ABSTRACT NOTIFICATION - EASL - THE INTERNATIONAL LIVER CONGRESS™ 2017

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Geneva, Tuesday, 24 January 2017

Dear Dr GEORGE,

On behalf of the Scientific Programme Committee of The International Liver Congress™ 2017 to be held in Amsterdam, the Netherlands from 19 to 23 April 2017, we are very pleased to inform you that your abstract entitled “Nanovesicle mediated delivery of combination of anticancer agents effectively induced cell death in HCC cell lines” has been accepted for both **ePoster** (electronic poster) **and Paper Poster Presentation**.

EASL will take care of the following;

- Free printing of your paper poster
- Free delivery to the Amsterdam RAI venue
- Free hanging and display of your abstract on poster board in the poster area

Your Poster number is: FRI-090. Your paper poster will be displayed on Friday 21 April 2017 and the poster board number corresponds to the 3 last digit of the Poster number. You will be able to retrieve your poster by removing it from the poster board between 18:00 and 18:30 on the day it is displayed.

Note that any **changes** related to your abstract need to be sent to the abstract office by **8 February 2017 at** ILC.abstracts@easloffice.eu. No changes will be possible after that date.

ePosters and Paper Posters (Exclusively Landscape Format)

You are required to submit your poster file that will be used for both ePoster and printing on the poster submission website. For this, you will shortly receive a notification providing guidelines and deadlines relating to ePoster preparation and presentation from the company MULTIEPOSTER who has been mandated by EASL.

Once your poster is submitted, EASL will **print it and display it** in the congress venue. Your poster has been scheduled to be displayed on Friday 21 April 2017 between 08:00 and 18:00. **Presenters** should stand next to their poster during the morning and afternoon coffee breaks and at lunch time for informal discussions.

Guidelines for preparing your poster, including dimensions of the poster, can be found on the congress website: https://ilc-congress.eu/poster-presenters/.

ePosters will be made available on:

- e-Poster stations during the congress (available to all onsite delegates)
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Embargo Policy

Wednesday 30 March 2016 at 10:00 CET- a large quantity of abstracts showing abstract title, author's names and abstract data will be posted online. At that time, the released abstracts are publicly available and no longer under embargo.

A small quantity of abstracts will be retained and presented during the official EASL Press Office activities and/or materials. These abstracts are under **strict embargo** until 7:00 CET on the day the abstract is presented at the congress. Only the embargoed abstract titles, author's and institute's names will be made available on the congress website on Wednesday 30 March. You will be notified if your abstract falls into this category.

In order to respect the EASL embargo policy, it is crucial that you do not, under any circumstances, disclose any information related to your abstract before the data is made available on the conference website.

Young Investigator Bursary:

If the presenting author applied for a bursary upon submission of your abstract, further information will be sent shortly in a separate email to the presenting author. EASL bursaries are granted only to those who have complied with and fulfilled all requirements as indicated in the abstract instructions.

Confirmation of attendance and registration to the congress for the presenting author is mandatory.

If you are unable to attend the ILC or you are not the presenting author, please advise the Congress Secretariat immediately at ILC.abstracts@easloffice.eu.

If you have not already registered and paid your registration fees you are requested to do so online via the Registration (https://ilc-congress.eu/registration/) page on the congress website. Please use the special code below before 8 February 2017 to benefit from an early registration fee.

Special Code: *y3wCDb*

Only abstracts of participants who have confirmed their participation and paid their fees will be included in the scientific programme.

We encourage you to book your accommodation promptly, as availability may be limited in some hotels. Please visit the ILC website for information on the congress website (https://ilc-congress.eu/hotels/).

We look forward to this exciting congress and thank you again for your important contribution.

There is no doubt that your enthusiasm, your scientific achievements and your willingness to share the best and latest research results will make the ILC in Amsterdam a huge success.

Yours sincerely,

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progression and monitored apoptosis *in vivo* using fluorescence molecular and micro-computed tomography (FMT, µCT).
Results: Single dose injection (0.2 mg/kg body weight) revealed a significant reduction of *Jnk2* on mRNA and protein levels in wildtype mice after 1 week. Moreover, 4 week *siJnk2* treatment had no influence in JNK1$^{\Delta hepa}$ livers. Next, we sought to investigate the effects in an acute model of Nemo$^{\Delta hepa}$ mice. Treatment with *siJnk2* caused hepatocyte hypertrophy, mitotic catastrophe, karyomegaly, exacerbated cell infiltration, hepatic fibrogenesis and ductular proliferation. These effects were evident by high alkaline phosphatase levels, cleaved caspase-3 positive cells alongside with increased compensatory proliferation. Furthermore, our data indicated that proinflammatory monocytes massively infiltrate the liver after hepatocyte-specific *Jnk2* inhibition. Interestingly, decreased compensatory proliferation, cleaved Caspase-3 protein levels and markers of hepatic stellate cell activation/matrix deposition were observed in a chronic model of Nemo$^{\Delta hepa}$ mice injected over 8 weeks.
Conclusions: *siJnk2* therapy successfully depleted the levels of *Jnk2* both *in vivo* and *in vitro*. *Jnk2* knockdown induced significant changes in liver parenchyma and a therapeutic option by reducing HCC progression. These results open ew opportunities for precision medicine of CLD treatment with potential translation into humans.

FRI-113
Histological subtypes of hepatocellular carcinoma are related to gene mutations and molecular tumor classification
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Background and Aims: Our increasing understanding of hepatocellular carcinoma (HCC) biology holds promise for personalized care, however its translation into clinical practice requires a precise knowledge of its relationship to tumor phenotype. We aimed at investigating molecular-phenotypic correlations in a large series of HCC.
Methods: Surgically resected HCC (n = 343) were investigated by pathological review, immunohistochemistry, gene expression profiling and sequencing.
Results: *CTNNB1* (40%) and *TP53* (21%) mutations were mutually exclusive and defined two major groups of HCC characterized by distinct phenotypes. *CTNNB1* mutated-tumors were large (P = 0.001), well-differentiated (P < 0.001), cholestastic (P < 0.001), with microtrabecular (P < 0.001) and pseudoglandular (P < 0.001) patterns and without inflammatory infiltrates (P < 0.001). *TP53* mutated-tumors were poorly-differentiated (P < 0.001) with compact pattern (P = 0.02), multinucleated (P = 0.01) and pleomorphic (P = 0.02) cells and frequent vascular invasion (P < 0.001). World Health Organization (WHO) histological subtypes were also strongly related to molecular features. The scirrhous subtype was associated with *TSC1/TSC2* mutations (P = 0.005), epithelial-to-mesenchymal transition and a progenitor expression profile. The steatohepatitic subtype showed frequent IL-6/JAK/STAT activation without *CTNNB1*, *TERT* and *TP53* pathway alterations (P = 0.01). Pathological review identified a novel subtype, designated as "macrotrabecular-massive" associated with HBV infection (P = 0.01), poor overall survival (P < 0.001), high alphafoeto-protein serum level (P = 0.01), angiogenesis activation (P = 0.007), *FGF19* amplifications (P = 0.02), *TP53* (P < 0.001) and *ATM* (P = 0.03) mutations. Finally, integration of HCC pathological characteristics with the transcriptomic classification showed phenotypically distinct tumor subclasses closely related to G1-G6 transcriptomic subgroups.
Conclusions: HCC phenotypes are tightly associated with gene mutations and transcriptomic classification. These findings may help in translating our knowledge of HCC biology into clinical practice.

FRI-114
Nanovesicle mediated delivery of combination of anticancer agents effectively induced cell death in Hepatocellular carcinoma cell lines
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Background and Aims: Hepatocellular carcinoma (HCC) is a primary malignant hepatic tumor and highly resistant to treatment owing to tumor heterogeneity. The current treatment modalities for HCC are not effective due to lack of efficient and organ specific drug delivery system. We studied the efficacy of milk-derived nanovesicles (MNV) to deliver the anticancer agent doxorubicin into HCC cells in culture as well as intrahepatic tumors induced in immunodeficient mice.
Methods: MNVs were isolated from skim milk using ultracentrifugation and characterized with nanoparticle tracking analysis (NTA) and electron microscopy. MNVs were loaded with doxorubicin (dox-MNV), purified by ultracentrifugation, and characterized using spectrophotometry and NTA. HepG2, Hep3B, and PLC/PRF/5 HCC cells in culture were treated with dox-MNV and evaluated the rate of cell death. Intrahepatic tumors induced in nude mice were injected with dox-MNV through tail vein and assessed tumor regression using in-vivo imaging system.
Results: Cellular uptake studies depicted plain and dox-MNV attained saturation within 4 h of treatment. Cell toxicity studies on HepG2, Hep3B, and PLC/PRF/5 HCC cells with MNV-dox at 1 µM depicted around 20% cell death at 24 h, 50% at 48 h, and 80% at 72 h. HepG2 cells treated with fluorescent-tagged dox-MNV exhibited nuclear disintegration and apoptosis within 24 h. Treatment of intrahepatic tumors with dox-MNV resulted in significant regression and increased survival rate in nude mice.
Conclusions: Our studies demonstrated that MNVs could be effectively used for successful delivery of anticancer agents into HCC cells and intrahepatic tumors. MNV mediated delivery of anticancer agents through intravenous system would be an effective method for the treatment of primary hepatic tumors.

FRI-115
Genetic and epigenetic bases of the relationship between reduced OCT1 expression and poor response to sorafenib in hepatocellular carcinoma and cholangiocarcinoma
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Background and Aims: The organic cation transporter-1 (OCT1, *SLC22A1* gene) plays a key role in sorafenib uptake and interaction with its molecular targets. Its expression has been found decreased both in hepatocellular carcinoma (HCC) and cholangiocarcinoma (CCA). Here we have aimed at characterizing the genetic and