21st Annual Congress of the Belgian Society of Internal Medicine

Circulating miRNAs as biomarker for liver fibrosis in chronic hepatitis B and C virus infection

P.J. Poortmans[1], J. Lambrecht[2], L.A. van Grunsven[2], R. Reynaert[1,2]

(1) Department of Gastro-Enterology and Hepatology, UZ Brussel, Brussels, Belgium

(2) Liver Cell Biology Lab, Department of basic (bio-)medical sciences, Vrije Universiteit Brussel (VUB), Brussels, Belgium

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Cell biology lab livr

Liver fibrosis

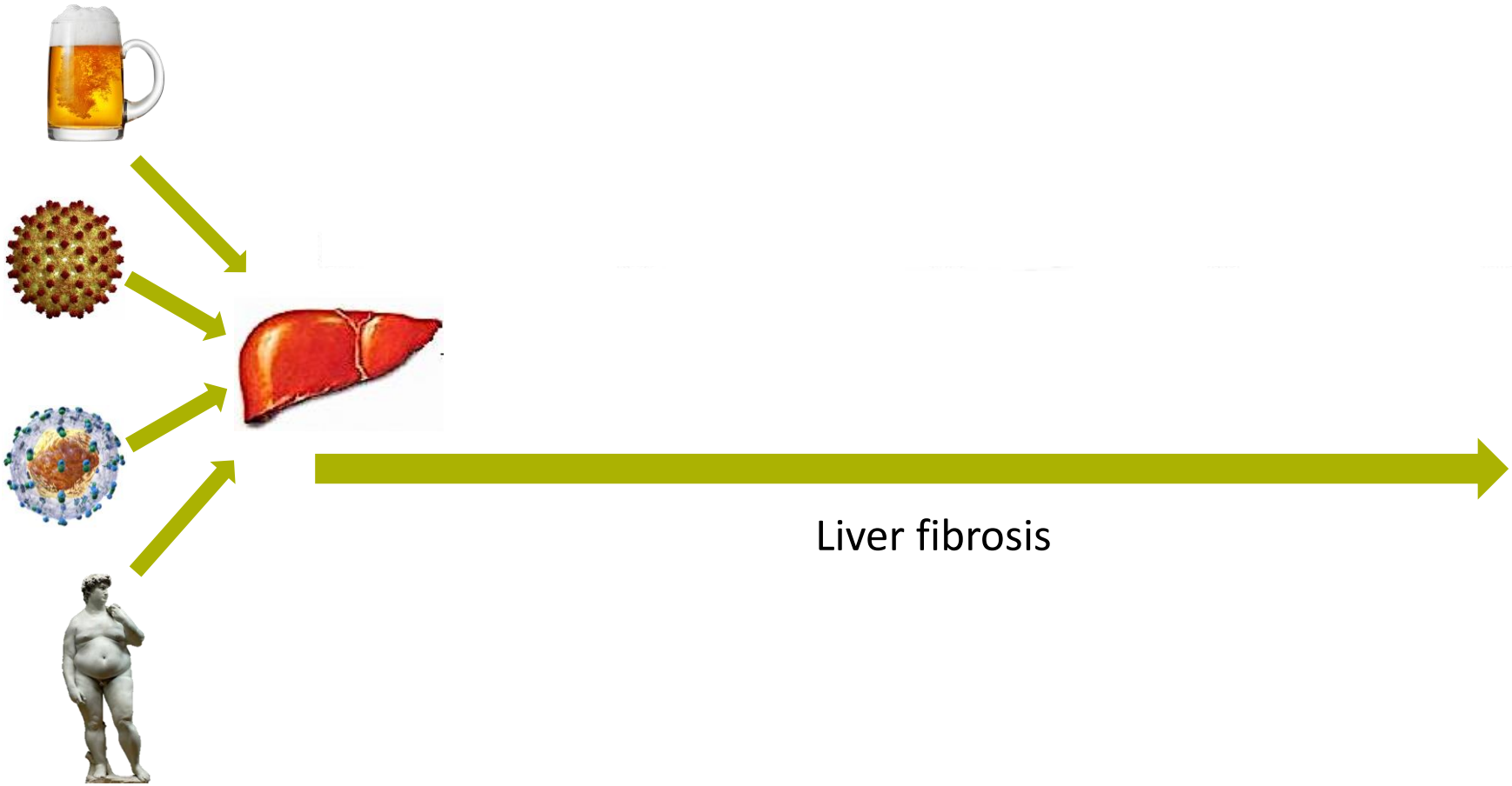

Image source: Adapted from *Ramos-Lopez et al. Genetic, metabolic and environmental factors involved in the development of liver cirrhosis in Mexico. World J Gastroenterol, 2015; 21(41):11552-66*

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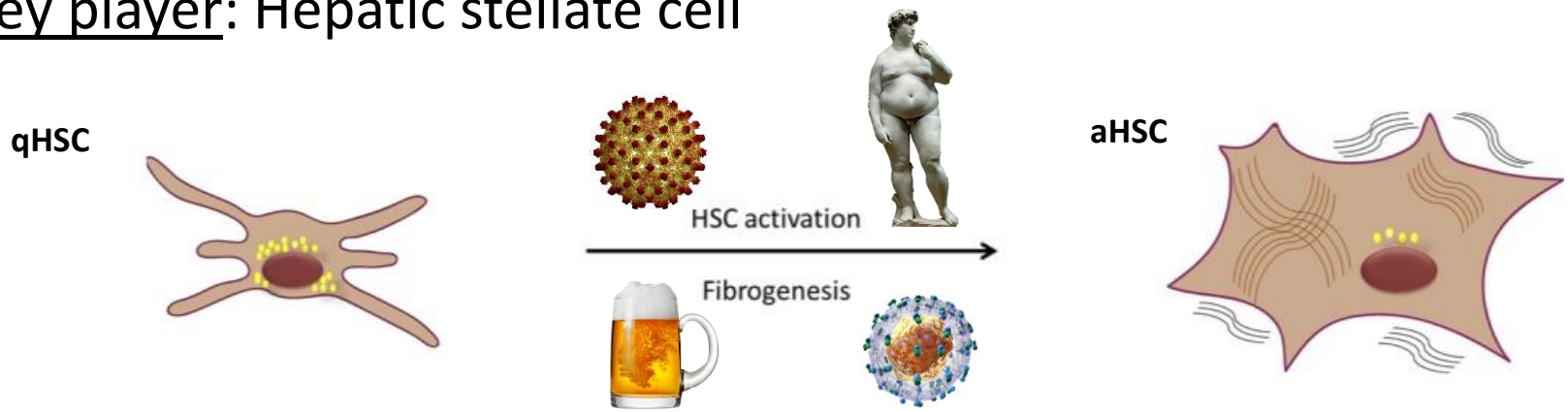
Liver fibrosis

- <u>Key player</u>: Hepatic stellate cell



- Frequent complications, high mortality rates

- *Diagnosis and staging*: Liver biopsy, FibroScan®, ALT, AST, …

→ More accurate non-invasive tools are needed

<u>Image source</u>: Adapted from *Lambrecht et al. The role of miRNAs in stress-responsive hepatic stellate cells during liver fibrosis. Front. Physiol. 2015; 6:209: doi: 10.3389*

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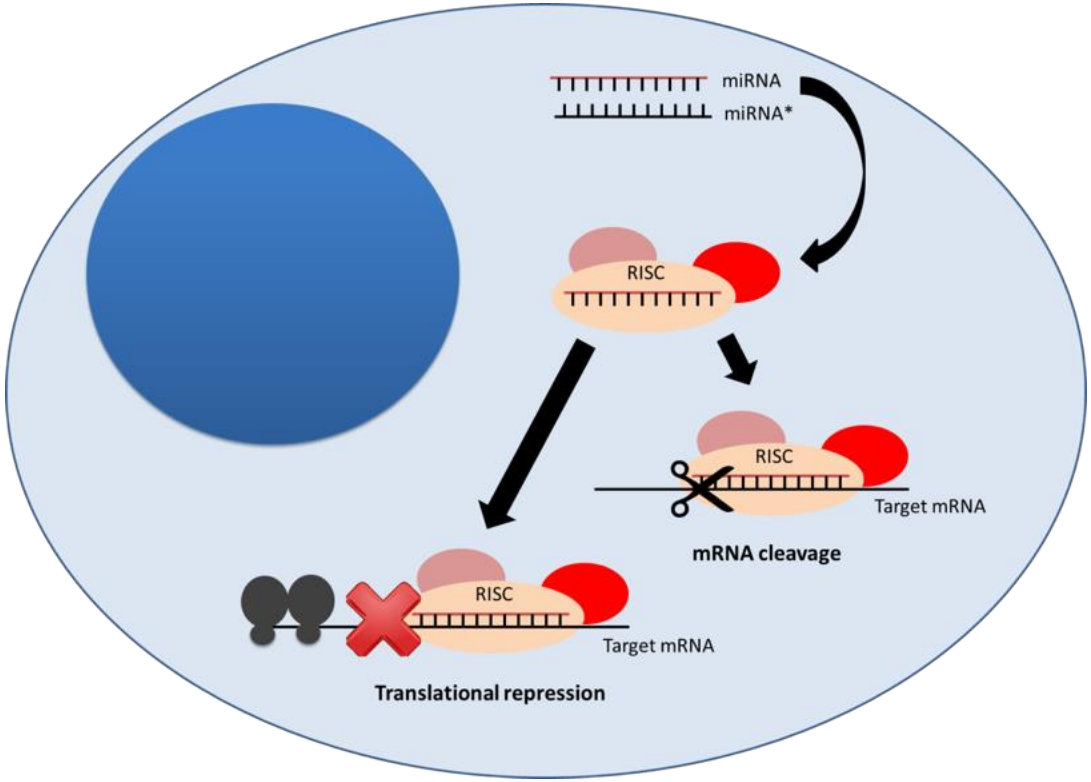
MicroRNA



→ Stably present in ECM, blood, urine, etc.

Image source: *Lambrecht et al. The role of miRNAs in stress-responsive hepatic stellate cells during liver fibrosis. Front. Physiol. 2015; 6:209: doi: 10.3389/fphys.2015.00209*

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Image source: *miRNA Body Map. Available at http://mellfire.ugent.be/public/body_map/index.php*

Circulating miRNAs in liver fibrosis

circulating miRNAs in liver fibrosis

HBV

Increased

miR-19b, miR-192, miR-22, miR-451, miR-92a, miR-572, miR-122, miR-575, miR-125b, miR-638, miR-150, miR-1974, miR-181b

Decreased

miR-29a, miR-486, miR-106b, miR-744, miR-223, miR-762

HCV

Decreased

miR-29a, miR-652, miR-451, miR-762

Increased

miR-16, miR-192, miR-20a, miR-320, miR-22, miR-513, miR-34a, miR-571, miR-92a, miR-1207, miR-122, miR-1225, miR-125b, miR-1275, miR-146a, miR-1974, miR-155

Alcohol

Increased

miR-135b, miR-571, miR-490, miR-761, miR-513

Decreased

miR-29a, miR-214, miR-203, miR-652

NAFLD

Decreased

miR-630, miR-762, miR-744

Increased

miR-16, miR-192, miR-19a, miR-223, miR-19b, miR-375, miR-34a, miR-572, miR-122, miR-575, miR-125b, miR-638

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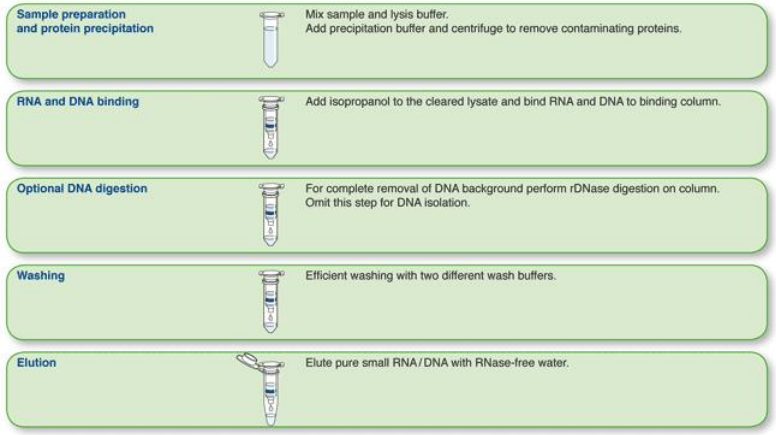
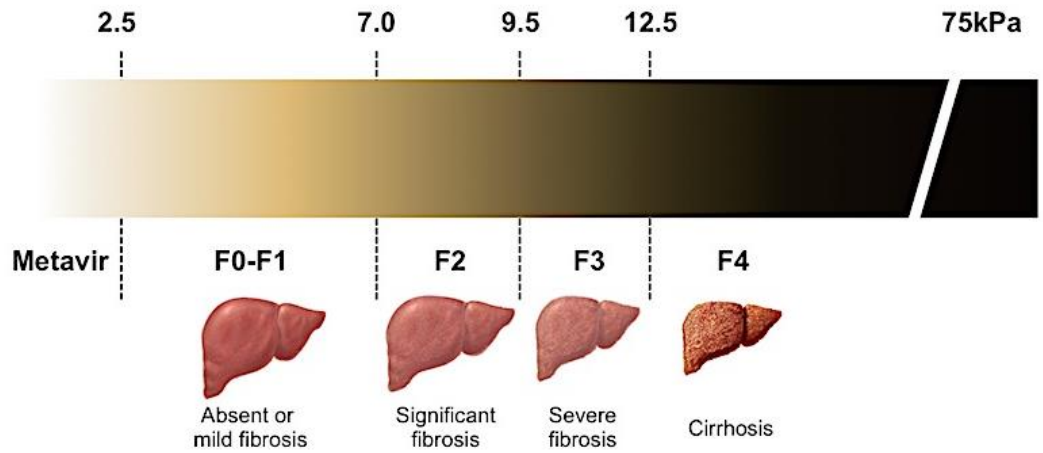
Aim of the study

To identify circulating miRNAs correlated to the degree of liver fibrosis in patients with chronic liver disease due to chronic viral hepatitis

Materials and methods

Patients with chronic viral hepatitis
UZ Brussels





Spiked-in

cel-miR-39-3p

RT-qPCR

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Study population

Total population: 42 patients

Healthy controls: 11 individuals

Fibrosis F-stage	HBV induced	HCV induced
F0-F1 No/minimal liver fibrosis	15	13
F2 Significant liver fibrosis	3	3
F3 Advanced liver fibrosis	1	3
F4 Cirrhosis	0	4
TOTAL	**19**	**23**

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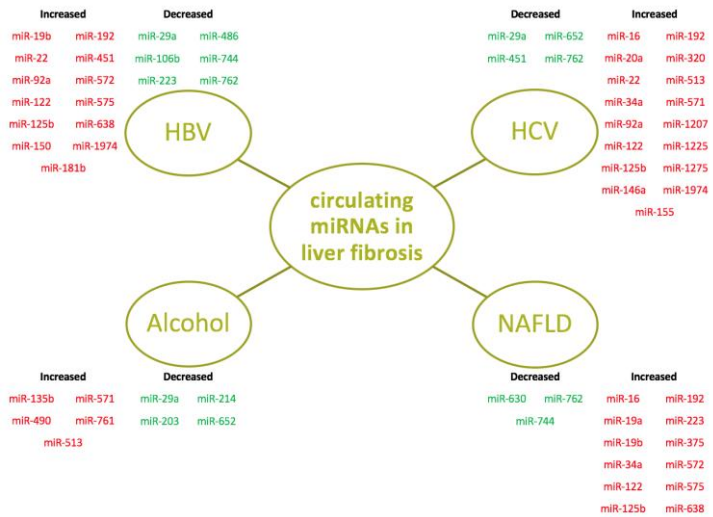
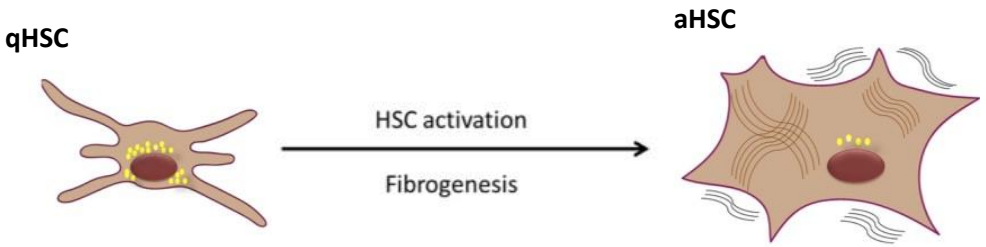
MiRNAs involved in HSC activation





Increased		Decreased	
miR-200b	miR-486	miR-19b	miR-223
miR-219a-1		miR-22	miR-375
		miR-29a	miR-483
		miR-125b	miR-571
		miR-139	miR-572
		miR-150	miR-638
		miR-185	miR-885
		miR-192	miR-1217

miRNA linked to pathways involved in HSC activation?

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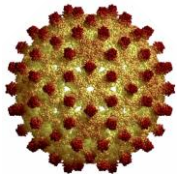
Selected miRNAs

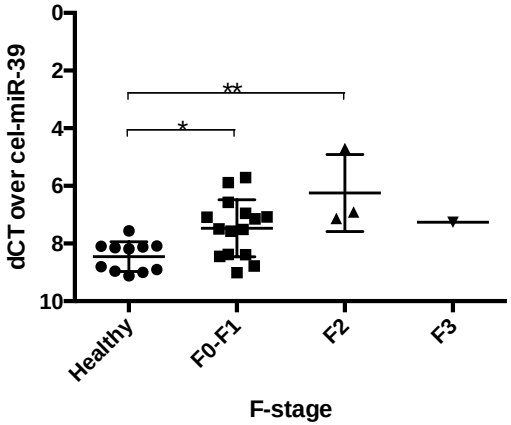
miRNA	Expression in aHSCs	Expression in blood	Associated liver disease
miR-19b-3p	decrease	increase	HBV infection, NAFLD
miR-150-5p	decrease	increase	HBV infection
miR-192-5p	decrease	increase	HBV infection, HCV infection, NAFLD
miR-200b-3p	increase	increase	NAFLD (murine model)
miR-142-3p	decrease	?	?
miR-219a-1-5p	increase	?	?

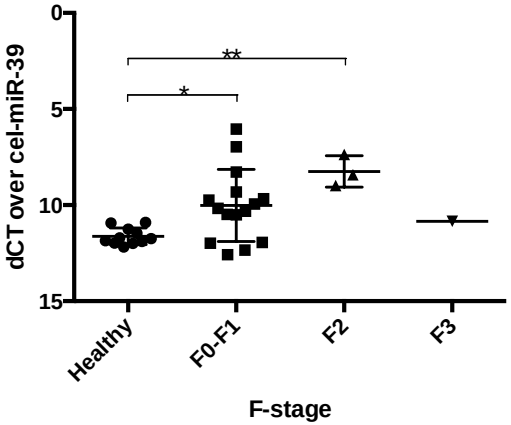
Circulating miR-150, -192 and-200b are upregulated in chronic viral hepatitis

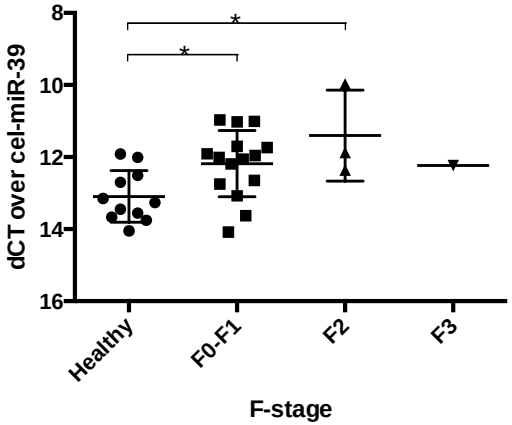
miR-150 | **miR-192** | **miR-200b**

Chronic HBV

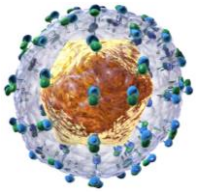


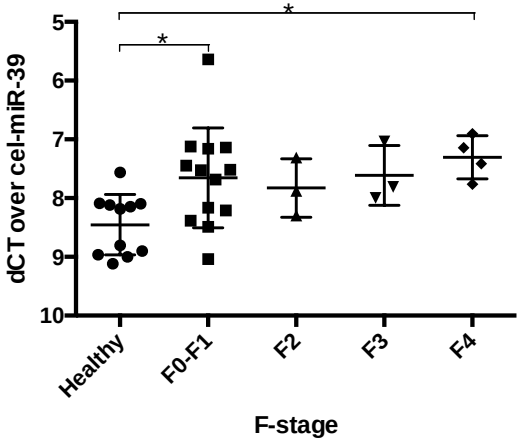


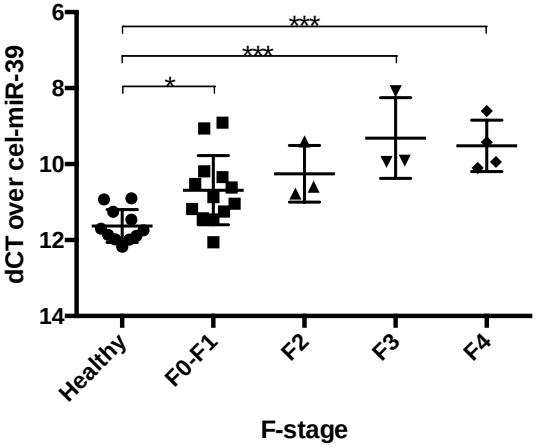


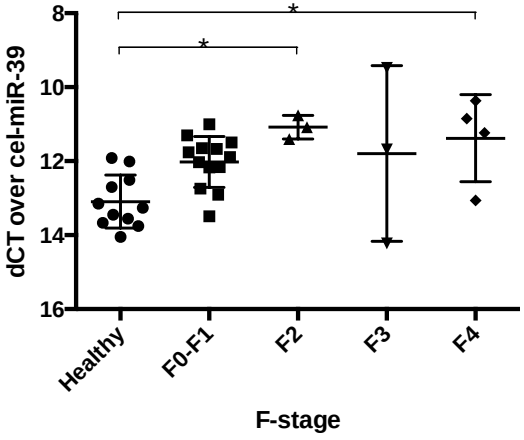


Chronic HCV

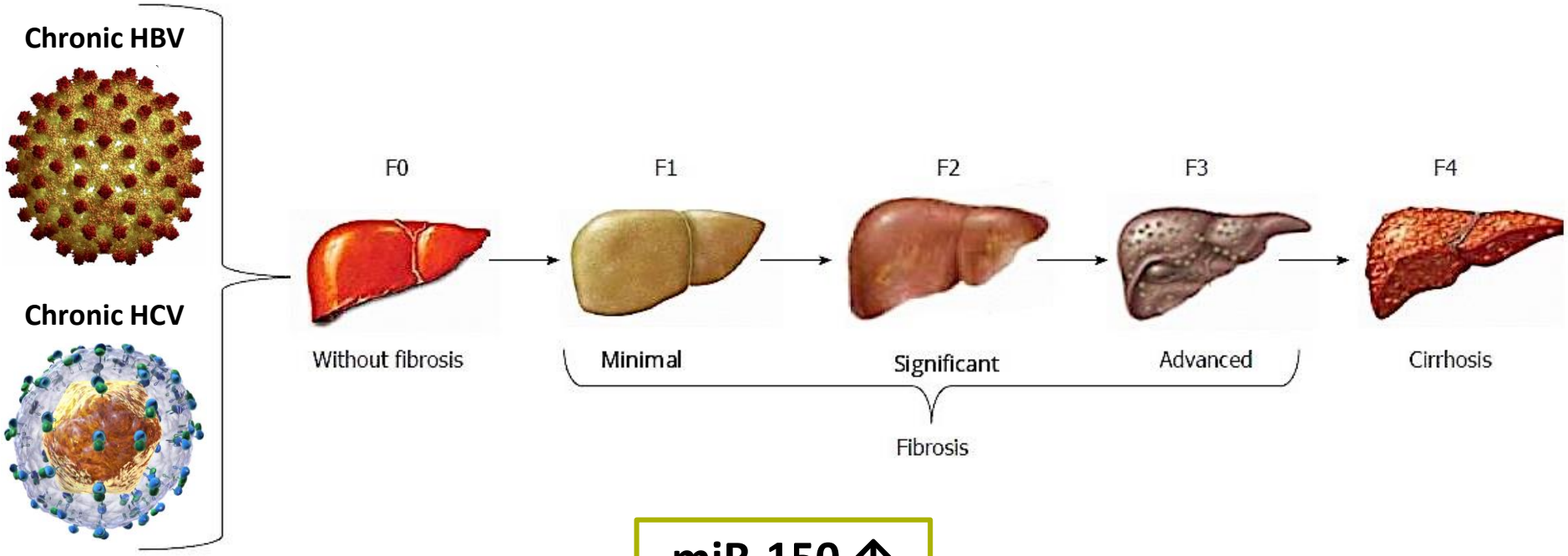








Conclusion



miR-150 ↑
miR-192 ↑
miR-200b ↑

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Perspectives and potential relevance

1. Validation in large cohorts of patients

miR-150 ↑
miR-192 ↑
miR-200b ↑

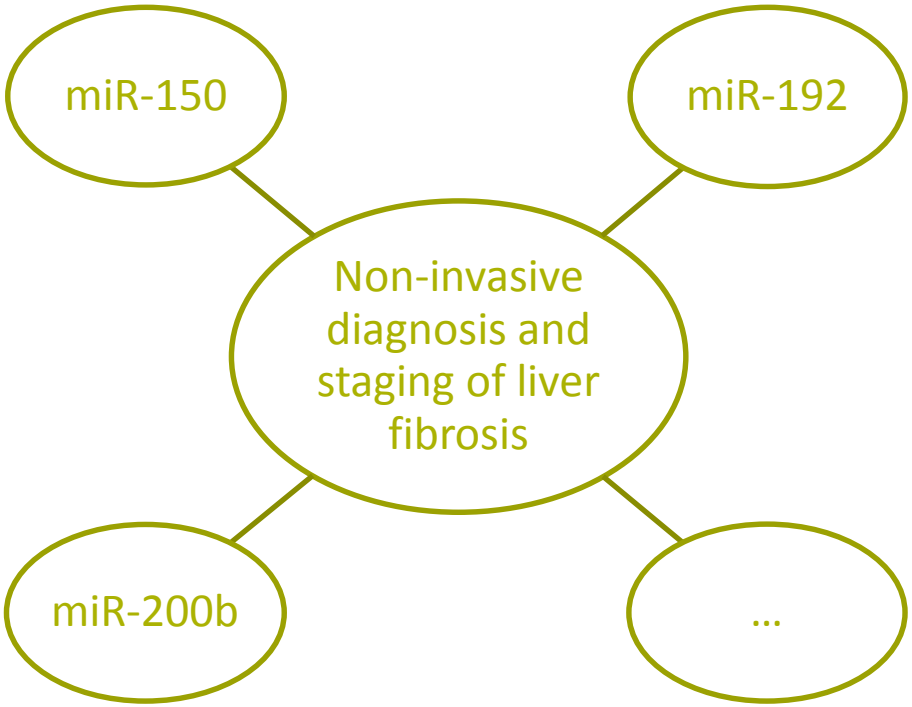
miR-150 ↑
miR-192 ↑
miR-200b ↑

?

Perspectives and potential relevance

1. Validation in large cohorts of patients

2. Biomarker panels



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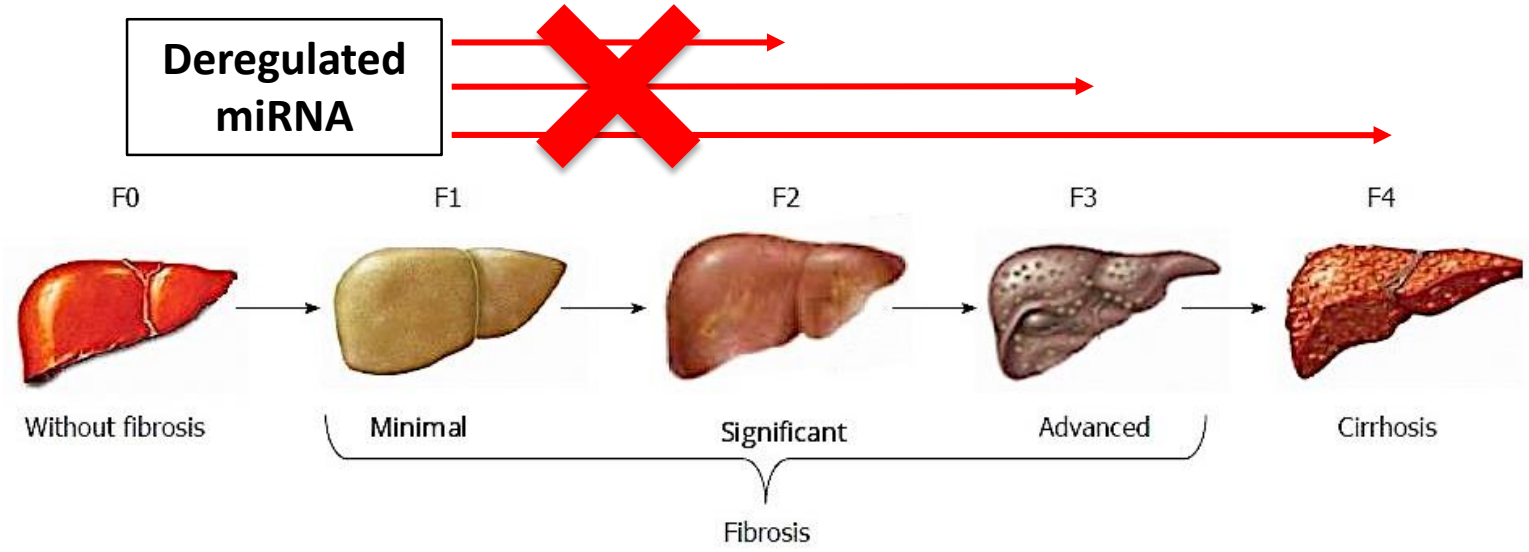
Perspectives and potential relevance

1. Validation in large cohorts of patients

2. Biomarker panels

3. <u>Prognostic</u>: fibrosis progression markers?



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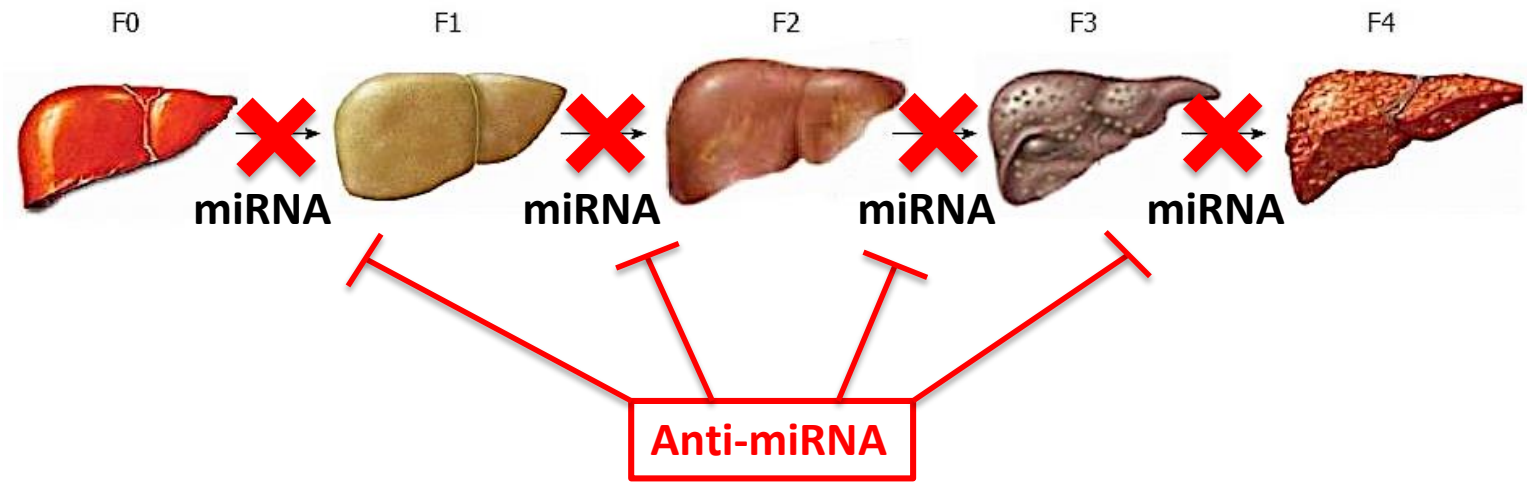
Perspectives and potential relevance

1. Validation in large cohorts of patients

2. Biomarker panels

3. <u>Prognostic</u>: fibrosis progression markers?

4. Therapeutic target



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Cell biology lab livr

Back-up slides

FibroScan®

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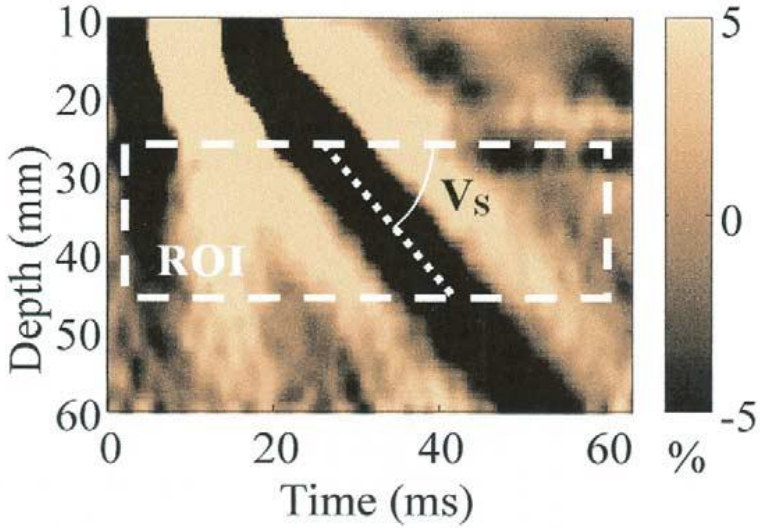
FibroScan®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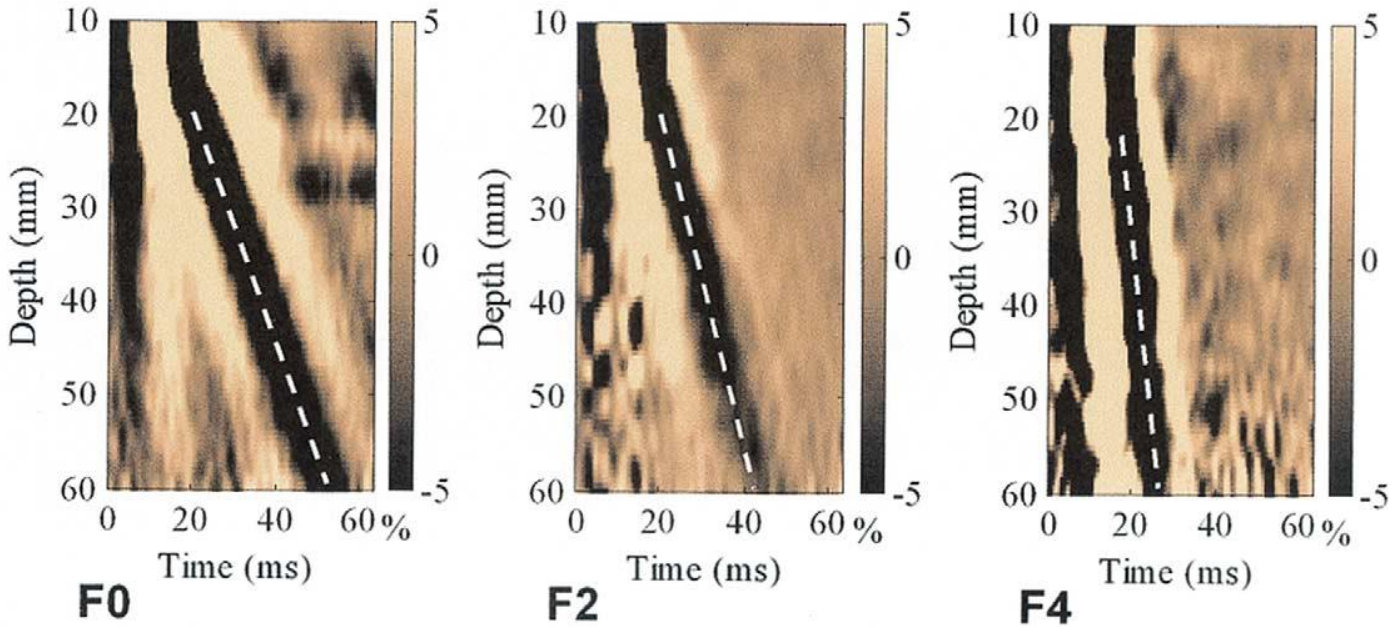
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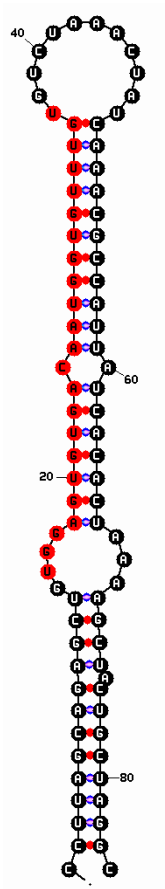
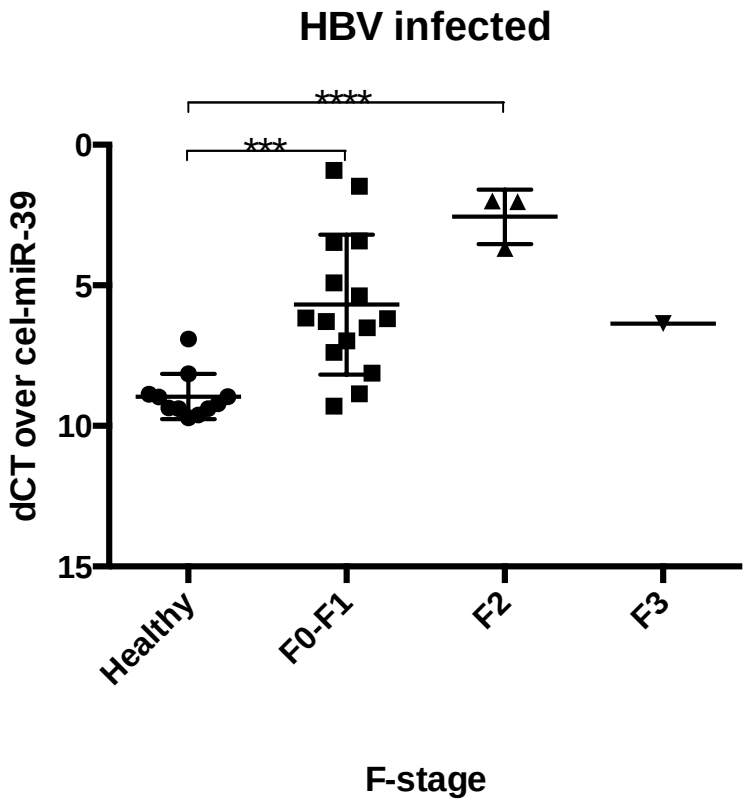
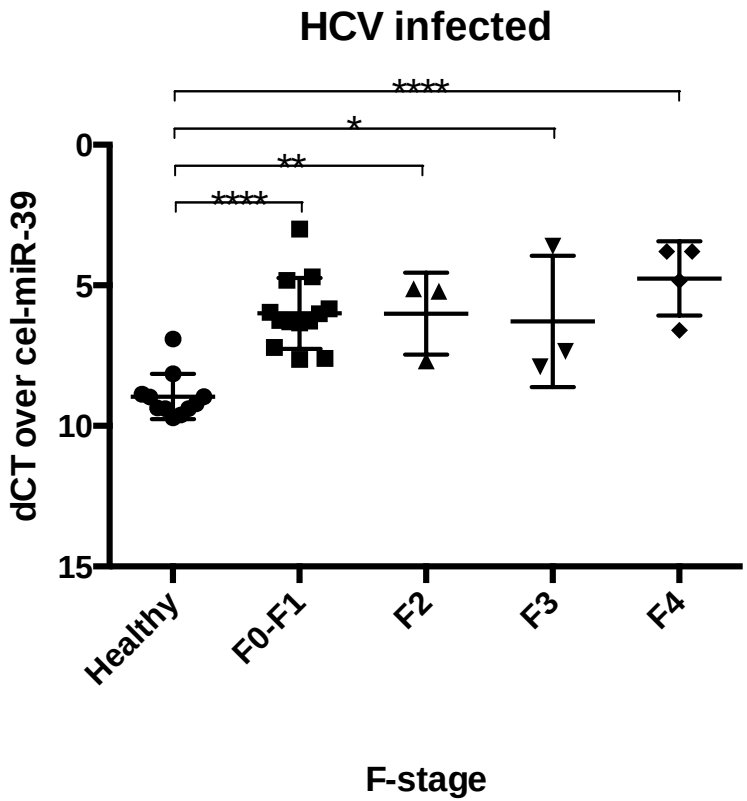
Validation of used methods

miR-122







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