Tissue morphogenesis relies on the autonomy and versatility of individual cells to proliferate and maintain tissue homeostasis. The information content of the genome gives rise to cellular plasticity as a result of the spatial and temporal cues that cells receive from the microenvironment. Physical cues from the microenvironment are translated into biochemical signals; however, environmental or cellular/molecular aberrations can alter mechanosignal transduction and initiate tumorigenesis. Cancer arises as a consequence of genetic mutations that divert cells toward acquiring abnormal phenotypes. Many of the aberrant intracellular signaling pathways that arise in cancer cells as a result of these genetic mutations have been mapped. The role played by the physical and mechanical parameters of tissue and vascular microenvironments in the regulation of tumor initiation, progression, and metastasis has received great attention over the past several years, accelerated by the National Cancer Institute’s formation of the Physical Sciences-Oncology Centers network.

The study of the role of physics in the regulation of cell physiology has a long and storied history. In his master work “On Growth and Form,” D’Arcy Thompson pioneered the thesis that physical parameters and forces regulate biological form and function. In the context of the metastatic process, cancer cells encounter dramatically different physical forces during their separation from the primary tumor mass, entry into the vascular or lymphatic space, circulation within the blood, exit into a new tissue, and colonization of the invaded microenvironment. The recent explosion in physical oncology research is enabled by technological advances such as multiscale computational modeling, microfabrication and nanotechnology, optical imaging and image processing, and tissue/protein engineering, to name a few. It is believed that a key to future breakthroughs in the field of cancer research will be to integrate knowledge across multiple scales, from the molecular to cellular to tissue to whole body and population scales in a seamless way.

This series of review articles, which are published together in this issue of American Journal of Physiology-Cell Physiology, highlights the efforts underway to understand the dynamics of the physical-biochemical drivers of tumorigenesis and cancer metastasis. This theme series was motivated by presentations at the Biomedical Engineering Society-sponsored Experimental Biology 2013 Symposium, entitled the “Physics of Cancer.” The first review in the series is an introductory article by Nicole M. Moore and Larry A. Nagahara, discussing the birth of a new field of study, physical oncology, positioned at the interface of physics/engineering and cancer biology/oncology. The following articles discuss the physical biology of cancer cells during circulation (Kevin G. Phillips, Peter Kuhn, and Owen J. T. McCarty), interaction with blood vessels and their glyocalyx layer (Michael J. Mitchell and Michael R. King), adhesion and extravasation at distant sites (Kimberly M. Stroka and Konstantinos Konstantopoulos), and finally, invasion (François Bordeleau, Turi A. Alcoser, and Cynthia A. Reinhart-King).

We hope that this series of review articles will be provocative and will also encourage readers to, in the words of D’Arcy Thompson, “hic artem remumque repono,” and turn their attention to Mechanics and to Physics. We welcome comments and thoughts regarding this theme series.

ACKNOWLEDGMENTS

O. J. T. McCarty is an American Heart Association Established Investigator (13EIA12630000).

GRANTS

This work was supported by National Institutes of Health National Cancer Institute Grants U54CA143906 and U54CA143876.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS


Address for reprint requests and other correspondence: O.J.T. McCarty, Dept. of Biomedical Engineering, Oregon Health & Science Univ., 3303 SW Bond Ave, Portland, OR 97239 (e-mail: mccartyo@ohsu.edu).