20. Tumor formation and malignant invasion: role of basal lamina

D. E. INGBER and J. D. JAMIESON

1. Introduction

Carcinoma is by far the most commonly occurring form of cancer and is a neoplasm of epithelial cell origin. In any neoplasm, local invasion and metastasis are the two most reliable criteria that designate the tumor as malignant. Direct invasion is the first and most crucial step in the malignant process and is defined in carcinomata by local disruption of basal lamina with tumor cell infiltration into the underlying connective tissue space (Figure 1).

Classically, basal lamina has been viewed as a host barrier through which a malignant tumor must gain the ability to invade and its dissolution has been commonly accepted as an end result of the neoplastic disorganization process. Over the past decade, basal lamina has been shown to be a product of epithelial cells [1–3] which serves to stabilize epithelial cell differentiation and orientation during organogenesis [1, 4]. In addition, this structure is most likely an architectural foundation for cell anchorage in vivo and so may play a central role in cell growth regulation. As the early stages of oncogenesis are characterized by a deregulation of cell differentiation, orientation, and proliferation, it is possible that the gradual loss of basal lamina integrity that precedes its complete disruption may be involved in neoplastic disorganization prior to the onset of malignant invasion. Thus, the main goal of this discussion is to present the biology of invasion in perspective of the entire neoplastic process and to hopefully raise some new questions regarding the role of basal lamina in the development of invasive carcinomata.

Neoplasia is commonly viewed at a cellular level as a disease which results from loss of control of cell proliferation and differentiation. Cancer is essentially a disease of 'self', as it results from a deregulation of the finely coordinated symbiotic processes by which independent cells are integrated into tissues, tissues into organs, and organs into a functional living organism. Discussion of the biology of malignant invasion in the past relied heavily upon alterations of such general cellular characteristics as intercellular adhesion, motility, proliferative capacity, and production of lytic products. We believe that examination of the malignant process at a tissue level will serve to more accurately place these isolated cellular qualities in perspective of the biologic mechanism that underlies neoplastic invasion in vivo.
Figure 1. Schematic diagram of the process by which normal epithelial architecture becomes disorganized during the development of invasive carcinomata. The solid line represents the basal lamina beneath the epithelium.

All tissues exhibit characteristic patterns of structural and functional organization which are determined during embryologic development and are normally maintained throughout adult life. Thus, understanding of the principles which underlie morphogenetic organization facilitates analysis of neoplastic disorganization of adult tissue morphology. We will review the biology of normal