Dual-Use Concerns in Precise Nanomedicines

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CONDENsE

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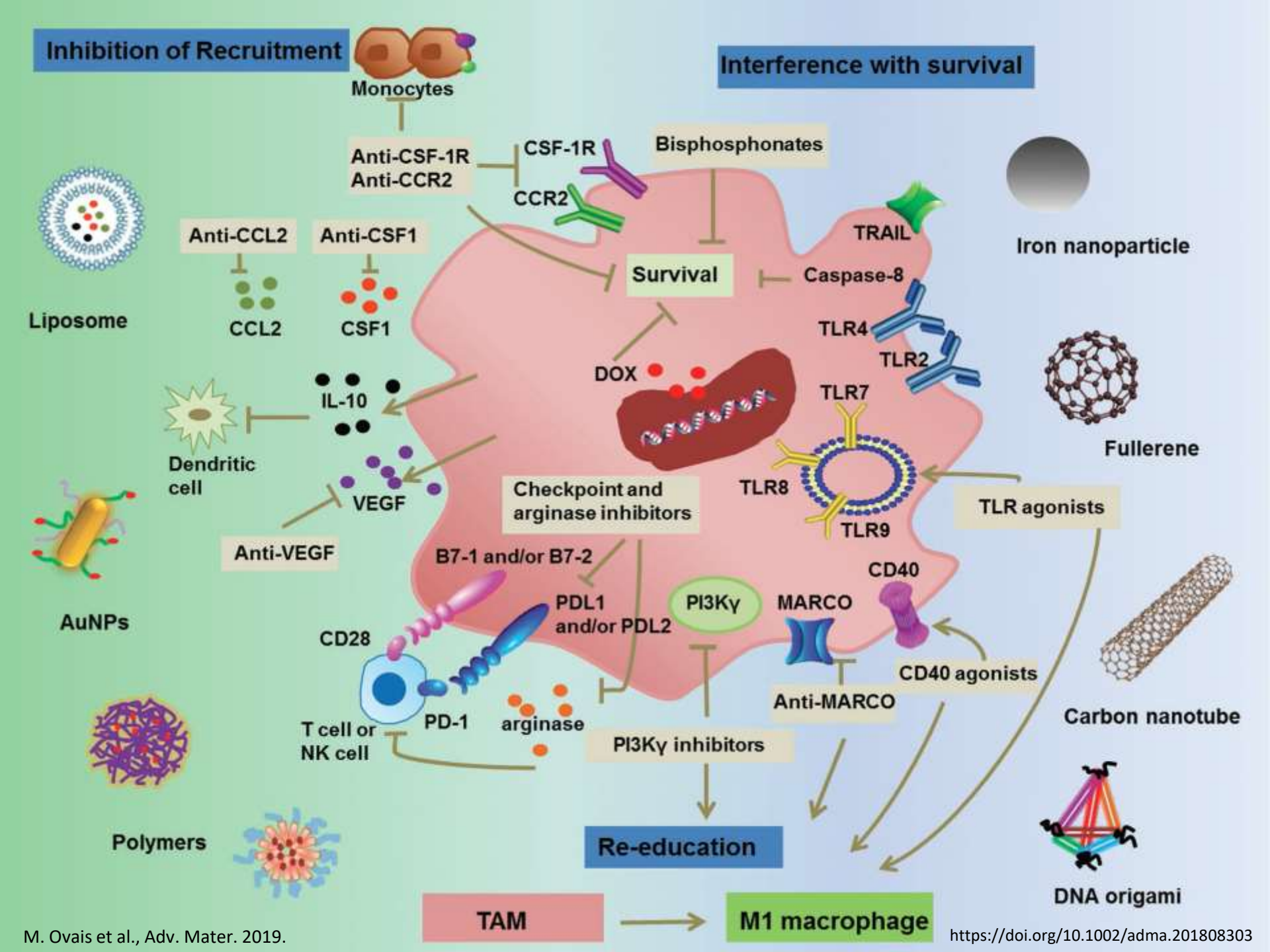

M. Ovais et al., Adv. Mater. 2019.

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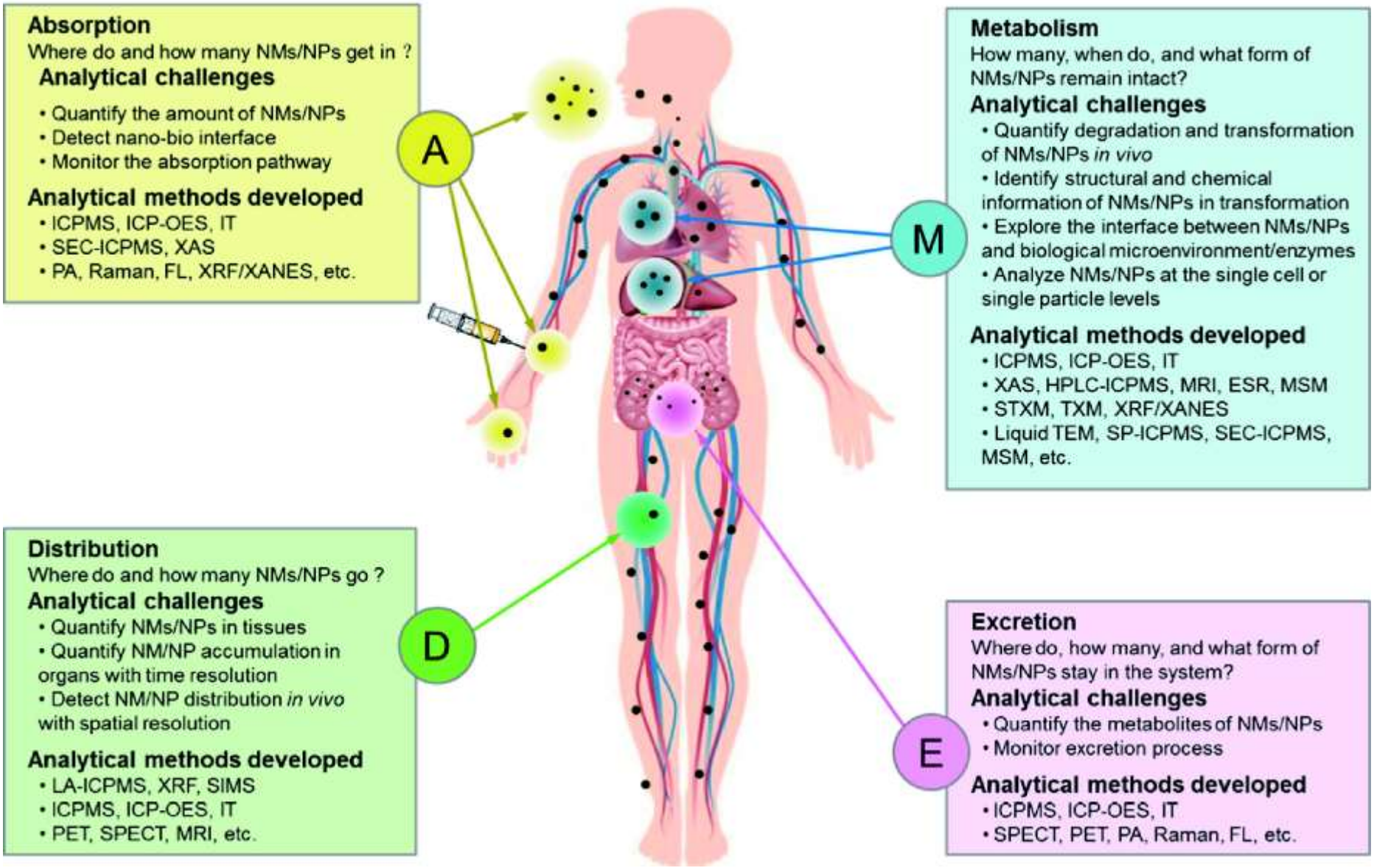

Chen H et al., Sci China Chem, 2018.

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Editorial

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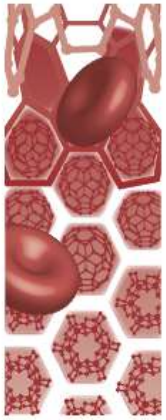

Safety considerations for nanoparticles in tumor treatment

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"many vital biological factors determines the faith and toxicological impact of NPs: NP–protein interaction, blood circulation, interaction with TME, tumor tissue penetration and internalization inside tumor cell. Furthermore, morphology, composition and surface chemistry of NPs are also the key influencers in the aforementioned biological processes"

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Keywords: cancer nanomedicine • nanoparticles trafficking • nanotoxicity

LETTERS

nature biotechnology

A DNA nanorobot functions as a cancer therapeutic in response to a molecular trigger *in vivo*

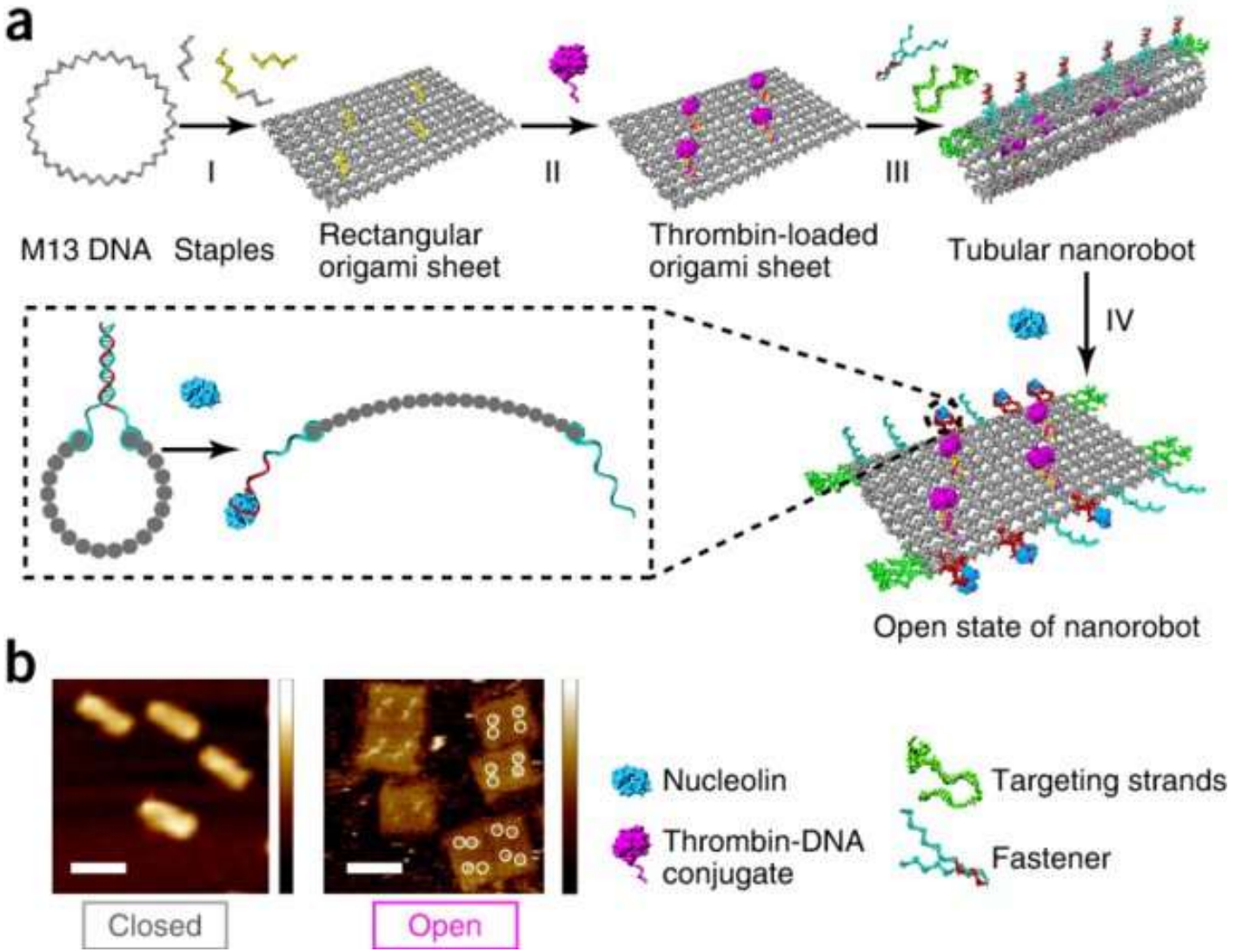
Suping Li[1,2,10], Qiao Jiang[1,10], Shaoli Liu[1,2,10], Yinlong Zhang[1,3,10], Yanhua Tian[1,4], Chen Song[1], Jing Wang[1], Yiguo Zou[1], Gregory J Anderson[5], Jing-Yan Han[6], Yung Chang[7], Yan Liu[7], Chen Zhang[8], Liang Chen[9], Guangbiao Zhou[8], Guangjun Nie[1,2], Hao Yan[7], Baoquan Ding[1,2] & Yuliang Zhao[1,2]

Nanoscale robots have potential as intelligent drug delivery systems that respond to molecular triggers[1–4]. Using DNA origami we constructed an autonomous DNA robot programmed to transport payloads and present them specifically in tumors. Our nanorobot is functionalized on the outside with a DNA aptamer that binds nucleolin, a protein specifically expressed on tumor-associated endothelial cells[5], and the blood coagulation protease thrombin within its inner cavity. The nucleolin-targeting aptamer serves both as a targeting domain and as a molecular trigger for the mechanical opening of the DNA nanorobot. The thrombin inside is thus exposed and activates coagulation at the tumor site. Using tumor-bearing mouse models, we demonstrate that intravenously injected DNA nanorobots deliver thrombin specifically to tumor-associated blood vessels and induce intravascular thrombosis, resulting in tumor necrosis and inhibition of tumor growth. The nanorobot proved safe and immunologically inert in mice and Bama miniature pigs. Our data show that DNA nanorobots represent a promising strategy for precise drug delivery in

thrombus formation in tumor vessels, and carries a decreased risk of resistance development. Moreover, vascular occlusion is a strategy that can be used for many types of cancer, as all solid tumor-feeding vessels are essentially the same[11,12].

The coagulation protease thrombin regulates platelet aggregation by activating platelets and converting circulating fibrinogen to fibrin[14], ultimately leading to obstructive thrombosis. Naked thrombin is short-lived in the circulation and induces coagulation events indiscriminately, and has not been used in cancer treatment. For therapeutic use, it is therefore critical to precisely deliver thrombin solely to tumor sites in a highly controlled manner to minimize its effects in healthy tissues.

DNA origami is a method that enables the rational design and production of DNA nanostructures with controlled size, shape and spatial addressability[15–18], producing functional platforms for biological applications[3,4,6,19–22]. Using DNA origami, we constructed a DNA nanorobotic system to overcome the challenges associated with thrombin delivery to tumors. Our nanorobot protects thrombin until exposure is triggered by the interaction with the tumor vessel marker



Design and characterization of thrombin-functionalized DNA nanorobot

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Acknowledgments

"Nanoscience and Technology is likely to change almost everything—from vaccines to computers to automobile tires to objects not yet imagined—is designed and made"

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