

Book report

The molecular basis of breast cancer prevention and treatment

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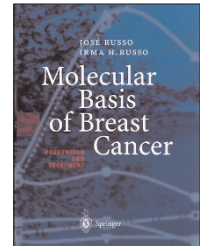
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The incidence of breast cancer is still rising, and the disease remains largely incurable once it becomes malignant. It is the most prevalent cancer in Europe and USA, with 41,000 new cases each year in the UK [1]. Fortunately we are beginning to gain insights into the origins of breast cancer, and now know that many of the key risk factors are related to life-styles associated with the hectic, consumer-based trends of Western cultures. For example, we consume more calories, eat fewer nutritive foods, and do less exercise than our forebears, leading to early menarche, obesity, and ingestion of fewer naturally occurring compounds that quench free radicals and reduce oxidative stress on DNA. Moreover, many women have their first full-term pregnancies when they are older. Paradoxically this knowledge is a reason to be optimistic about the future, because the implication is that breast cancer is a disease that is largely preventable; it is not common in some Far Eastern countries although women from those societies become prone if they migrate to the West. If we can identify how these risk factors impact on breast development and in particular understand the molecular changes within breast epithelium that lead to genomic alterations, then we have a chance to establish preventative strategies to ameliorate the disease.

José and Irma Russos' new book on the *Molecular Basis of Breast Cancer: Prevention and Treatment* tackles the problem by following a logical path of first introducing the disease from the epidemiological point of view, before discussing how the breast develops and becomes altered in cancer, and how we might seek to understand it through both *in vivo* and culture models. The book ends with two chapters on possible modalities for how the disease might be inhibited in the first place. Some of these are very interesting, and I particularly liked the chapters on *Epidemiological considerations*; the first half of the one on *The (human) breast as a developing organ*, where relatively few studies have been published in comparison to the mouse; and the chapter on *Preventive strategies*, which delves into the structure and activities of many naturally-

occurring chemopreventives as well as anti-inflammatories, anti-estrogens, and other compounds that are likely to have properties to protect against the onset of cancer.

The central idea in the book comes from the observation that early pregnancy protects against breast cancer, and posits that a treatment to artificially induce differentiation within mammary epithelial cells could represent a radical new approach to prevent much of the disease. The epidemiological data from which this hypothesis arises is supported strongly by experimental observations that a state of pregnancy induced naturally, or by estrogen/progesterone treatment, or by human chorionic gonadotropin (hCG, a hormone that stimulates ovaries to produce higher levels of estrogen and progesterone) has a dramatic inhibitory effect on carcinogen-induced mammary cancer. The authors argue a case for ectopic administration of hCG as a possible preventative strategy. However, although this might be a neat strategy for eliminating tumours in rats, it is rather premature to consider it as preventative in humans. The likely targets for neoplastic genomic modifications are breast stem cells and we have no idea how hCG might affect the behaviour of these cells. A succession of breast cancer prevention trials began in 1985, and it would have been good to see a discussion of these. There is no mention, for example, of the STAR trial, which is one of the largest breast cancer preventative studies ever, examining the comparative effectiveness of tamoxifen and raloxifene. In a book where 'prevention' of breast cancer features in the title, one might have expected a broad debate on all the existing strategies, exploring the way that they work as well.

There are several other aspects of the book that are also rather problematic. First, with reams of new data in the literature and the resultant emergence of novel concepts, I would expect a long textbook (448 pages) on the basis of breast cancer to include a wide-ranging and in-depth look at its molecular control. We know that cancer is largely due to genomic instability that arises within populations of

(as yet undefined) stem cells, and involves the escape of protective apoptosis and immune surveillance mechanisms, deregulated proliferation, and inappropriate sampling of the environment so that tumour cells ignore normal positional cues and thereby migrate to and survive at distant metastatic sites. However, the contemporary ideas on many key topics, including mechanisms of genomic instability and telomere rescue, apoptosis avoidance, cell cycle regulation in cancer, and malignant spread, are not covered in any degree of depth in this book; indeed, most are hardly mentioned. Currently there are no other individual volumes that consider the basis of breast cancer at the molecular level and so, although this is a lavishly produced and well illustrated text in the typical quality style of Springer-Verlag, these omissions seriously limit its usefulness.

As one progresses through the book, it becomes apparent that most of the chapters evolve from general overviews of each topic into mini-reviews of different aspects of the authors' own work. Most of the chapters include multiple reprints of previously published data, and the authors present their hypotheses based on the conclusions to their own experiments. In the absence of a reasoned discussion of this work in the light of the studies from the many other labs working on breast cancer, the book is rather one-dimensional.

Although preventing breast cancer is an ideal that should always be kept in sight, there are many individuals who contract the disease and therefore need to be treated. There is no doubt that improvements in detection and surgical methods have and will continue to reduce breast cancer mortality. However, there will always be a significant cohort whose disease cannot be cured surgically and for these, their tumours require treatment using biological modalities. This has not proved to be particularly successful and fewer than 5% of those individuals with a recurrent metastatic breast cancer can expect to survive more than 10 years after detection. Many of the current strategies prolong life by a year or so and alleviate symptoms, but what we really need are novel therapies that eliminate primary and secondary tumours with targeted efficiency. The good news is that understanding mechanisms of cancer progression provides new opportunities for designing smart drugs that target specific enzymes. Anastrozole (aromatase), trastuzumab (cErbB2), gefitinib (epidermal growth factor receptor), and celecoxib (cyclooxygenase-2) are just a few examples that already look very promising as novel therapeutics. Most of these, and why they are good drugs, are ignored in this book, so unfortunately a critical aspect of its aim, to look at breast cancer treatment, has been omitted.

This is an exciting time to be involved with research on breast cancer and mammary gland biology, since novel technologies are bringing us more information, and devel-

opments such as new mouse and cell models have encouraged a number of biologists from diverse backgrounds to enter the field. With the excellent prospects for the future of breast cancer research, it would be timely to have a thorough text on the molecular basis of breast cancer, summarizing the situation within a single volume. Unfortunately this new book focuses far too much on the authors' own work in this area and fails to examine much of the contemporary literature. We have good reason to hope that the next two or three decades will see a dramatic reduction in the number of deaths arising from breast cancer, but there is still scope for other authors to bring our current knowledge into focus.

Competing interests

None declared.

Reference

1. **Cancer Research UK** [<http://www.cancerresearchuk.org/>]