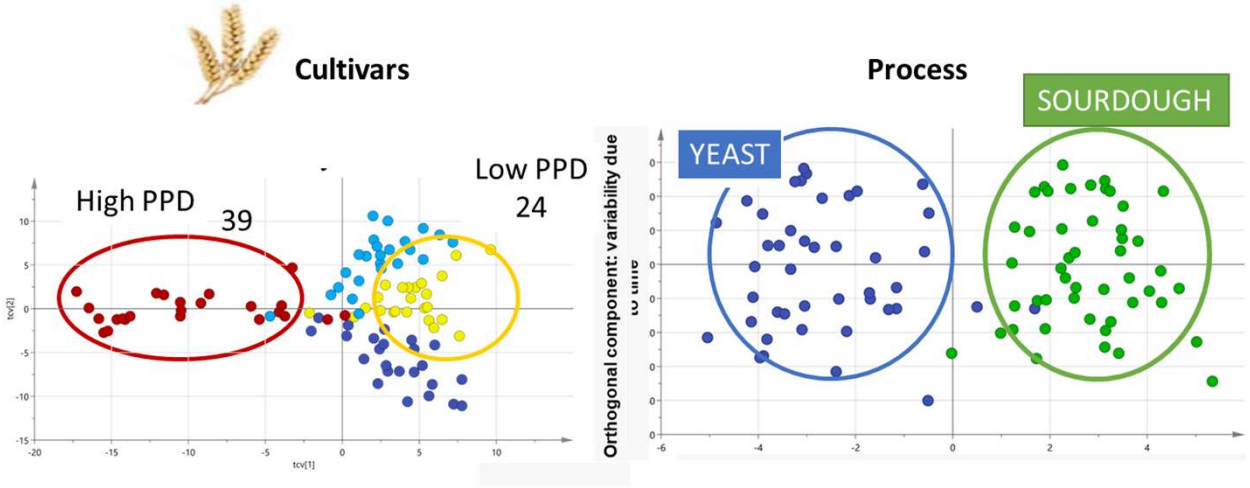
Fructanes are controlled

20 patients have completed the trial

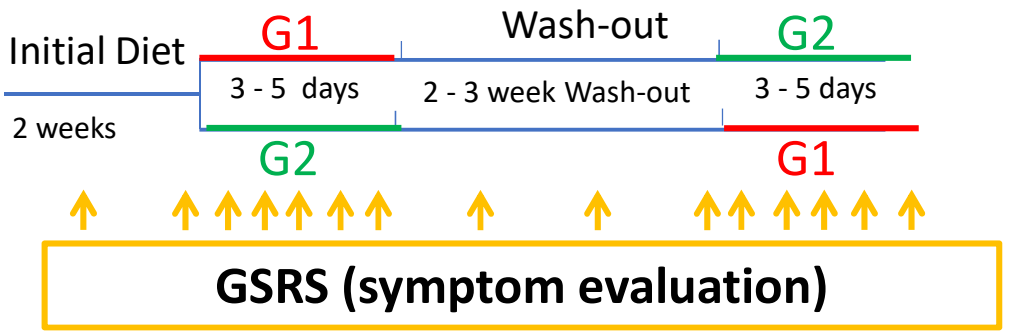
A Clinical trial in two steps: the second step (in progress)

2. Could specific bread be developped 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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Objectives for the «fork »

- ❑ Etiology: Is gluten the causal element of NCWS (and more)?

- ❑ Developping biomarkers to objectively diagnose the NCWS

- ✓ Assessing occurence

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

Thank you for your attention
Thank you to all the partners

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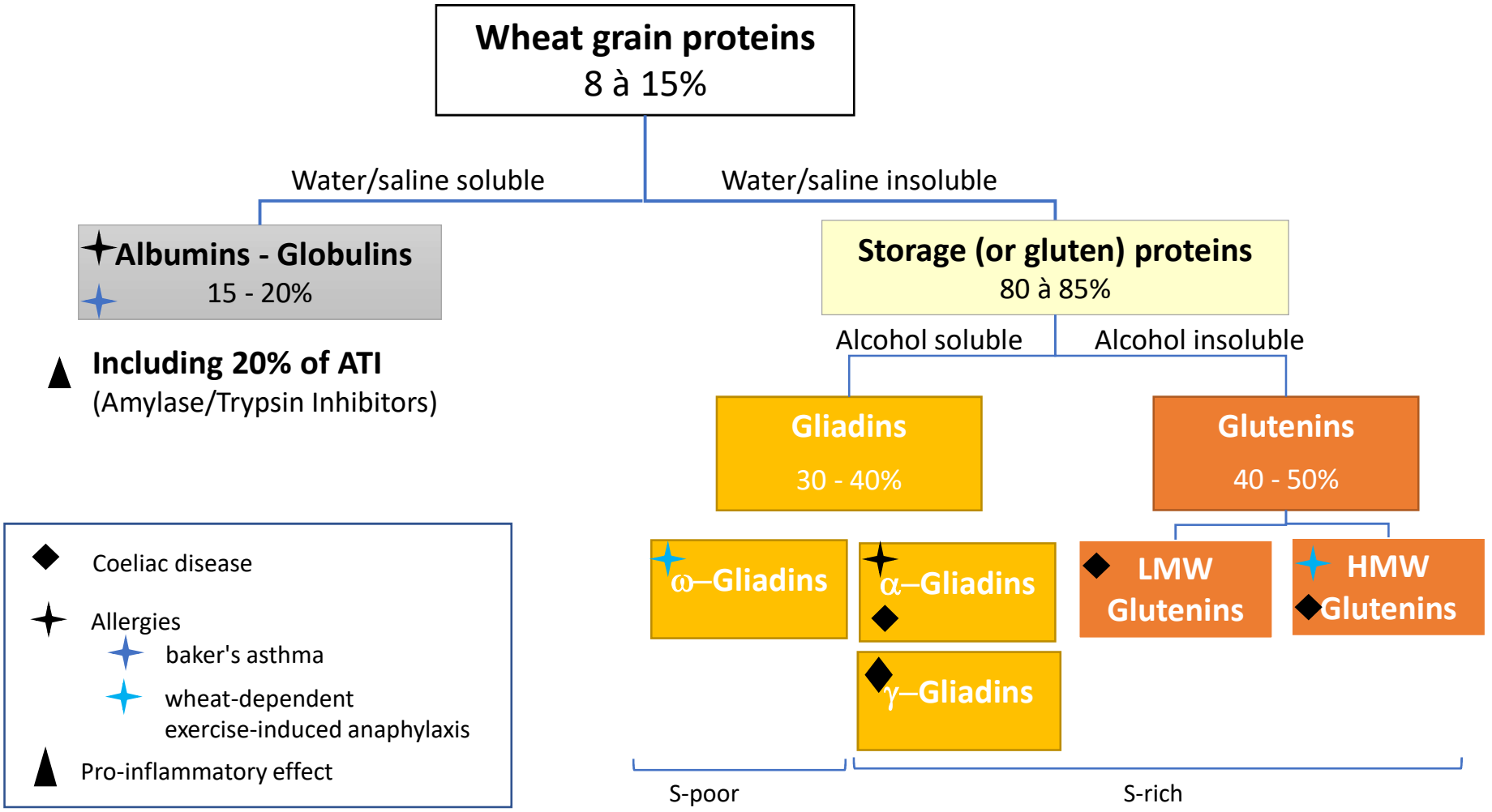
Wheat protein-related disorders



What does reveal the bread protein digestibility

E. Bancel
C. Ravel

2

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They were genotyped and phenotyped

Markers SNP	Protein content (%) and composition	Flour polymer characteritcs	Technological properties

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

1

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www.etude-nutrinet-sante.fr

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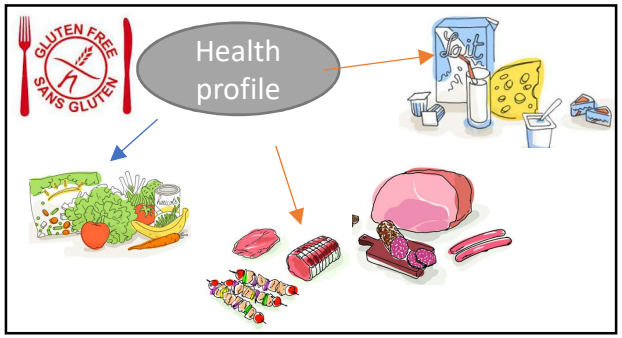

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