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RESEARCH Open Access

Robust circulating microRNA signature for the diagnosis and early detection of pancreatobiliary cancer

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Abstract

Background A new circulating biomarker superior to carbohydrate antigen 19–9 (CA19-9) is needed for diagnosing pancreatobiliary cancer (PBca). The aim of this study was to identify serum microRNA (miRNA) signatures comprising reproducible and disease-related miRNAs.

Methods This multicenter study involved patients with treatment-naïve PBca and healthy participants. The optimized serum processing conditions were evaluated using *t*-distributed stochastic neighbor embedding (*t*-SNE) visualization. Serum miRNA candidates for disease association were selected using weighted gene coexpression network analysis (WGCNA). A miRNA signature combining multiple serum miRNAs was tested in exploratory, validation, and independent validation sets. The synthesis and secretion of diagnostic miRNAs were evaluated using human pancreatic cancer cells.

Results In total, 284 (150 healthy and 134 PBca) of 827 serum samples were processed within 2 h of blood collection before freezing, distributed in the same area as that in the *t*-SNE map, and assigned to an exploratory set. The 193 optimized samples were assigned to either the validation (50 healthy, 47 PBca) or independent validation (50 healthy, 46 PBca) set. Index-1, a combination of five serum miRNAs (hsa-miR-1343-5p, hsa-miR-4632-5p, hsa-miR-4665-5p, hsa-miR-665, and hsa-miR-6803-5p) with disease association in WGCNA, showed a sensitivity and specificity of > 80% and an AUC outperforming that of CA19-9 in the exploratory, validation, and independent validation sets. The AUC of Index-1 was superior to that of CA19-9 (0.856 vs. 0.649, $p = 0.038$) for detecting T1 tumors. miR-665, a component of Index-1, was expressed in human pancreatic cancer cells, and its transfection inhibited cell growth.

Conclusions The serum miRNA signature Index-1 is useful for detecting PBca and could facilitate the early diagnosis of PBca. These findings can help improve clinical PBca detection by providing an optimized biomarker that overcomes the limitations of the current standard.

Keywords Pancreatobiliary cancer, Circulating microRNA, Biomarker

nature medicine

Brief Communication

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Ultrasensitive ctDNA detection for preoperative disease stratification in early-stage lung adenocarcinoma

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Check for updates

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Allan Hackshaw[1,2], Nicholas McGranahan[1,3], Mariam Jamal-Hanjani[1,4,5], Alexander M. Frankell[1,2], Richard O. Chen[3,113] & Charles Swanton[1,2,11,113]

Circulating tumor DNA (ctDNA) detection can predict clinical risk in early-stage tumors. However, clinical applications are constrained by the sensitivity of clinically validated ctDNA detection approaches. NeXT Personal is a whole-genome-based, tumor-informed platform that has been analytically validated for ultrasensitive ctDNA detection at 1–3 ppm of ctDNA with 99.9% specificity. Through an analysis of 171 patients with early-stage lung cancer from the TRACERx study, we detected ctDNA pre-operatively within 81% of patients with lung adenocarcinoma (LUAD), including 53% of those with pathological TNM (pTNM) stage I disease. ctDNA predicted worse clinical outcome, and patients with LUAD with <80 ppm preoperative ctDNA levels (the 95% limit of detection of a ctDNA detection approach previously published in TRACERx) experienced reduced overall survival compared with ctDNA-negative patients with LUAD. Although prospective studies are needed to confirm the clinical utility of the assay, these data show that our approach has the potential to improve disease stratification in early-stage LUADs.

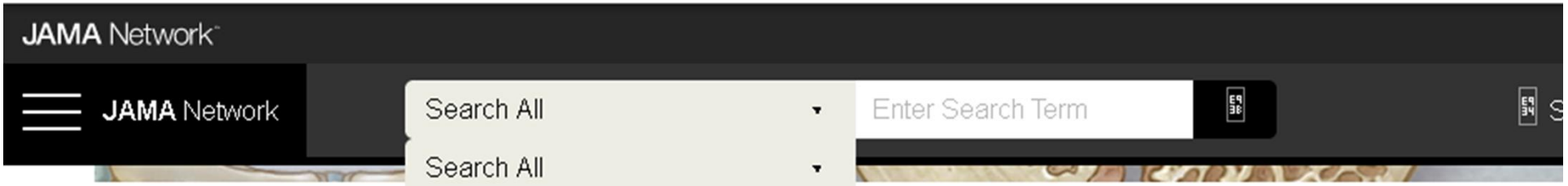
tumor DNA (ctDNA, namely

ctDNA detection can be tumor-informed or tumor-agnostic.

REVIEW

Circular RNAs in cancer

Yang Guo[#] | Qiang Huang[#] | Yu
Chengzhi Xu | Chunping Wu[*] | Le



JAMA | Screening for Osteoporosis

Navigating the new USPSTF Osteoporosis Screening recommendations:
Insights and Comprehensive Resources from *JAMA* and the JAMA Network

Population	Recommendation	Grade
Women 65 years or older:	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures.	B
Postmenopausal women younger than 65 years with 1 or more risk factors for osteoporosis:	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than 65 years who are at increased risk for an osteoporotic fracture as estimated by clinical risk assessment.	B
Men:	The current evidence is insufficient to assess	I

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Editorial

The use of transient elastography for predicting hepatocellular carcinoma in chronic hepatitis B patients: Editorial on "Risk assessment of hepatitis B virus-related hepatocellular carcinoma development using vibration-controlled transient elastography: Systematic review and meta-analysis"

Mirko Zoncapè and Emmanuel A. Tsochatzis

Chronic hepatitis B (CHB) virus infection continues to pose a significant global public health challenge, influenced by evolving epidemiological patterns due to several factors, such as vaccination policies and migration. The diagnosis of hepatitis B is established by the presence of hepatitis B surface antigen (HBsAg), and chronic hepatitis B infection is confirmed when HBsAg persists in the bloodstream for at least 6 months.[1-4] The global prevalence of HBsAg varies greatly across different countries.[5] Almost 296 million people worldwide have CHB, with the highest rates observed in Africa and Asia.[1] Such patients require lifelong monitoring and potentially antiviral treatment. In 2022, hepatitis B virus (HBV)-related complications resulted in approximately 1.1 million deaths, and these numbers

the risk of developing hepatocellular carcinoma (HCC) in patients with CHB is still a challenge nowadays, as this might develop even in patients who do not have cirrhosis or in patients who are responding to antiviral treatment.

Given this, it becomes crucial to identify those patients who are at a higher risk of developing HCC, to ensure they receive timely and effective care. Effective risk stratification can play a pivotal role in this regard, allowing for HCC surveillance and potentially improving outcomes. In this context, a meta-analysis by Jin et al.[6] has provided interesting insights on the efficacy of transient elastography (TE) as a non-invasive test (NIT) for predicting HCC development in this patient population.

TE performed using the Fibroscan is a well validated NIT for assessing liver fibrosis in CHB[7] and is recommended in

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Clinical Practice Guidelines

JOURNAL
OF HEPATOLOGY

EASL Clinical Practice Guidelines on the management of hepatocellular carcinoma☆

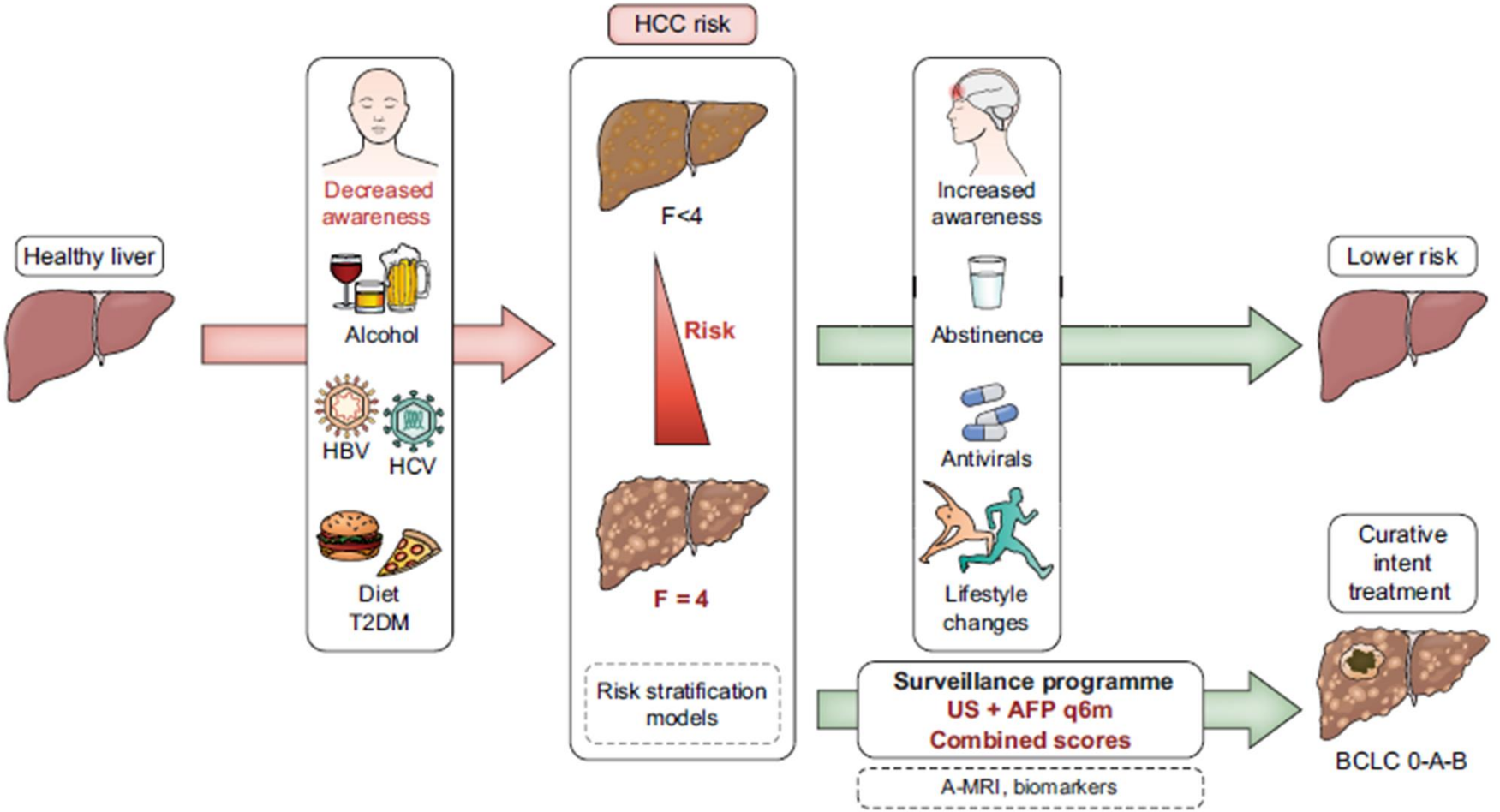
European Association for the Study of the Liver*

Summary

Liver cancer is the third leading cause of cancer-related deaths worldwide, with hepatocellular carcinoma (HCC) accounting fo

Summary

Liver cancer is the third leading cause of cancer-related deaths worldwide, with hepatocellular carcinoma (HCC) accounting for approximately 90% of primary liver cancers. Advances in diagnostic and therapeutic tools, along with improved understanding of their application, are transforming patient treatment. Integrating these innovations into clinical practice presents challenges and necessitates guidance. These clinical practice guidelines offer updated advice for managing patients with HCC and provide a comprehensive review of pertinent data. Key updates from the 2018 EASL guidelines include personalised surveillance based on individual risk assessment and the use of new tools, standardisation of liver imaging procedures and diagnostic criteria, use of minimally invasive surgery in complex cases together with updates on the integrated role of liver transplantation, transitions between surgical, locoregional, and systemic therapies, the role of radiation therapies, and the use of combination immunotherapies at various stages of disease. Above all, there is an absolute need for a multiparametric assessment of individual risks and benefits, considering the patient's perspective, by a multidisciplinary team encompassing various specialties.


HCC risk
Healthy liver
Decreased awareness
Alcohol
HBV
HCV
Diet
T2DM
F<4
Risk
F = 4
Risk stratification models
Increased awareness
Abstinence
Antivirals
Lifestyle changes
Lower risk
Curative intent treatment
Surveillance programme
US + AFP q6m
Combined scores
A-MRI, biomarkers
BCLC 0-A-B

Recommendation	Consensus
Patients with HBV infection should be treated with nucleoside or nucleotide analogues to reduce the risk of developing HCC (both *de novo* and recurrence) and the type and time of treatment should follow EASL guidelines on HBV infection **(LoE 2, strong recommendation).**	100%
Patients with HCV infection and liver fibrosis should be treated with direct-acting antivirals to reduce the risk of cirrhosis-related complications, including HCC **(LoE 2, strong recommendation).**	100%
Patients with HBV and HCV co-infection can be treated following the same criteria as for mono-infected patients **(LoE 3, weak recommendation).**	100%
Weight loss in patients with obesity, alcohol cessation, and tobacco cessation are recommended to reduce the risk of liver-related and other adverse outcomes and may be recommended to reduce the risk of HCC **(LoE 3, weak recommendation).**	100%
Coffee consumption may be recommended to reduce the risk of HCC **(LoE 3, weak recommendation).**	94%
Owing to a lack of evidence, the use of statins, aspirin and metformin cannot currently be recommended to reduce the risk of HCC development **(LoE 3, weak recommendation).**	96%
High-risk seronegative people should be vaccinated against HBV to decrease HCC incidence and HCC-related death and improve overall survival **(LoE 3, strong recommendation).**	100%
Patients with cirrhosis should be offered surveillance for HCC unless they have a relatively high risk of death from non-HCC causes, or they could not be offered a curative-intent treatment for HCC (*e.g.*, patients with Child-Pugh class C cirrhosis ineligible for liver transplantation) **(LoE 2, strong recommendation).**	96%
Patients with chronic liver disease and advanced fibrosis without cirrhosis have a higher risk of HCC than the general population, but HCC surveillance cannot currently be recommended in this group owing to insufficient evidence **(LoE 3, weak recommendation).**	95%
An ultrasound examination of the liver every 6 months is recommended for screening of HCC. The combined use of ultrasound with AFP increases sensitivity while decreasing specificity and is a reasonable option. There is limited data to support the use of other promising imaging modalities such as abbreviated MR or serum biomarkers **(LoE 3, strong recommendation).**	78%
The LI-RADS should be used to favour standardisation in the acquisition, description and reporting of liver imaging examinations **(LoE 3, strong recommendation).**	96%
Non-invasive diagnosis of HCC should be based on the LI-RADS CT/MR v2018 or the LI-RADS CEUS v2017 criteria. With CT/MRI, the following major imaging features are combined to reach the diagnosis: tumour size, rim and non-rim arterial hyperenhancement, peripheral and non-peripheral washout (in the portal venous or delayed phases on CT and MRI using extracellular contrast agents or gadobenate dimeglumine, or in the portal venous phase only with MRI using gadoxetic acid), enhancing capsule and threshold growth. With CEUS, non-rim arterial hyperenhancement with late-onset (>60 s) and washout of mild intensity are combined to reach the diagnosis	95%

ment did not impact the result.

In summary, the analyses published to date have applied differing methodology to varying data sets which include a wide range of trial phases, lines of treatment and drug classes. Overall, there is at best a moderate correlation between PFS and OS, but a wide variation is seen between individual trials suggesting that PFS is not a robust surrogate for OS. The identification of a surrogate is most important for first-line trials where OS is longest. For advanced HCC, the OS in recent trials remains around 20 months. By comparison with other tumours this is relatively short, and OS remains appropriate under these circumstances.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Oral Regimens for Rifampin-Resistant, Fluoroquinolone-Susceptible Tuberculosis

L. Guglielmetti, U. Khan, G.E. Velásquez, M. Gouillou, A. Abubakirov, E. Baudin, E. Berikova, C. Berry, M. Bonnet, M. Cellamare, V. Chavan, V. Cox, Z. Dakenova, B.C. de Jong, G. Ferlazzo, A. Karabayev, O. Kirakosyan, N. Kiria, M. Kunda, N. Lachenal, L. Lecca, H. McIlleron, I. Motta, S.M. Toscano, H. Mushtaque, P. Nahid, L. Oyewusi, S. Panda, S. Patil, P.P.J. Phillips, J. Ruiz, N. Salahuddin, E.S. Garavito, K.J. Seung, E. Ticona, L. Trippa, D.E.V. Vasquez, S. Wasserman, M.L. Rich, F. Varaine, and C.D. Mitnick, for the endTB Clinical Trial Team*

RESULTS

Among the 754 participants who underwent randomization, 699 were included in the modified intention-to-treat analysis, and 562 in the per-protocol analysis. In the modified intention-to-treat analysis, 80.7% of the patients in the standard-therapy group had favorable outcomes. The risk difference between standard therapy and each of the four new regimens that were found to be noninferior in the modified intention-to-treat population was as follows: BCLLfxZ, 9.8 percentage points (95% confidence interval [CI], 0.9 to 18.7); BLMZ, 8.3 percentage points (95% CI, −0.8 to 17.4); BDLLfxZ, 4.6 percentage points (95% CI, −4.9 to 14.1); and DCMZ, 2.5 percentage points (95% CI, −7.5 to 12.5). Differences were similar in the per-protocol population, with the exception of DCMZ, which was not noninferior in that population. The proportion of participants with grade 3 or higher adverse events was similar across the regimens. Grade 3 or higher hepatotoxic events occurred in 11.7% of participants overall and in 7.1% of those receiving standard therapy.

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CONCLUSIONS

Consistent results across all the analyses support the noninferior efficacy of three all-oral shortened regimens for the treatment of rifampin-resistant tuberculosis. (Funded by Unitaid and others; endTB ClinicalTrials.gov number, NCT02754765.)

Table 3. Safety Analysis at Week 73.*

Adverse Events	BLMZ (N= 126)	BCLLfxZ (N= 122)
Any adverse event — no. (%)	126 (100)	122 (100)
Grade 3 or higher adverse events		
≥1 event — no. (%)	69 (54.8)	68 (55.7)
No. of events related to trial drug or drugs/total no. of events (%)†‡	49/136 (36.0)	57/166 (34.3)
Serious adverse events		
≥1 event — no. (%)	18 (14.3)	16 (13.1)
No. of events related to trial drug or drugs/total no. of events (%)†‡	7/26 (26.9)	11/29 (37.9)
Death from any cause — no. (%)	3 (2.4)	1 (0.8)
Adverse events of special interest		
≥1 event — no. (%)	35 (27.8)	33 (27.0)
Any grade 3 or 4 increase in ALT or AST — no. (%)	23 (18.3)	17 (13.9)
Any grade 3 or 4 leukopenia, anemia, or thrombocytopenia — no. (%)	11 (8.7)	9 (7.4)
Any grade 3 or 4 peripheral neuropathy — no. (%)	4 (3.2)	5 (4.1)
Any grade 3 or 4 optic neuritis — no. (%)	0	1 (0.8)
Any grade 3 or 4 QT corrected interval prolonged — no. (%)‡‡	0	4 (3.3)
Permanent discontinuation of any drug due to adverse event — no. (%)	26 (20.6)	32 (26.2)

* The safety population included all participants who underwent randomization and receiv
aspartate aminotransferase.
† An event was considered to be related if there was at least a reasonable possibility that it
‡ The QT interval was corrected according to Fridericia's formula.

CLINICAL NEWS | ULTRASOUND

Samsung Medison debuts AI-

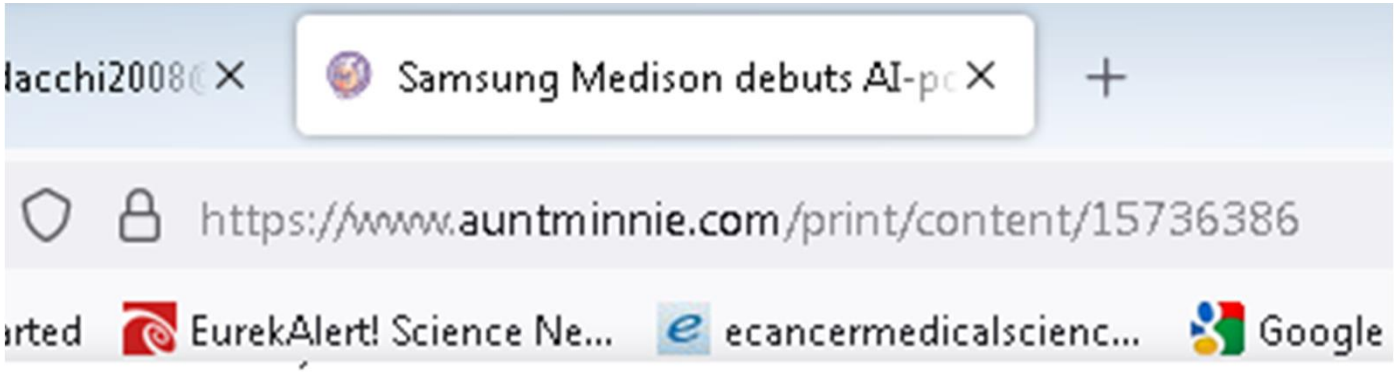
powered ob/gyn ultrasound system

Korea-based Samsung Medison has launched a new AI-powered ob/gyn ultrasound syst

1 of 3

By —

Tags — Samsung Medison



The company debuted Samsung Z20 at the Society for Maternal-Fetal Medicine (SMFM) 2025. The system features Live ViewAssist, a real-time deep learning tool that enhances precision and simplifies advanced obstetrical exams, according to the firm. Its other capabilities include automatic identification and labeling, real-time quality evaluation, and measurements.

The device is designed to reduce the risk of work-related musculoskeletal disorders, Samsung Medison said, adding that it also addresses the challenges of diagnosing patients with a high body mass index.

Also at SMFM, Sonio joined Samsung to showcase its cloud-based ultrasound reporting and image management software. Samsung acquired Sonio last year.

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THE END