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Extracellular vesicles as biomarkers in cirrhosis

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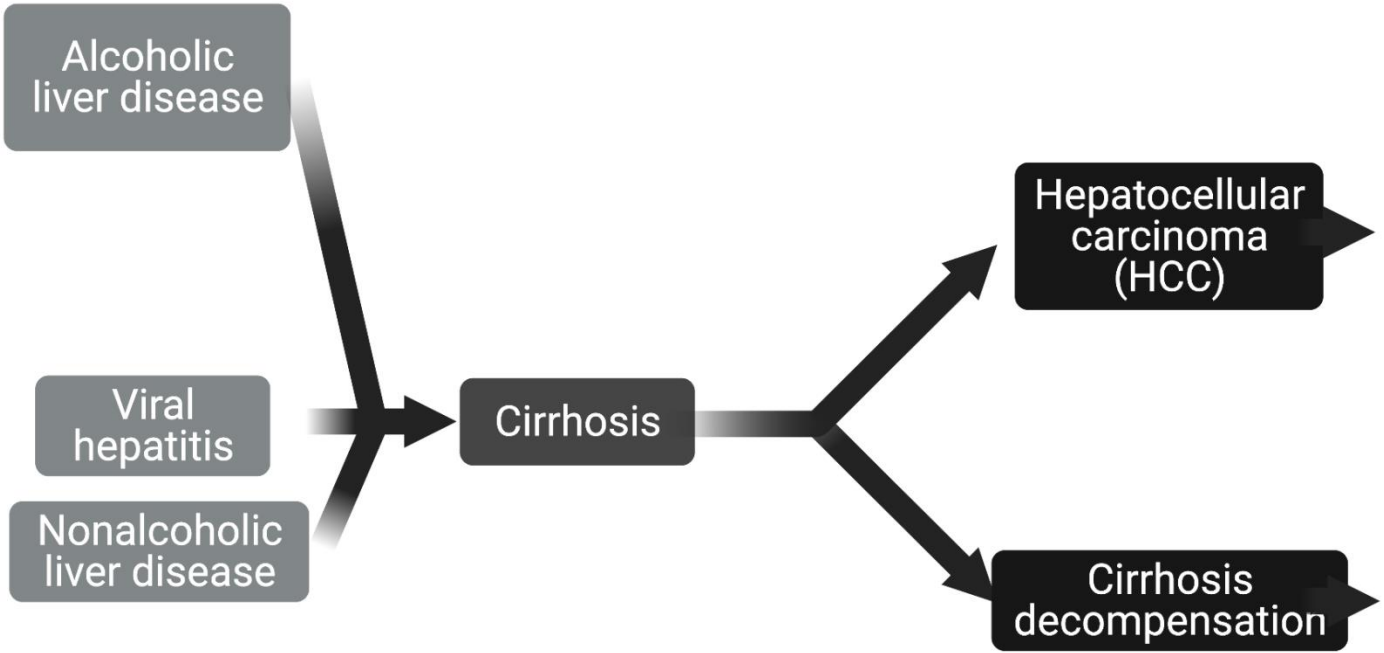
MVF CENTRE DE RÉFÉRENCE MALADIES VASCULAIRES DU FOIE

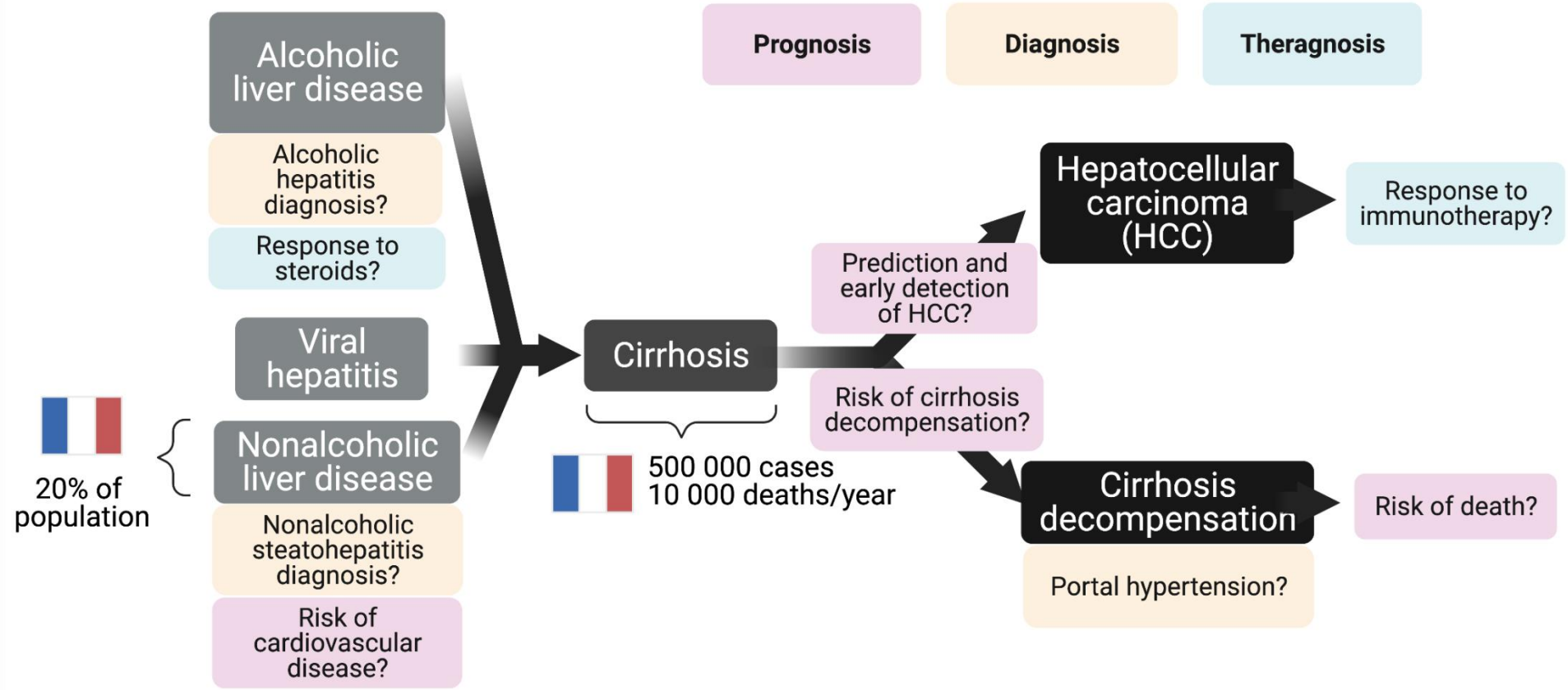
Instituts thématiques Inserm Institut national de la santé et de la recherche médicale

CRI CENTRE de RECHERCHE sur l'INFLAMMATION

Chronic liver diseases: a pubic health issue



Chronic liver diseases: a pubic health issue



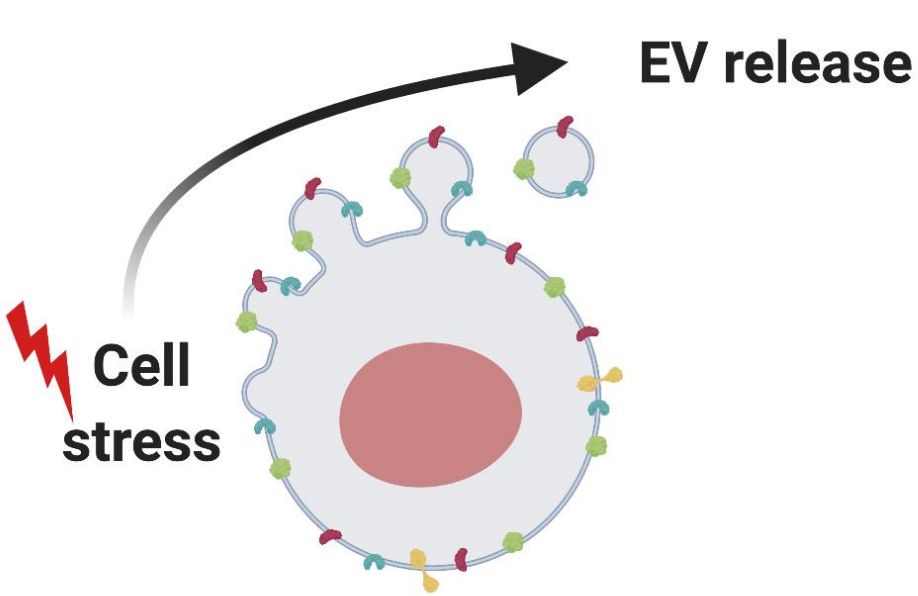
EVs as biomarkers in liver diseases

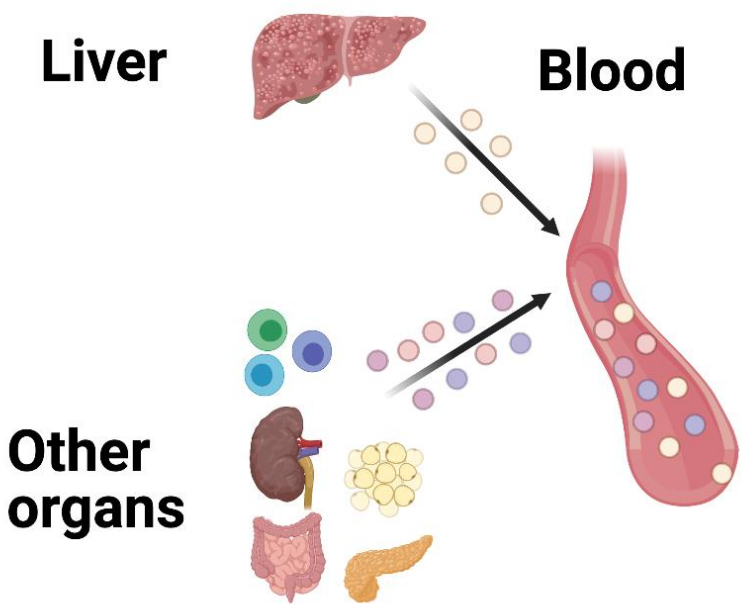
- Rational
- Hypothesis driven approach
- Agnostic approach

Extracellular vesicles (EV) as biomarkers in liver diseases

Kostallari et al, Adv Drug Deliv Rev. 2021

Extracellular vesicles (EV) as biomarkers in liver diseases





Signatures **including** EV subpopulations could be useful biomarkers

Thietart & Rautou, J Hepatol 2020

EVs as biomarkers in liver diseases

- Rational
- Hypothesis driven approach
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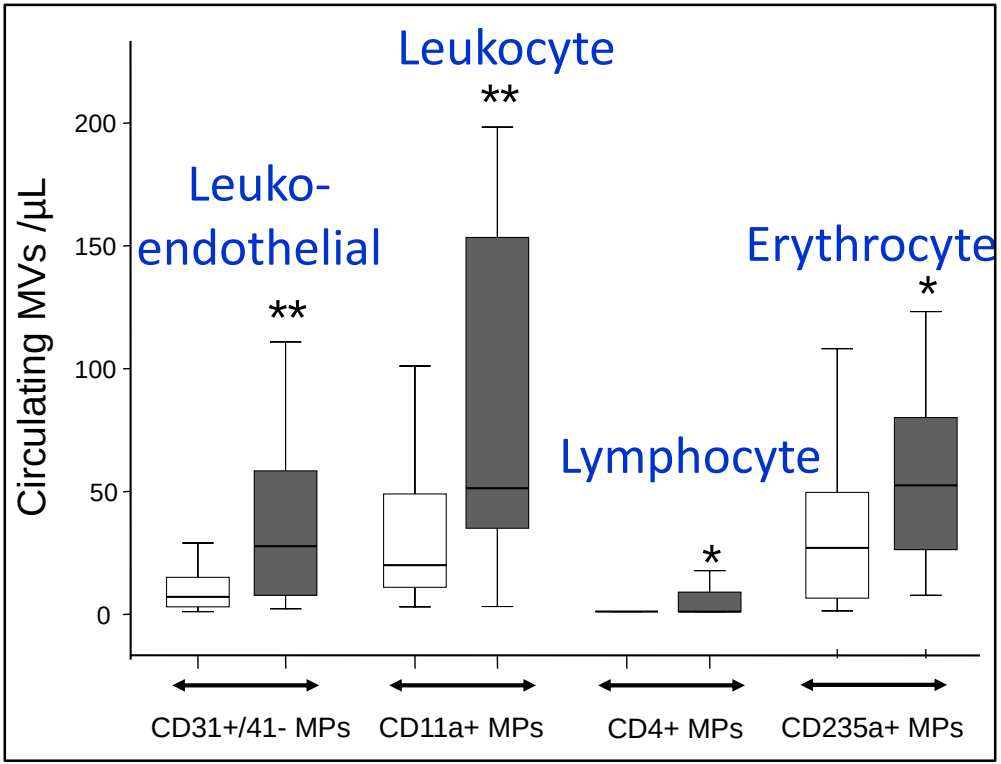
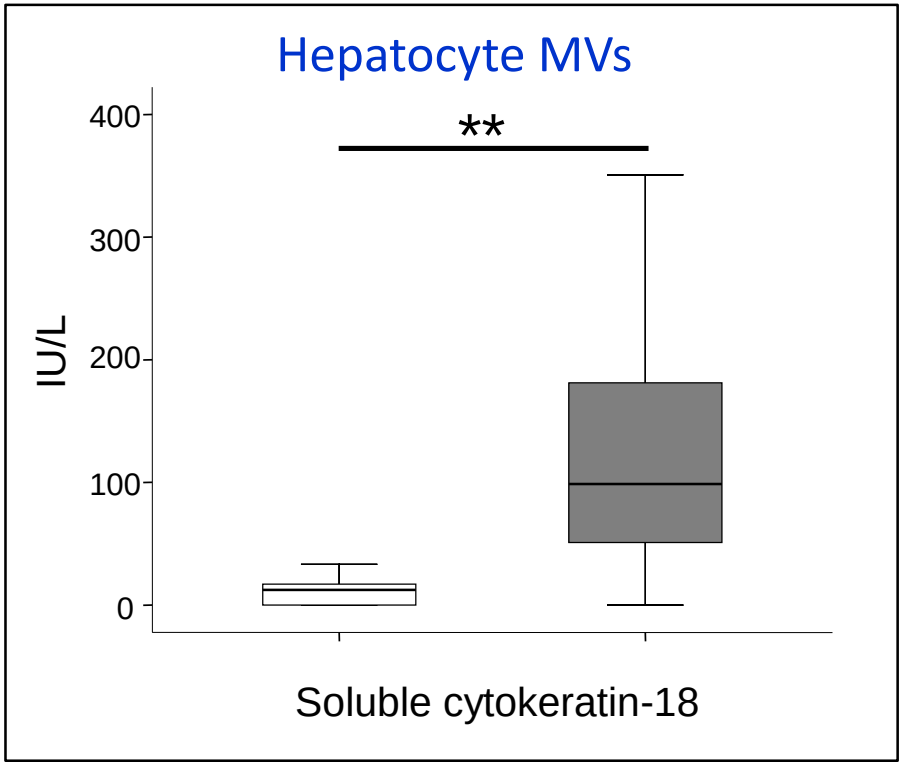
↑ levels of subpopulations of EVs in cirrhosis





☐ Controls (n=30)

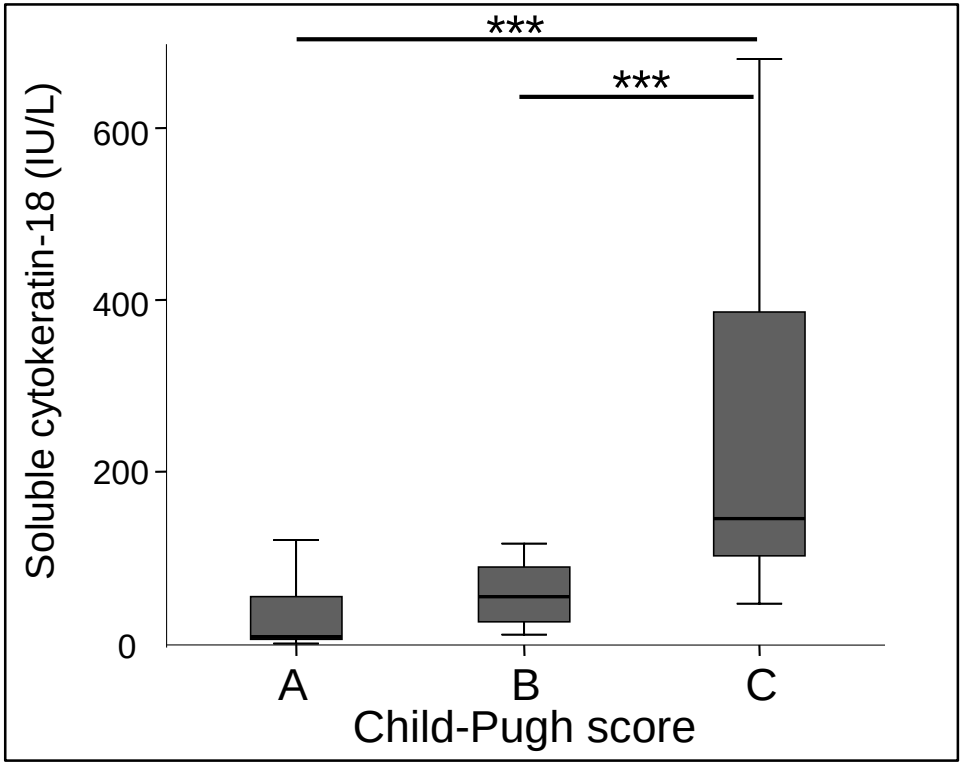
■ Patients with cirrhosis (n=91)

Rautou *et al.*, J Hepatol 2013

Rautou *et al.*, Gastroenterology 2012

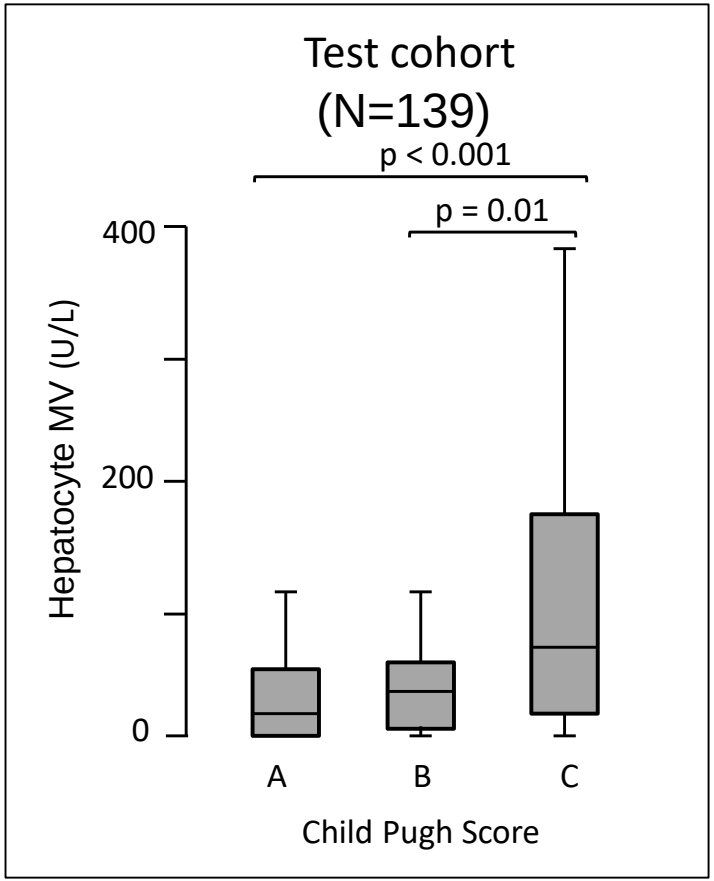
↑ levels of subpopulations of EVs in cirrhosis

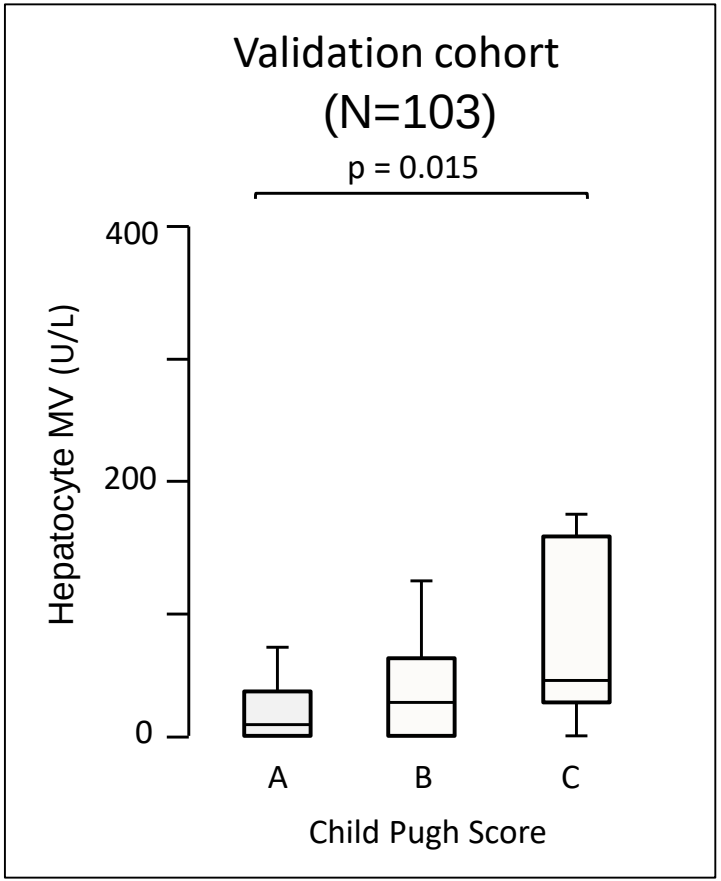
Hepatocyte MVs in cirrhosis



Rautou *et al.*, Gastroenterology 2012

Increased levels of hepatocyte MVs in cirrhosis

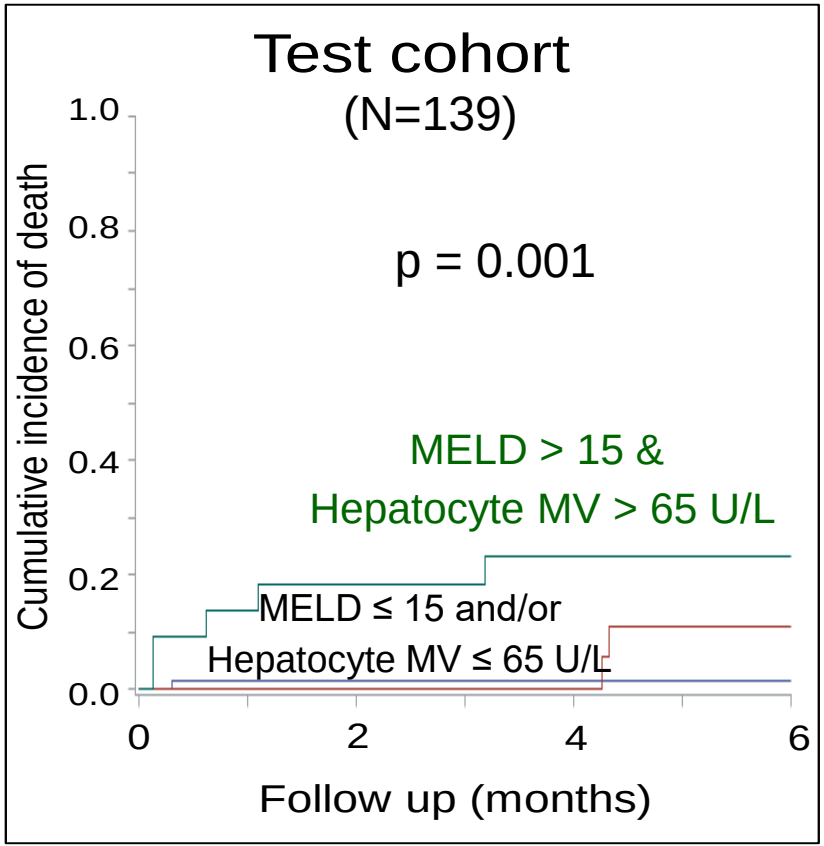


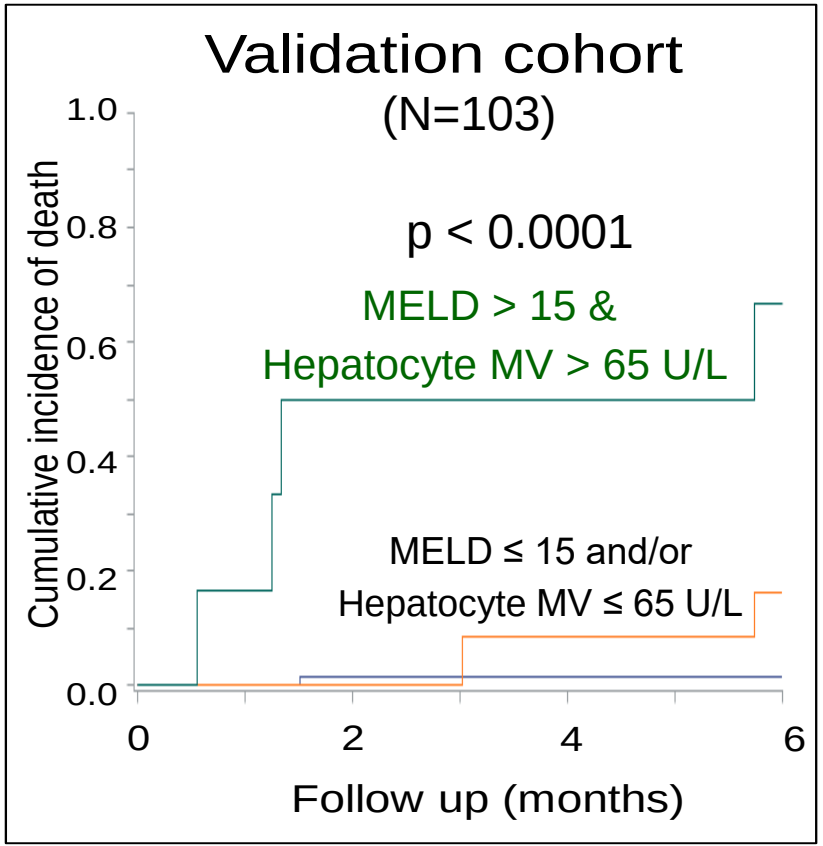


Collaboration: G Silva-Junior & JC Garcia-Pagan

Payancé *et al*, Hepatology 2018

Hepatocyte MVs predict patients' survival

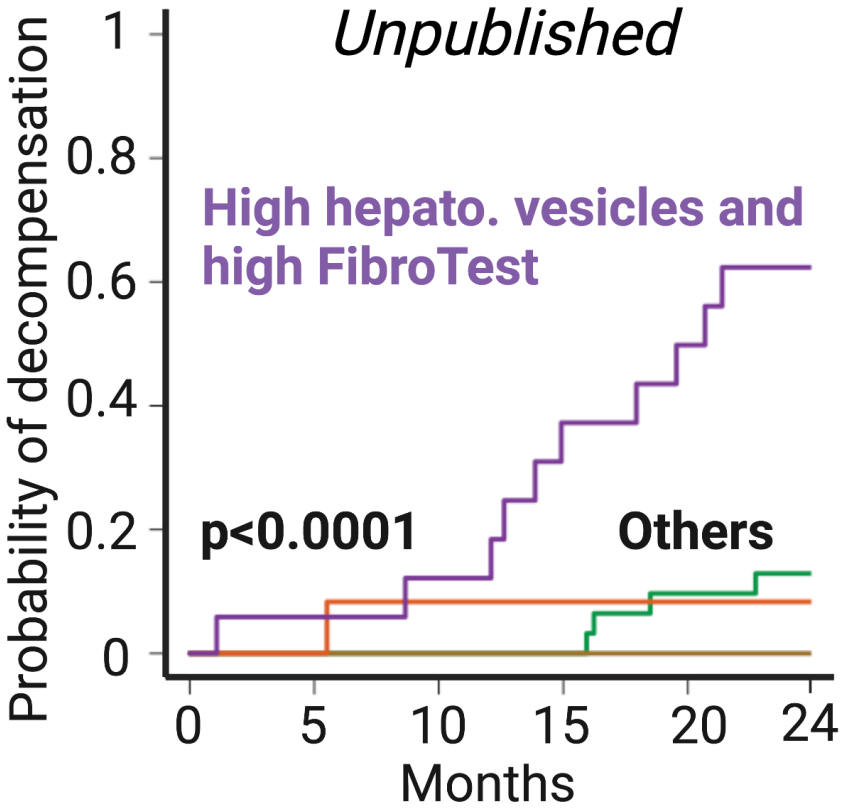




Competing risk analyses

Payancé *et al*, Hepatology 2018

Hepatocyte MVs predict decompensation of cirrhosis



N=81 patients with **compensated** cirhosis (CIRRAL cohort)

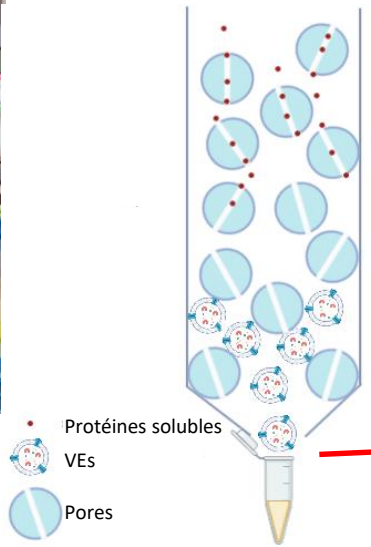
Elkrief et al, submitted

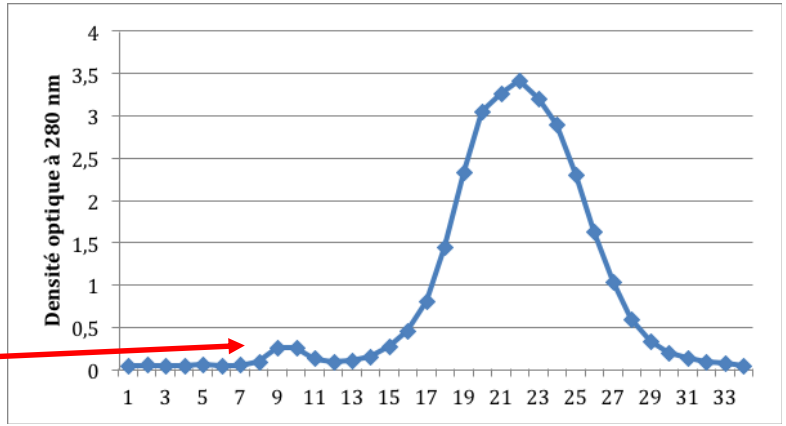
EVs as biomarkers in liver diseases

- Rational
- Hypothesis driven approach
- Agnostic approach

Proteomics analysis of EVs

Platelet poor plasma (2 mL) → Size exclusion chromatography → Fractions 5-11 collected → Centrifugation 20 500g 2h → Lysis in triton

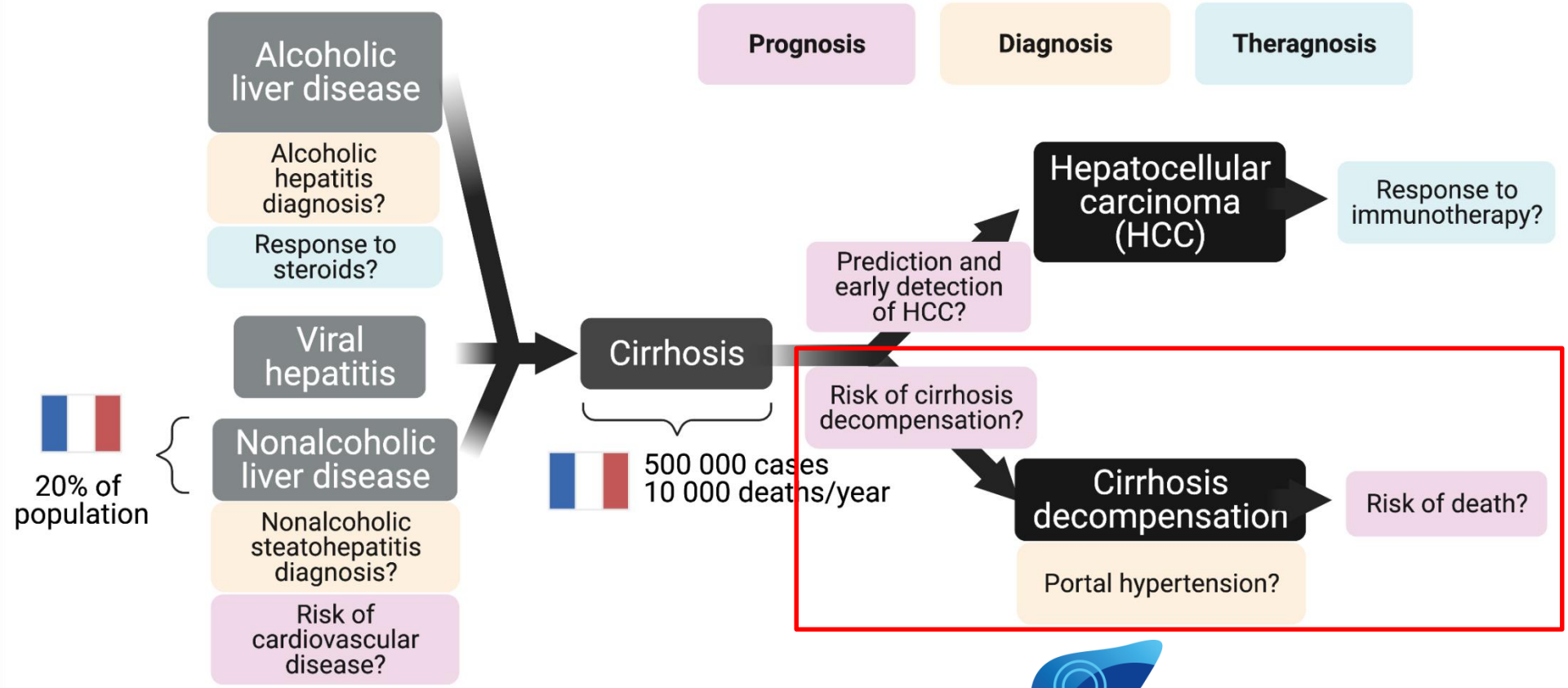




Mass stectometry

institutCurie

Chronic liver diseases: a pubic health issue

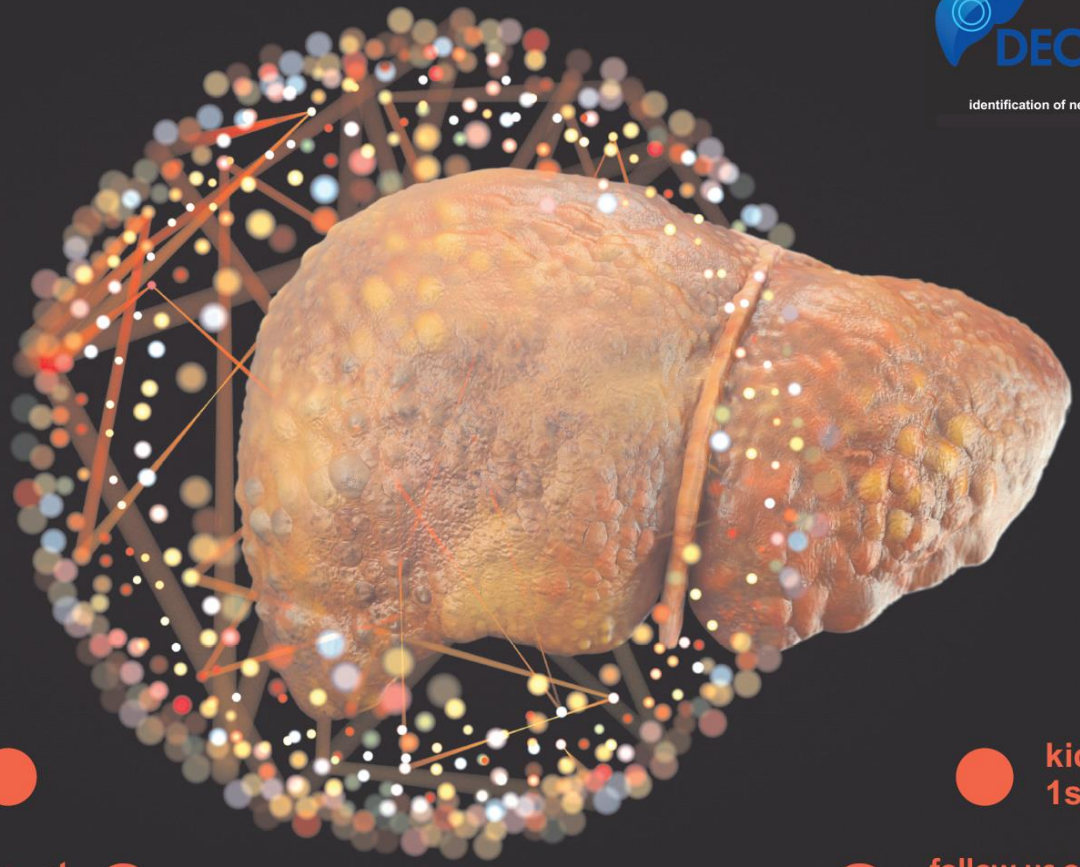


https://decision-for-liver.eu/

DECISION

DECISION

DEcompensated CIrrhoSIs:
identification of new cOmbiNatorial therapies based
on systems approaches



project duration
5 ½ years

kick-off
1st April 2020

grant amount
6 million €

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10 countries
21 institutions

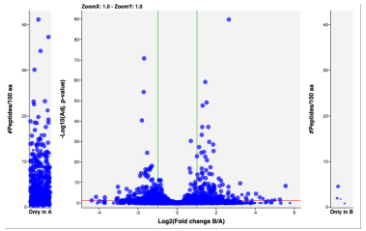
www.decision-for-liver.eu

EVs in patients with acute decompensation of cirrhosis

Proteomics
Discovery

High throughput measurement (filtration-ELISA)

Set up | Pilot cohort | Large cohorts



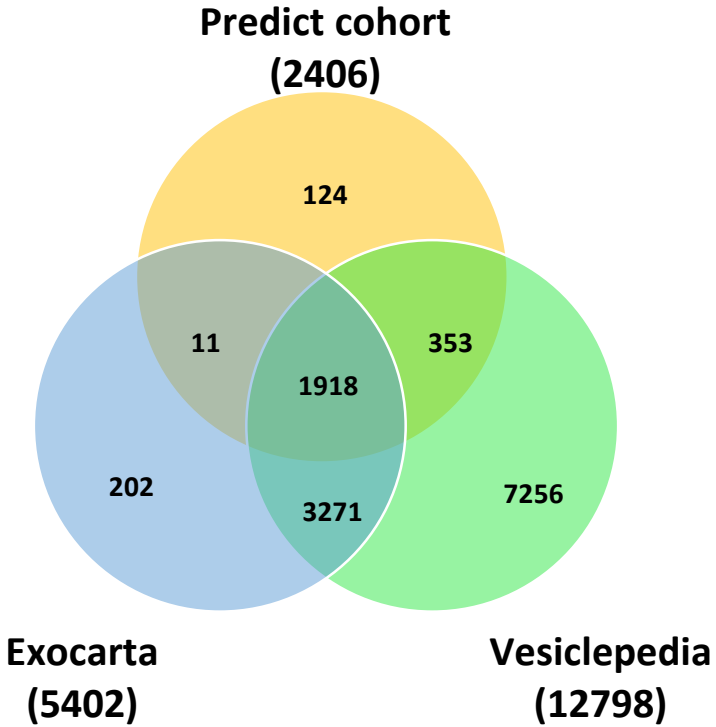
N=37
PREDICT

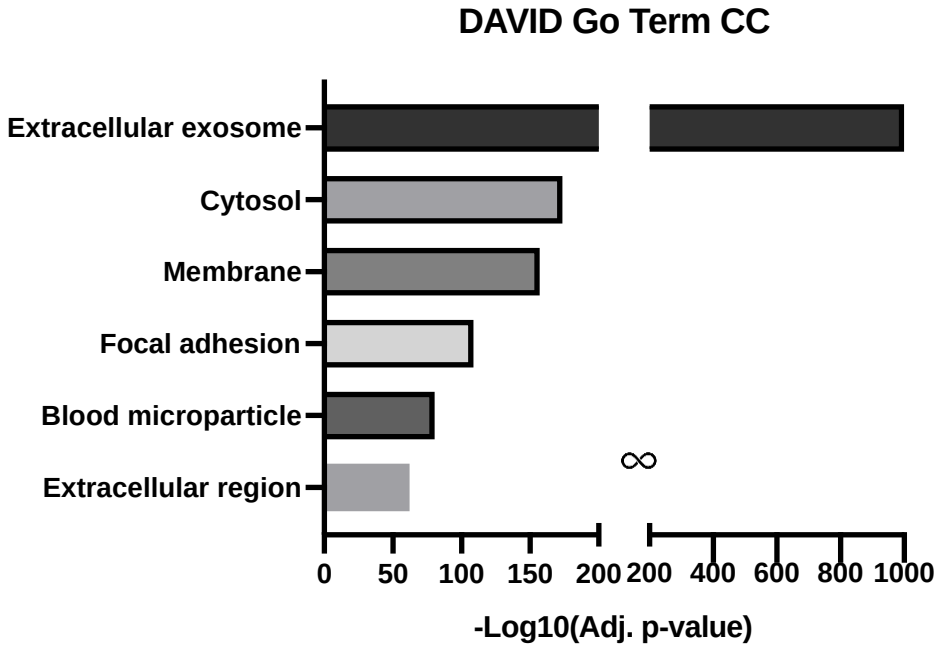
7 EV subpopulations
N=21
Beaujon

7 EV subpopulations
150 AD patients
(PREDICT)

4 EV subpopulations
Healthy n=10
PREDICT n=765*
ACLARA n=589

EVs proteomics in the PREDICT cohort

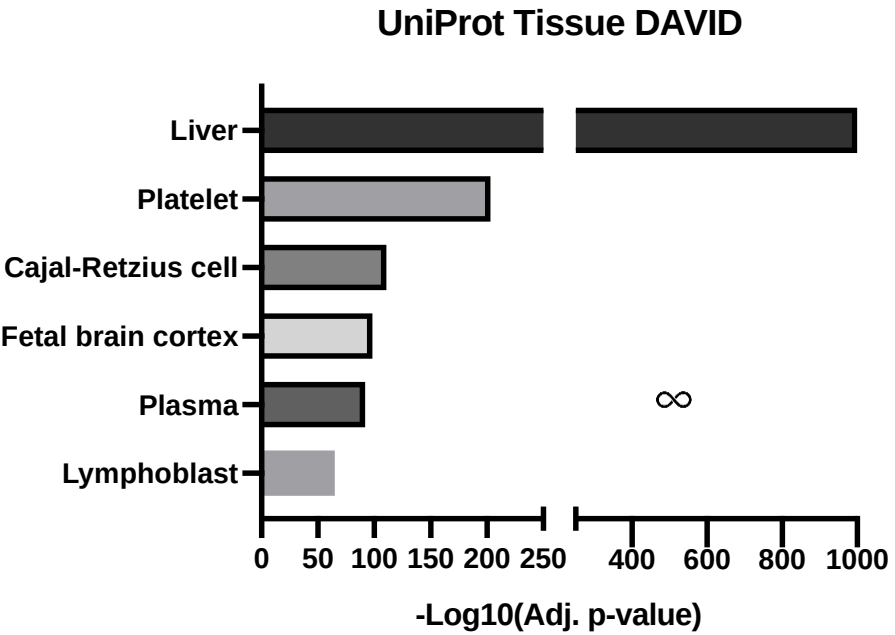


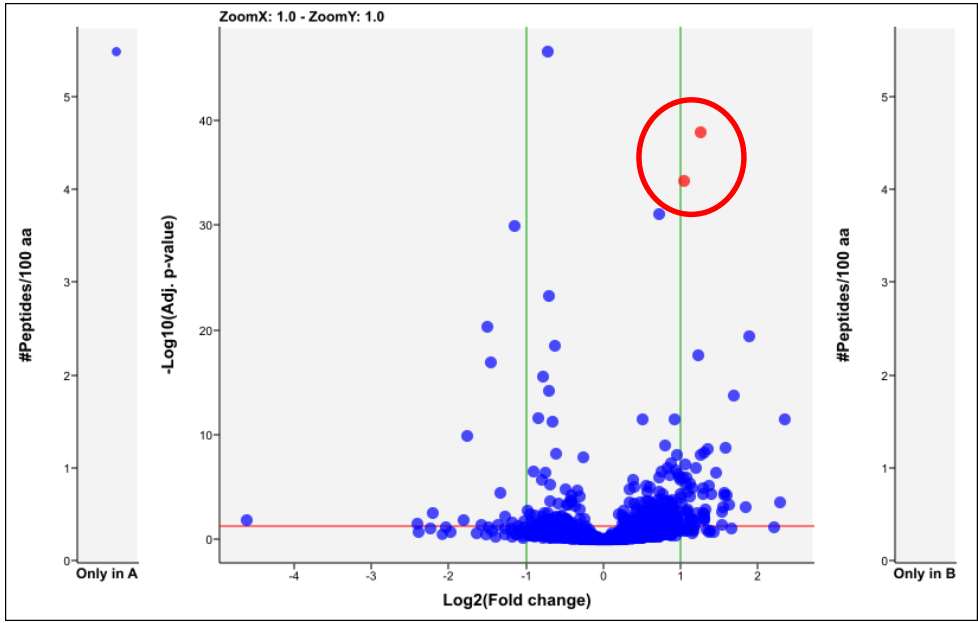


Proteins commun with exocarta et vesiclepedia

Valainathan, Tanguy et al.

EVs proteomics in the PREDICT cohort





Alive at 3 months

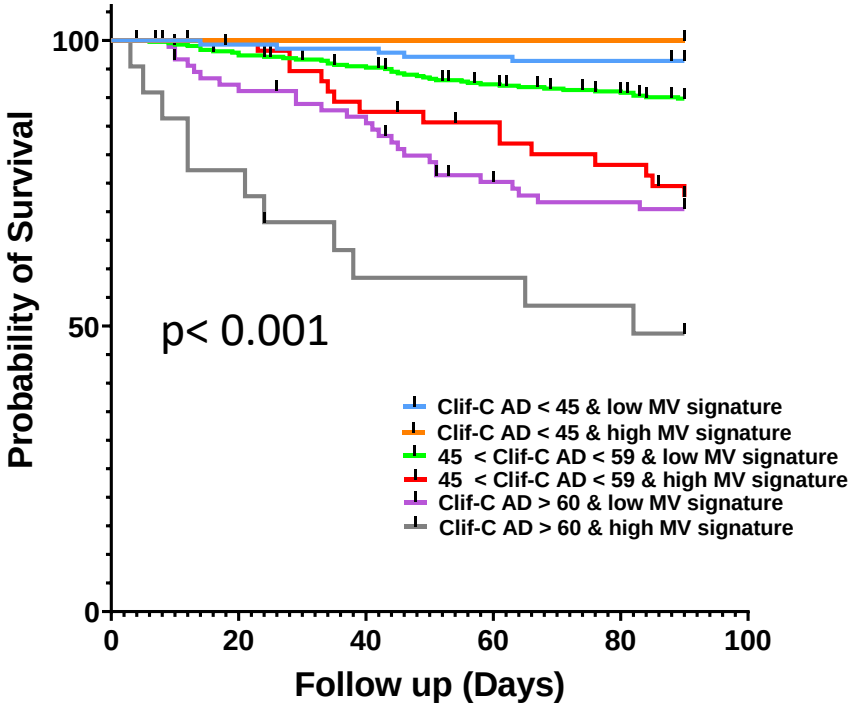
Dead at 3 months

Valainathan, Tanguy et al.

From EVs proteomics to improved prediction

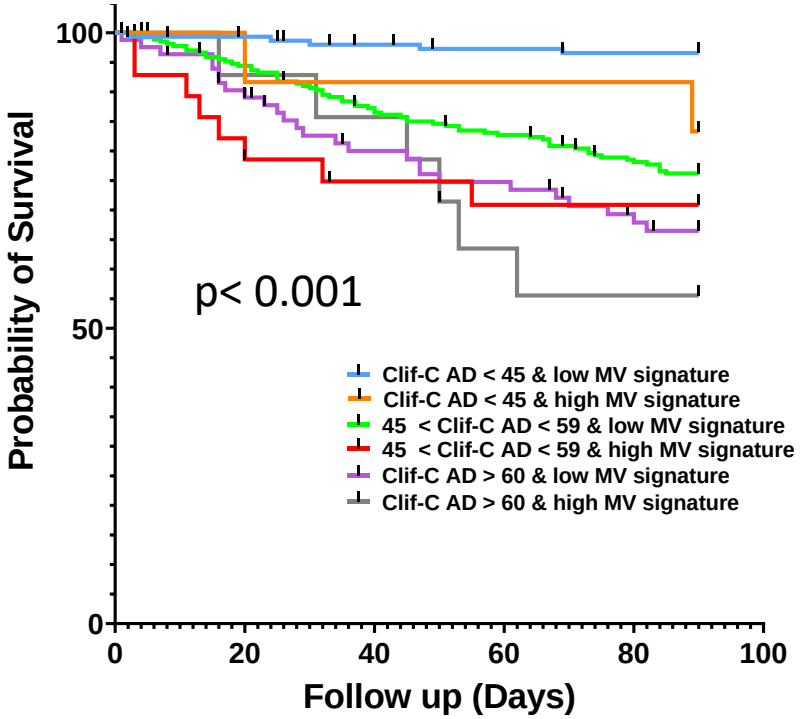
PREDICT prospective European cohort

N=752



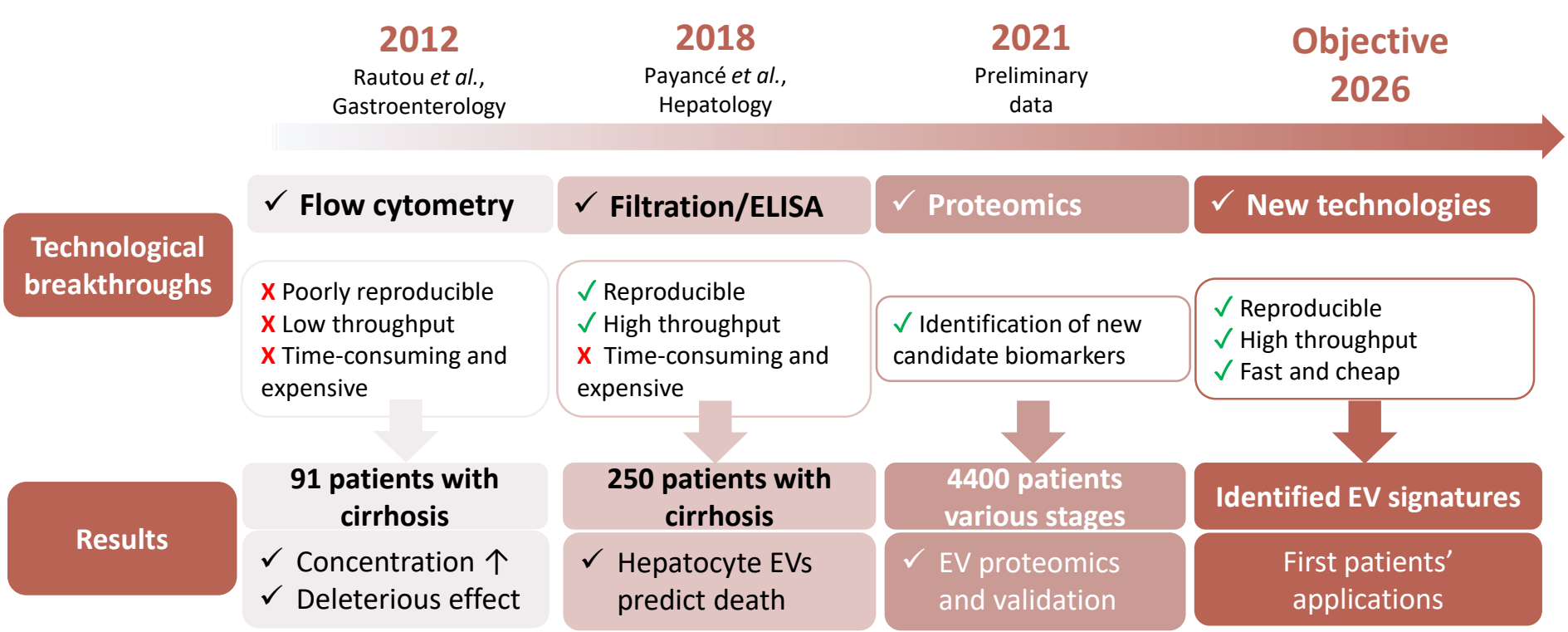
ACLARA prospective South America cohort

N=578



Valainathan, Tanguy et al.

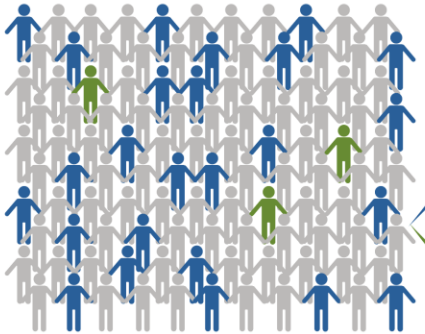
Achievements and future directions



EV in cirrhosis: our next challenge

CIRRHOSIS

Asymptomatic patients
10-12 years
life expectancy



5 million cases
170 000 deaths/year

Market size: 26 billion€

RISKS

Decompensation
1-2 years life expectancy

Hepatocellular Carcinoma (HCC)
1-2 years life expectancy

CURRENT TOOLS

Liver stiffness
X Only 15% positive predictive value

Liver ultrasonography
X Only 48% sensitivity

LIVER-TRACK

Blood tests repeated every 6 months

Decompensation test

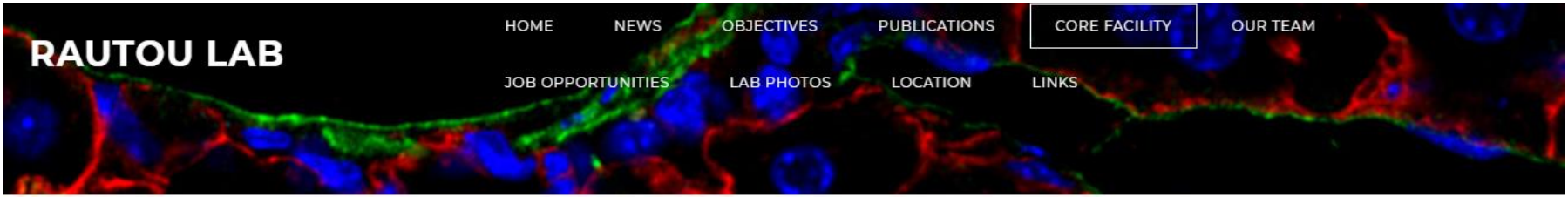
HCC test

Ge, NEJM, 2016
Trebicka, Gut, 2021
Tzartzeva, Gastroenterology, 2018

Conclusion

- Circulating levels of several subpopulations of MVs are increased in patients with cirrhosis
- MVs might reflect ongoing liver injury and thereby predict patients' outcome
- Preanalytics is key and new detection techniques available
- A **EV signature** might be a valuable tool in cirrhosis

EV core facility



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We can offer for your projects:

Isolation or generation of vesicles

Detailed and extensive vesicle characterization

Identification and quantification in large patient cohorts

Université de Paris

IVETh – Plateforme d'expertise technologique de Production, d'Ingénierie, et de Caractérisation de Vésicules Extracellulaires

Marion Tanguy

Instituts thématiques

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de la santé et de la recherche médicale

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CRI
CENTRE de RECHERCHE sur l'INFLAMMATION

Hepatology unit, Beaujon Hospital
Reference center for vascular liver diseases

Inserm U1149 – ATIP AVENIR, www.rautoulab.com/
Team "*vessels in liver diseases*"

AGENCE NATIONALE DE LA RECHERCHE ANR

EF Clif
EUROPEAN FOUNDATION FOR THE STUDY OF CHRONIC LIVER FAILURE

HORIZON 2020

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ASSOCIATION FRANÇAISE POUR L'ETUDE DU FOIE
(Association reconnue d'utilité publique)

Société Nationale Française de Gastro-Entérologie
SNFGE

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AMVF

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