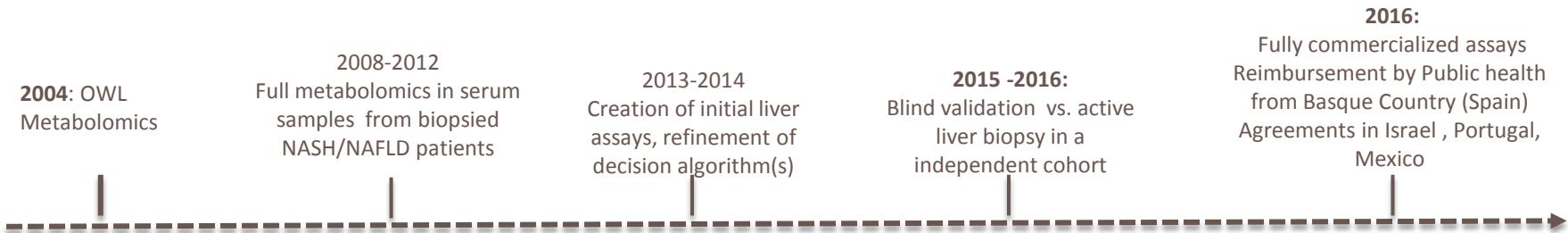


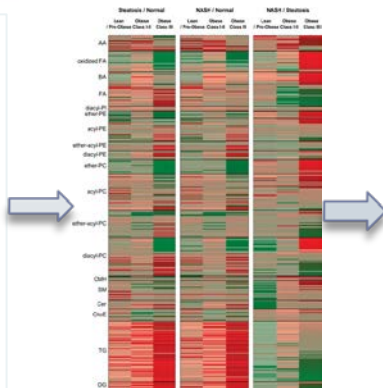


NASH – Novel Biomarkers & Metabolomics Platform

Developmental Milestones



Pioneer translational work on selected model and human samples were performed by parallel analyses among Gmmt-KO mice, NAFLD patients and healthy individuals



- Separating simple NAFLD from NASH with **540 metabolites**
- BMI-dependent NASH diagnosis with **ca. 40 metabolites**
- Further refinement of metabolite selection

Continued assay validation & refinement:

... OWLiver Care 1.0/2.0/3.0 for NAFLD discrimination

... OWLiver 1.0/2.0/3.0 for NASH diagnosis

OWLiver[®] Care

Non-invasive test for screening fatty liver disease from normal individuals

OWLiver[®]

The world's 1st non-invasive test for diagnosing NASH

Estudio Multicéntrico: 12 Hospitales

Keck Hospital
of USC



467 pacientes
biopsiados

Inserm



Hospital Universitario Reina Sofía

Área Hospitalaria de Valme

Hospital Universitario
Virgen de la Victoria



NAFLD Assay Evolution



OWLiver[®] *Care*

Version	1.0	2.0	3.0
Metabolites N	540 (L+AA)	25 TAG	11 TAG
BMI	Stratified	Stratified	Continuum
AUROC ± se Sensitivity Specificity	0.93 ± 0.02 (all BMI)	<u>Lean/Pre-obese:</u> 0.98 ± 0.02 1.00 0.91 <u>Obese class I-II:</u> 0.99 ± 0.02 0.98 1.00	0.90 ± 0.02 0.98 sen 0.78 spec

L= Lipids, AA= Amino Acids, TAG= Triglycerides

NASH Test evolution



Separating simple NAFLD from NASH



Version	1.0	2.0	3.0
Metabolites N	540 (L+AA)	25 TAG	20 TAG
BMI	Stratified	Stratified	Continuum
AUROC ± se	0.87 ± 0.02 (all BMI)	<u>Lean/Pre-obese:</u> 0.99 ± 0.01	0.95 ± 0.01
Sensitivity		0.93	
Specificity		1.00	
		<u>Obese class I-II:</u> 0.90 ± 0.04	
	0.71	0.89	
	0.92	0.75	
		<u>Obese class III:</u> 0.91 ± 0.02	
		0.87	
		0.90	

L= Lipids, AA= Amino Acids, TAG= Triglycerides

OWLiver Care® 3.0

Blind validation in new cohort

ROC curve

N	No NAFLD	NAFLD
181	30	151

AUC **0.91 ± 0.04**

Sensitivity: 0.92

Specificity: 0.87

**Pos Pred
Value:** 0.97

**Neg Pred
Value:** 0.68

OWLiver[®] 3.0

Blind validation in new cohort

ROC curve

N	Steatosis	NASH
139	59	80

AUC **0.88 ± 0.03**

Sensitivity: 0.78

Specificity: 0.95

Pos Pred Value: 0.95

Neg Pred Value: 0.76

Experiencia Introducción OWLiver



Sept- Dic 2011

2012

2013-2014

2015

2016

CLÍNIC
BARCELONA
Hospital Universitari

Informe de
Evaluación
por Dirección de
Innovación Hosp.
Clínic
introducción
OWLiver,

Petitorio Hosp. Clínic
(Enero 2012)



Proyecto
piloto
"uso clínico"
test OWLiver

- Consejería de Salud GV
- Dir. Investigación e Innovación Sanitaria
- Dirección de Asistencia Sanitaria
- Red de Diagnóstico Biológico (RDB)
- Gerentes
- Servicios de Hepatología de Osakidetza

Petitorio Osakidetza



Hospitales:

Cataluña, Madrid,
Cantabria, Castilla-
León, Andalucía y
Navarra

Petitorio hospital por
hospital