Message from the FLIP Coordinator:
Dear Partners,
This is a crucial moment in the life of the FLIP project. As we are hitting the half-time benchmark, the group becomes more cohesive and all the work done so far starts giving concrete results. We are rapidly increasing the numbers of the FLIP prospective cohort, hopefully our future major tool for large scale collaborative projects on NAFLD in Europe. The HCC observatory has been implemented and running in many of the prominent HCC centers. Large numbers of DNA samples are now available for testing in Newcastle. The first results on diagnostic strategies from our group seem encouraging and were submitted to the AASLD. EASL granted us a slot for a FLIP symposium during next year’s meeting, which is a major sign of recognition of our consortium. However much more work needs to be done. First, the cohort is useless if data is not entered in the e-CRF and serum is not readily available. Same for the HCC Observatory. Then there is a very annoying delay in implementing FibroTest in the FLIP cohort despite this test being free of charge or supported by Biopredictive, a full partner of the consortium. Also, coherent and consensual decisions need to be taken regarding new exploratory markers of NAFLD. Finally, we need to seriously start prospecting for new funding for after the EC funding period. Lots of work but very exciting! And in the meanwhile let’s keep our door open for groups or individuals with genuine interest in NASH! See you all in Newcastle, the European heavyweight NASH City!

Vlad Ratziu

FLIP news!
This year for the first time our FLIP consortium was present at the International Liver Congress in Berlin!
A short summary of our activity, future plans and the history of our application for FP7 was presented during the “EU Grants Session: Improving Liver Research Funding from the EU”. We created a link from the EASL website allowing all visitors of the EASL site to find information about FLIP project www.easl.eu/_newsroom/latest-news/nafld-and-the-the-flip-consortia.

The Liver Meeting will take place in San Francisco, November 4-8 2011.

Next FLIP meeting : Month 24 FLIP meeting: in winter 2012! Half of the project is over, now we have to think about our results and publications. Location – to be decided!

USE THE e-CRFs!
It is very important for our common work to enter all included patients of both NAFLD and HCC cohort at the e-CRFs. One person in each clinical site will be responsible for the CRF and an update to should be done every 3/6 months.
If you have some questions or problems with e-CRFs, you can contact Claus Holst (ch@ipm.regionh.dk), from the DataHub in Copenhagen.

FLIP publication policy!
Don’t forget to add our official FLIP logo on your posters, letters and any communications, thus reinforcing the identity of our consortium. You can download the logo from Mindshere.
Don’t forget to submit your journal article, poster or abstract related to FLIP to the FLIP publication portal so that the results of our work can be seen by everyone!
You can send an e-mail with all details (title, authors...) of your publication to Ann Hasting at ann.hasting@eu.astellas.com or Tania Langon tliong@almacq.com.
Partner news:

**BIOPREDICTIVE**

An independent validation of noninvasive biomarkers FibroMax (FibroTest, SteatoTest, ActiTest and NashTest) in 288 patients with morbid obesity was recently published (Lassailly et al. Eur J Gastroenterol Hepatol 2011). The strength of the study is the methodology which uses weighted AUROCs (by the Obuchowski method) comparing for a test all combinations of stages two by two. The diagnostic performances of FibroTest, SteatoTest, and ActiTest were statistically significant; thereby authors concluded that is possible to reduce the need for biopsy in this population.

In an overview of FibroMax (submitted AASLD 2011, accepted oral session AFEF September 2011, Paris) Poynard et al. found the same significant results for the prediction of liver injury in patients with severe obesity; the overview included the FLIP cohort of morbid obese patients, the previously published independent cohort of Lassailly et al. another independent cohort (Diaz et al. Gastroenterol Clin Biol 2007) with a total of 494 patients.

In the prospective Parisian cohort of type 2 diabetic patients without history of liver disease (694 subjects), FibroTest has a significant prognostic value for the 5-year survival without liver and cardiovascular-related complications and deaths. FibroTest remained significant after adjustment for Framingham score, both for the prediction of overall survival and for the survival without complications. (Submitted to AASLD 2011, accepted in oral session in AFEF September 2011 in Paris).

Last but not least, since June 19th 2011, FibroTest is reimbursed by the French National Health Insurance.

### Recruitment status M18!

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<th>Name</th>
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np : not participating
sio : site initiation ongoing

TOTAL 322 83

### Liste of publications

**FLIP Posters:**

1. NAFLD and the changing face of hepatocellular cancer (HCC), Debashish Das, Dipankar Chattopadyhay, Tahira Islam, Diane Walia, Bryon Jaques, Derek Manas, Mark Hudson, Helen L. Reeves. EASL 2011


**FLIP Publications:**

1. Manuel Romero-Gómez, APOC3 polymorphisms and non-alcoholic fatty liver disease: resolving some doubts and raising others, Journal of Hepatology, 2011

2. Bechmann, Lars; Gastaldelli, Amalia; Vetter, Diana; Patman, Gillian; Pascoe, Laura; Hannivoort, Rebekka; Lee, Ursula; Fiel, M. Isabel; Munoz, Ursula; Ciociaro, Demetrio; Lee, Youngmin; Buzzigoli, Emma; Miele, Luca; Hui, Kei; Bugianesi, Elisabetta; Burt, Alastair; Day, Christopher; Reeves, Helen. Glucokinase links Krüppel-like factor 6 to the regulation of hepatic insulin sensitivity in non-alcoholic fatty liver disease, Journal of Hepatology, 2011


5. ABSENCE OF ADIPOSE TRIGLYCERIDE LIPASE PROTECTS FROM HEPATIC ER STRESS, Claudia Fuchs, Thierry Claudel, Pooja Kumari, Guenter Haemmerle, Tatjana Stojakovic, Hubert Scharnagl, Emina Halilbasic, Judith Gumhold, Dagmar Silbert, Harald Koefeler, and Michael Trauner, submitted to JBC


7. C-reactive protein levels in relation to various features of non-alcoholic fatty liver disease among obese patients, Zimmermann E, Anty R, Verrijken A, Van Gaal L, Sørensen T and Jess T.

**Abstract submitted:**

1. Janine Graham, Tahira Aslam, Dipankar Chattopadyhay, Debasish Das, Imran Patanwala, John Rose, Bryon Jaques, Derek Manas, Mark Hudson, Helen Reeves. NAFLD related HCC is rising dramatically in the North of England. June 2011 to AASLD (American Association for Study of Liver Disease) and BASL (British Association for Study of Liver Disease).

2. Raluca Pais, Randa Bittar, Lyudmila Mateeva, Dan Dumitrascu, Larysa Fedchuk, Thierry Poynard, Dominique Bonnefont-Rousselot, Vlad Ratziu, Fibroblast growth factor 21 is a predictor of advanced disease in patients with NAFLD, June 2011 to AASLD