How liver cells enable colorectal cancer spread: New study unveils crucial details

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crucial details

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Discovery of proteins Plexin-B2 and semaphorin's role in colorectal cancer metastasis sheds light on potential treatment targets.

Article

In vivo interaction screening reveals liver-derived constraints to metastasis

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It is estimated that only 0.02% of disseminated tumour cells are able to seed overt metastases[1]. While this suggests the presence of environmental constraints to metastatic seeding, the landscape of host factors controlling this process remains largely unclear. Here, combining transposon technology[2] and fluorescence niche labelling[3], we developed an in vivo CRISPR activation screen to systematically investigate the interactions between hepatocytes and metastatic cells. We identify plexin B2 as a critical host-derived regulator of liver colonization in colorectal and pancreatic cancer and melanoma syngeneic mouse models. We dissect a mechanism through which plexin B2 interacts with class IV semaphorins on tumour cells, leading to KLF4 upregulation and thereby promoting the acquisition

EDITORIAL

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The New Nomenclature for Fatty Liver Disease

Sven M Francque[1,2], Bogdan Procopet[3,4]

Non-alcoholic fatty liver disease (NAFLD) and its more severe subtype non-alcoholic steatohepatitis (NASH), is the most common chronic liver disease (CLD) worldwide and represents an increasing burden of morbidity and mortality, and comes with a substantial individual patient suffering and a considerable societal cost [1]. In the past two decades, intensive research has been conducted to understand disease pathophysiology and clinical course better and develop diagnostic and therapeutic tools for disease management. Changing the name and the definition of the disease is, hence, something that could potentially have a huge impact and needs careful consideration of the pros and cons.

lesions, especially when alcohol is not the sole cause. Results from these studies may lead to refinements or revisions of the current nomenclature. Another criticism is that a diagnosis based on just one cardiometabolic criterion might be too lax or that certain metabolic criteria need adjustment. Recent analysis from the UK biobank suggests that patient groups with MASLD or MAFLD, with alcohol consumption < 20/30g/d, were largely identical.

Thresholds of glycaemic control, lipid levels considered "healthy" and "normal" transaminases, and the thresholds for pulmonary hypertension… all were not carved in stone and have been adjusted as needed with evolving knowledge. That will also be the case for the new NAFLD nomenclature. But for the time being, it offers the reference framework for clinical care and research in the fields covered by the SLD umbrella and represents a significant step forward in the research and management of the patients concerned.

Conflicts of interest: None to declare.

MAYO CLINIC

MAYO CLINIC PROCEEDINGS

Biett Sign as an Indicator of Secondary Syphilis

Pei-Chun Weng, MD, and Shu-Hao Li, MD

A man in his early 70s presented with a 5-day history of palmoplantar rashes. He reported no constitutional symptoms but a history of unprotected intercourse 3 months prior. Upon examination, there were multiple erythematous macules with annular collarettes of scales on the palms (Figure A) and soles (Figure B), consistent with Biett sign. Laboratory assessments revealed positive rapid plasma reagin and Treponema pallidum particle agglutination tests with titers of 1:256 and 1:1280, respectively, leading to a diagnosis of secondary syphilis. Screening for human immunodeficiency virus yielded negative results. An intramuscular injection of 2.4 million units of benzathine penicillin G was administered. The skin lesions resolved and a rapid plasma reagin test yielded negative results at the 1-month and 6-month follow-ups, respectively.

Syphilis is a sexually transmitted disease caused by *Treponema pallidum*. The initial painless chancre of syphilis appears at the

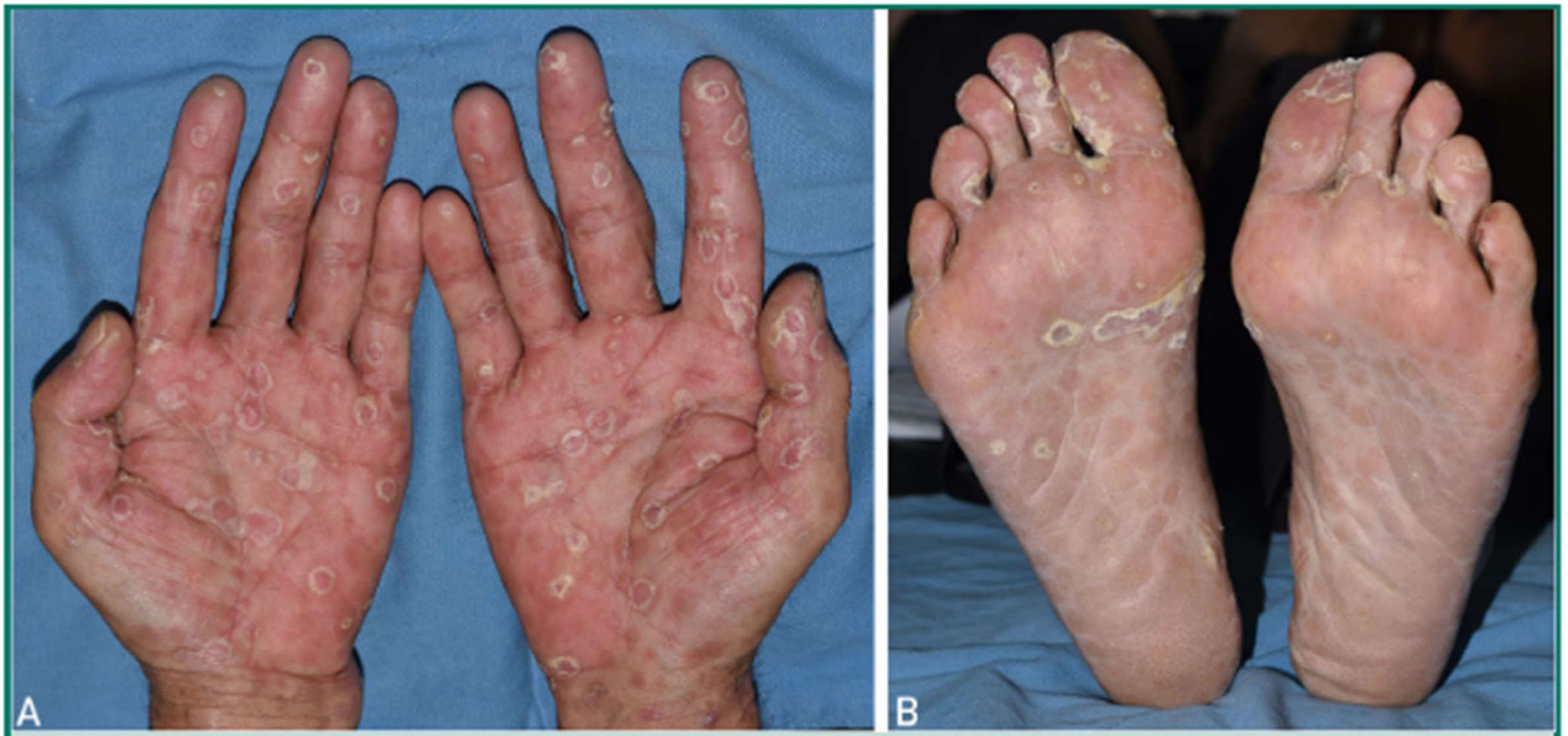

FIGURE. Diffuse erythematous macules with characteristic collarettes of scales on the palms (**A**) and soles (**B**), consistent with Biett sign of secondary syphilis.

Q: Should my patients with hypertension be referred for renal denervation?

A: Maybe. Select patients should be referred after informed and shared decision-making.

Patients with treatment-resistant hypertension or intolerance to further medication adjustments may be suitable candidates for renal denervation, as it demonstrates a blood pressure (BP)-lowering effect of 5 to 7 mm Hg, comparable to the effect of adding another antihypertensive agent (**Figure 1**).[1–5] Two renal denervation systems—ultrasound and radiofrequency based—are currently approved by the US Food and Drug Administration.[6,7] The European Society of Hypertension updated guidelines[8] state that renal denervation is a consideration for true treatment-resistant hypertension and for patients with drug intolerances and an estimated glomerular filtration rate (eGFR) greater than 40 mL/minute/1.73 m^2.

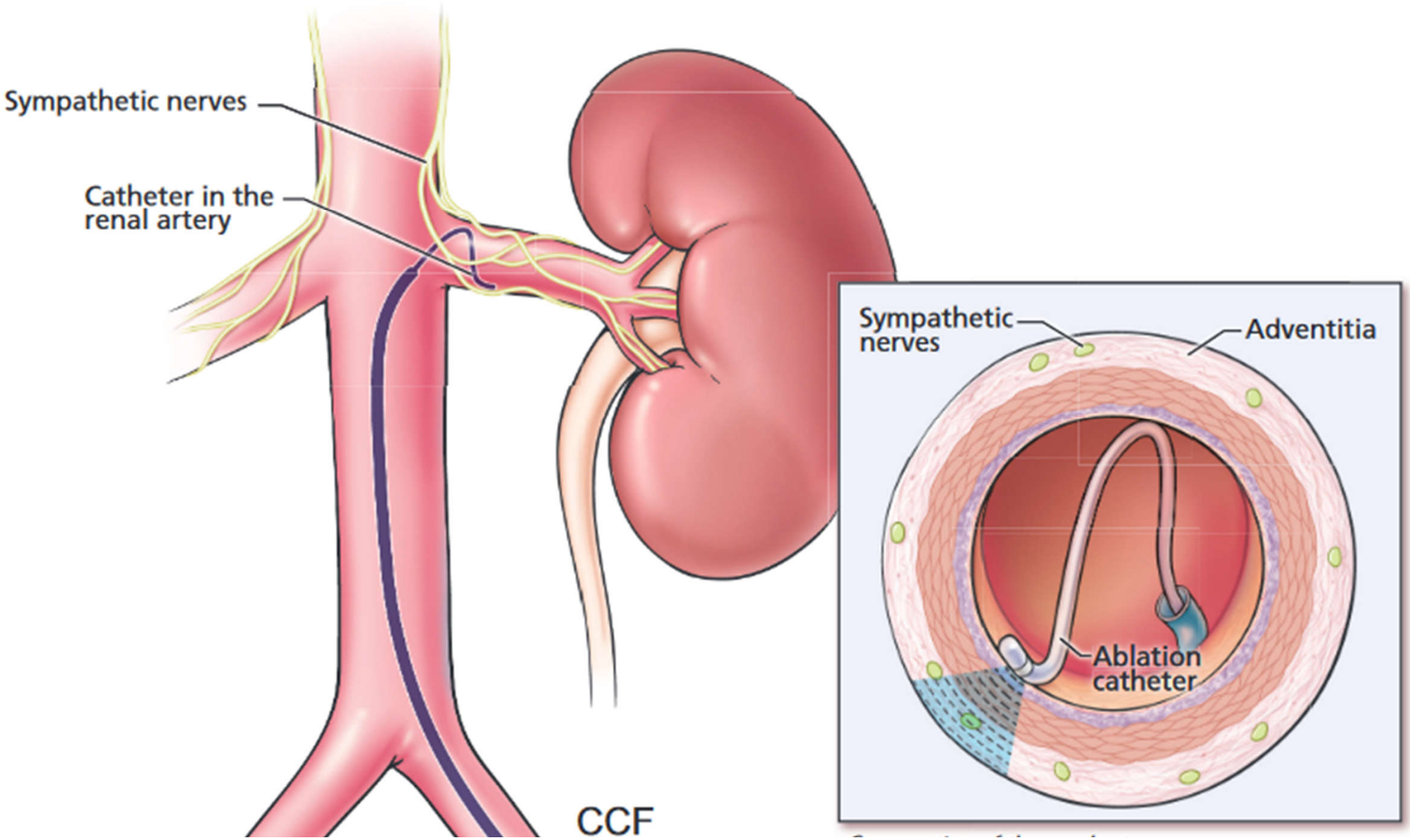
Sympathetic nerves
Catheter in the renal artery
CCF
Sympathetic nerves
Adventitia
Ablation catheter

TABLE 1

Patient characteristics for potential treatment with renal denervation

Exclusion criteria

White coat hypertension
Secondary hypertension
- Renovascular hypertension
- Primary aldosteronism
- Hyperthyroidism
- Pheochromocytoma
- Cushing syndrome
- Coarctation of the aorta

Isolated systolic hypertension
Pregnancy
Estimated glomerular filtration rate < 30 mL/minute/1.73 m^2
Inadequate renal artery anatomy

Characteristics of potential candidates

Treatment-resistant hypertension
Multiple medication intolerances
Medication adherence difficulty

THE BOTTOM LINE

Recent studies have demonstrated the efficacy and safety of catheter-based renal artery denervation with radiofrequency or ultrasound energy in reducing blood pressure across the hypertension spectrum, with multiple trials suggesting a significant and sustained reduction in BP. In some studies, BP reduction was sustained for up to 36 months after renal denervation. More data are needed to determine whether attenuating the renal sympathetic nervous system offers end-organ protection beyond BP reduction. Renal denervation may be offered as an alternative or adjunct to pharmacotherapy in patients with apparent treatment-resistant hypertension, multidrug intolerance, or nonadherence. Shared decision-making, including establishing realistic expectations regarding lowering BP, is crucial before proceeding with renal denervation.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Results after Four Years of Screening for Prostate Cancer with PSA and MRI

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prostate cancer was 0.84 (95% CI, 0.66 to 1.07). The number of advanced or high-risk cancers detected (by screening or as interval cancer) was 15 in the MRI-targeted biopsy group and 23 in the systematic biopsy group (relative risk, 0.65; 95% CI, 0.34 to 1.24). Five severe adverse events occurred (three in the systematic biopsy group and two in the MRI-targeted biopsy group).

CONCLUSIONS

In this trial, omitting biopsy in patients with negative MRI results eliminated more than half of diagnoses of clinically insignificant prostate cancer, and the associated risk of having incurable cancer diagnosed at screening or as interval cancer was very low. (Funded by Karin and Christer Johansson's Foundation and others; GÖTEBORG-2 ISRCTN registry number, ISRCTN94604465.)

Biopsy type performance			
Category of cancer	Systematic biopsy	MRI-targeted biopsy	Relative risk (with 1 as reference)
Screening-detected cancer and interval cancer, overall			
Clinically insignificant	2.4%	1%	0.43

THE END