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PREFACE

Human Ductal Carcinoma In Situ: from the Eyes of a Beholder

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"Why study DCIS if we can cure 97% of patients?" Most scientists studying DCIS will encounter this question. To patients that have faced this diagnosis and experienced the harsh and disfiguring consequences of currently-offered therapies, the answer is obvious. DCIS overdiagnosis and overtreatment is well documented in numerous studies, and the public health costs of unnecessary treatment are immense [1–3]. Most importantly, patient survival that stands at ~97% for non-invasive DCIS plummets to 80% or lower when later more advanced stages of breast disease are discovered. Studying DCIS and how to prevent its progression is not a choice, but a necessity. Fortunately, recent findings using advanced technologies point to significant variation at the molecular, epigenetic, cellular and microenvironmental levels that highlight exciting new avenues for investigation.

The reviews in this issue are intended to address the current state of knowledge in DCIS biology, the diagnostic and therapeutic approaches used, and clinical trials aimed at overcoming the issue of DCIS overtreatment and overdiagnosis. Sinha and colleagues focus on the contribution of intratumoral heterogeneity to DCIS progression, and put forward the idea that understanding intratumoral heterogeneity will lead to a better appreciation for the complex biology of DCIS and its evolution.

Nelson et al. review the current state of knowledge regarding how DCIS progression is impacted by the tumor microenvironment including myoepithelial, fibroblast and immune cells. They propose the intriguing idea that factors in the microenvironment surrounding DCIS may serve as future therapeutic targets for preventing its progression, as well as potential biomarkers for risk stratification.

The contribution of epigenetic factors including the impact of DNA methylation, histone modifications, enhancers and non-coding RNAs on DCIS and early stage breast cancer progression are reviewed by DeVaux et al.

Villanueva and colleagues discuss the controversial role of estrogen and progesterone and their cognate receptors in DCIS. They review findings from clinical and observational studies of steroid hormones as breast cancer risk factors and as biomarkers in patient DCIS. Finally, they describe the emerging experimental models of ER/PR positive DCIS.

This issue also includes two reviews dedicated to experimental models of human DCIS including an overview by Brock et al. focused on in vitro models for studying the invasive transitions of DCIS, and a review by Behbod et al. describing in vivo DCIS models.

Doke and colleagues review the current therapeutic approaches for treating DCIS, with a focus on the current clinical management of DCIS and a discussion on screening and detection and the possibility of overdiagnosis. A review of ongoing trials in the United States and Europe aimed at identifying low risk patients who would do well with lesser therapy is discussed by Han et al.

We anticipate that this issue will not only provide the scientific community with up to date information in the field of DCIS, but more importantly, will highlight the unknowns that need to be studied. We further hope that the content will convince researchers and funding agencies that we must continue to study DCIS with the promise that more personalized treatment strategies can be offered to today's increasing number of patients diagnosed with DCIS. It is certain that prevention of the transition of DCIS to invasive breast cancer will improve survival. Research must continue to better understand the pathophysiology of DCIS, design future personalized therapeutic strategies with fewer side effects, and identify biomarkers to create strategies for risk stratification.

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Finally, we dedicate this issue to Drs. Kenneth B. Deome, Daniel Medina, Charles W. Daniel, Robert Cardiff, and their colleagues and trainees who pioneered studies in the field of breast premalignancy. Their work has provided the scientific community with much needed experimental models for research related to the understanding of mechanisms underlying the development and progression of early stage breast cancer.

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