

New Hope for the Improvement of Liver Cancer Treatment: A Novel Platform for Drug Delivery

Dr Nadine Abi-Jaoudeh

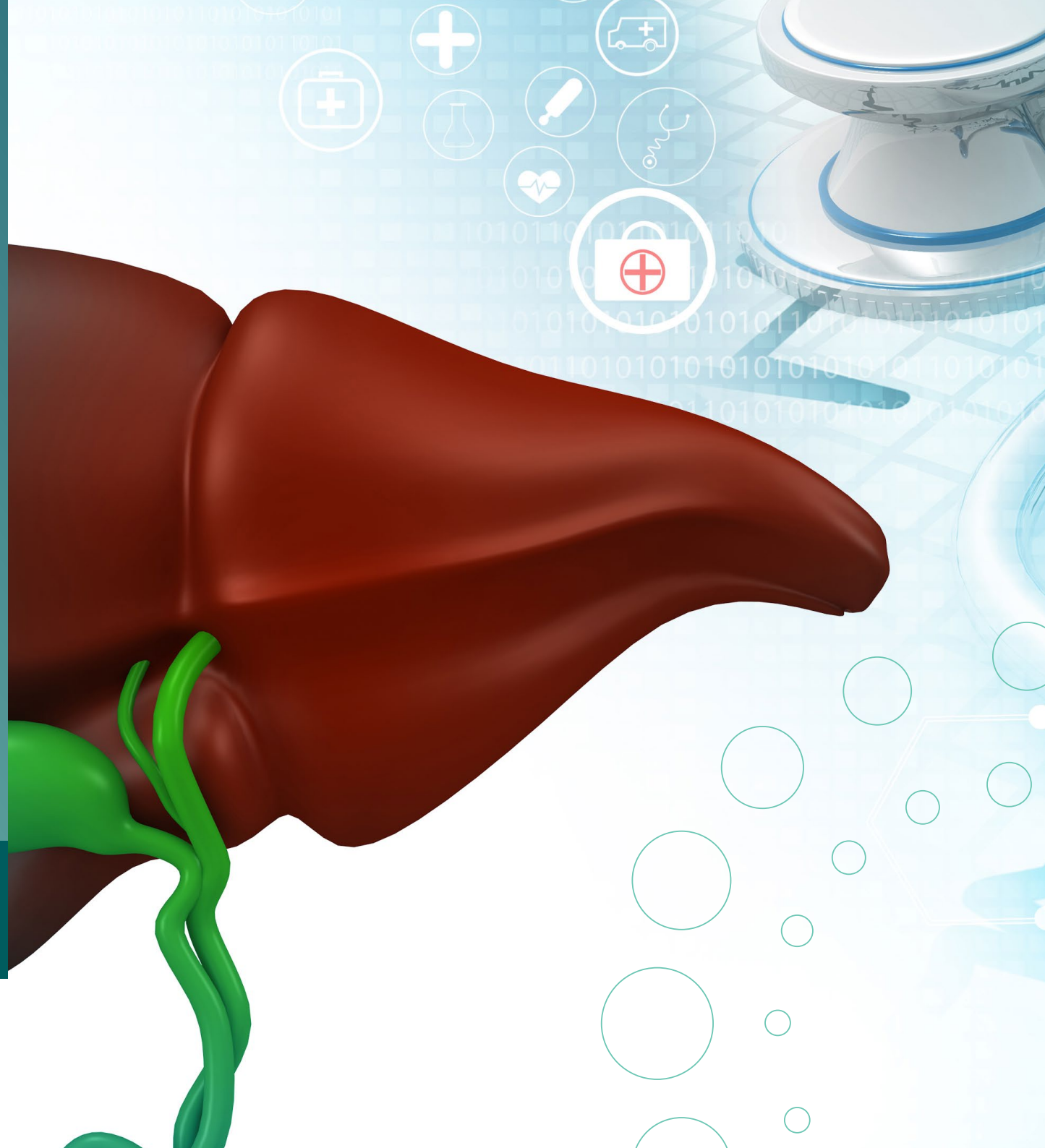
OCTOBER 2024

doi.org/10.33548/SCIENTIA1103



MEDICAL & HEALTH SCIENCES

 Scientia



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Dr Nadine Abi-Jaoudeh and Dr David Imagawa of the University of California Irvine are working with a team of researchers dedicated to improving treatment options and outcomes in hepatocellular carcinoma – a serious form of cancer associated with long-term liver diseases. Their early-stage research offers important hope that in the future, effective drugs such as sorafenib and regorafenib may be utilised in trans-arterial chemoembolisation thanks to their development of a novel platform for drug delivery.

Treating Hepatocellular Carcinoma

Hepatocellular carcinoma (HCC), more commonly known as liver cancer, is the fifth cause of cancer death worldwide. This serious form of cancer is most frequently found in individuals with underlying conditions and its incidence is increasing. As with all cancers, positive outcomes are most likely when the cancer is detected early and treatment commences rapidly.

An approach known as trans-arterial chemoembolisation (TACE) is recommended by several clinical guidelines for the treatment of intermediate HCC (defined as the presence of multiple lesions in the liver but with preserved liver function and absence of cancer-related symptoms). TACE is a minimally invasive procedure involving the delivery of chemotherapy directly to the tumour alongside embolic agents to block the blood supply from the branches of arteries that feed the tumour.

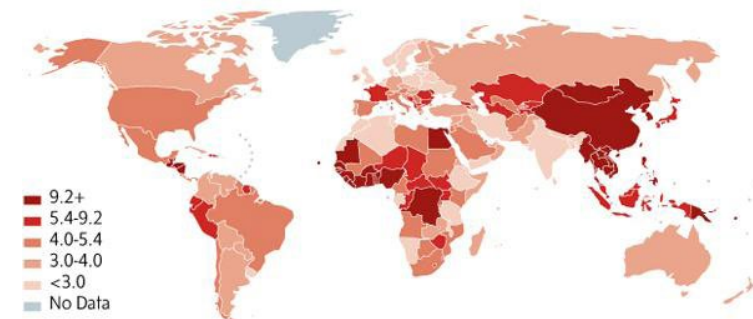
Despite being a recommended first-line approach for intermediate HCC, a standard methodology for TACE has not been established. In other words, the specific treatments that patients may receive can vary widely, with the upshot that outcomes can likewise vary considerably.

Dr Nadine Abi-Jaoudeh, Dr Imagawa of the University of California Irvine, and the dedicated team of researchers at Bruin Biosciences considered the evidence in support of the efficacy of TACE. They noted that several clinical trials have not demonstrated an added benefit by the addition of chemotherapy to the embolic agents in TACE. They were also concerned to note that the drugs used for chemotherapy as part of TACE (such as doxorubicin) are already known to be ineffective in the treatment of HCC.

How Can Outcomes be Improved?

The use of drugs with established efficacy in HCC would likely improve the treatment outcomes of TACE – if they can be safely incorporated into the intervention. Drugs that can inhibit the growth of new blood vessels (known as anti-angiogenic agents) effectively impair tumour growth by preventing the tumour from recruiting and growing blood supply. However, to be used during TACE, drugs need to be water-soluble, positively charged, and able to be loaded onto the tiny beads (microspheres) that block the arteries and slowly release from the microspheres over time into the tissue (elution process). For example, sorafenib and regorafenib are two drugs that can be very useful in the treatment of HCC, but due to their lipophilic nature and neutral charge, they cannot currently be loaded or eluted on the microspheres and are not part of TACE.

LIVER CANCER
Mortality rate per 100,000, both sexes



△ Credit: <https://bruinbio.com>.

A Novel Platform

To overcome this critical challenge to effective HCC treatment, the Bruin Biosciences team developed and patented a platform specifically designed to allow the loading and elution of lipophilic and/or neutral drugs such as sorafenib and regorafenib on microspheres for use in TACE. In 2023, they published a study in which they used the established VX2 rabbit tumour model to test the delivery of the targeted therapies loaded onto the beads.

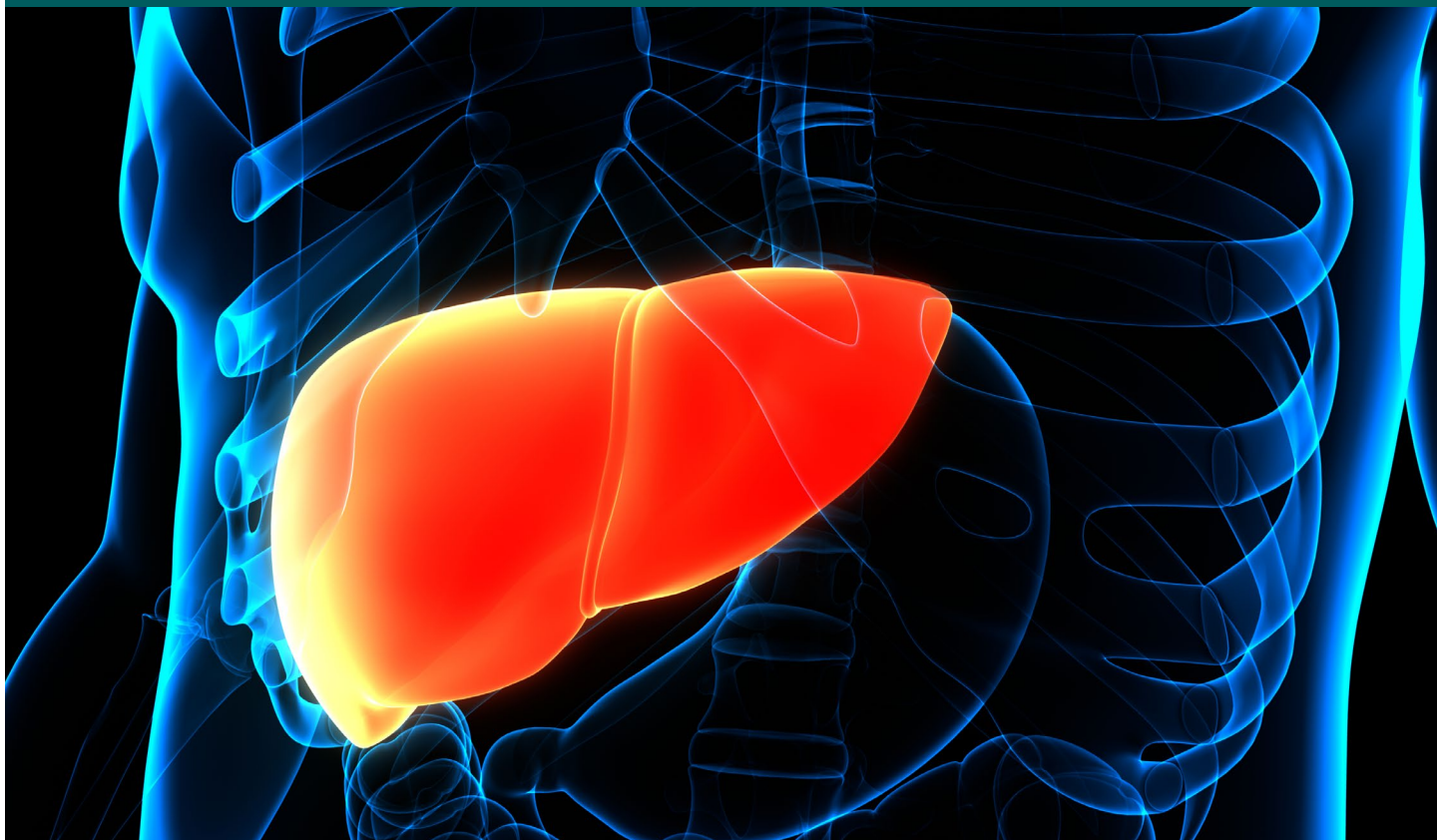
The outcomes were highly promising. First, the researchers confirmed that their idea of delivering lipophilic drugs via microspheres was achievable. Second, analyses confirmed that both sorafenib and regorafenib were effectively delivered directly to the tumours with minimal escape into the blood circulation.

Excitingly, the improvement of TACE through the use of lipophilic drugs may allow for better outcomes for patients with larger or more persistent tumours. Furthermore, the more targeted delivery of drugs such as sorafenib via TACE as opposed to oral or intravenous systemic administration will likely reduce the often significant side effects associated with these treatments. Of course, when side effects are reduced, the risk of dose reductions, interruptions, and poor patient compliance is also reduced.

Future research will need to expand the testing and validation of the platform in further animal and, eventually, human studies before the intervention can be offered as standard of care. Nonetheless, this early-stage work provides important hope that the treatment of HCC can be dramatically improved.



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MEET THE RESEARCHER



Dr Nadine Abi-Jaoudeh

Department of Radiological Sciences, University of California Irvine, Orange, CA, USA

Dr Nadine Abi-Jaoudeh is an American and Canadian board-certified vascular and interventional radiologist at the University of California Irvine. Dr Abi-Jaoudeh completed her medical degree at the University of Montreal, then took up an internship and residency at the University of Laval in Québec, and a fellowship in interventional radiology at the University of Virginia in Charlottesville. She then joined the National Institutes of Health, where she was a principal and associate investigator on several human trials. She also completed multiple animal and translational studies. In 2015, Dr Abi-Jaoudeh joined the University of California Irvine where she has progressed the research program. In 2018, she became the director of clinical research in the Department of Radiology. In late 2020, she became section chief of interventional radiology. She served as the inaugural chair of the diversity and inclusion committee of radiology from 2021–2024. She is principal investigator on multiple phase I, II and III trials as well as pre-clinical studies.

CONTACT

nadine@hs.uci.edu

<https://faculty.uci.edu/profile/?facultyId=6155>

<https://bruinbio.com/>

<https://bruinbio.com/our-team/>

<https://www.linkedin.com/in/nadine-abi-jaoudeh-55681066>



KEY COLLABORATORS

Dr Ben Sadeghi, Department of Radiological Sciences, University of California Irvine, Orange, CA, USA

Dr Hanna Javan, Department of Radiological Sciences, University of California Irvine, Orange, CA, USA

Dr Jim Na, Cullgen, Inc., San Diego, CA, USA

Dr Graham Beaton, Epigen Biosciences, San Diego, CA, USA

Dr Fabio Tucci, Epigen Biosciences, San Diego, CA, USA

Dr Satheesh Ravula, Epigen Biosciences, San Diego, CA, USA

Dr David K Imagawa, Department of Surgery, University of California Irvine, Orange, CA, USA



FUNDING

Funding for this work was provided by Dr David KImagawa, a seed grant from the Department of Radiological Sciences.



FURTHER READING

N Abi-Jaoudeh, *et al.*, Drug-Eluting Embolic Loaded with Tyrosine Kinase Inhibitor Targeted Therapies for Transarterial Chemoembolization in a VX2 Model, *Cancers*, 2023 15(12), 3236. DOI: <https://doi.org/10.3390/cancers15123236>

OUR TEAM



David Imagawa
Chief of the Division of Hepatobiliary and Pancreas Surgery at the University of California, Irvine Medical Center.



Fabio C. Tucci, Ph.D.,
Chief Operating Officer and co-founder



Dr Jim Na
Co-founder and COO of Bruin Biosciences



Satheesh B. Ravula Ph.D.,
Chief Business officer at Epigen Biosciences



Graham Beaton, Ph.D.,
Chief Scientific Officer



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