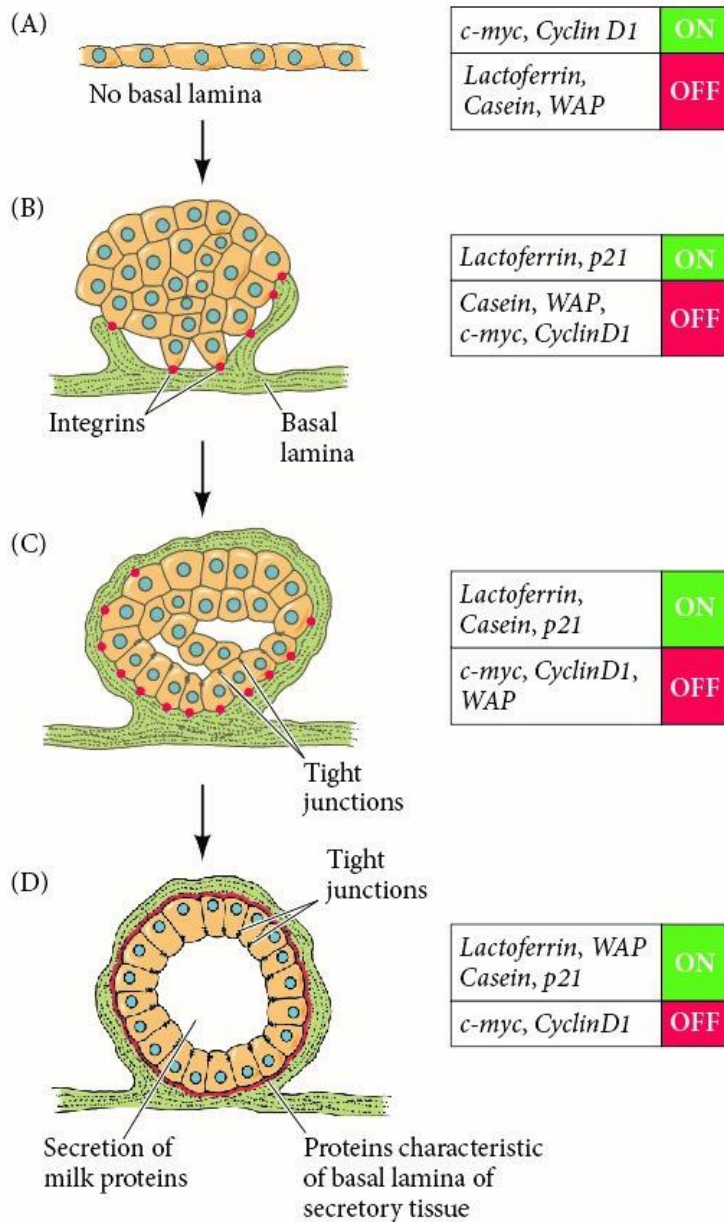


Integrins and Cell Death

The presence of bound integrin prevents the activation of genes that promote apoptosis, or programmed cell death (Montgomery et al. 1994; Frisch and Ruoslahti 1997). For instance, the chondrocytes that produce the cartilage of our vertebrae and limbs can survive and differentiate only if they are surrounded by an extracellular matrix and are joined to that matrix through their integrins (Hirsch et al. 1997). If chondrocytes from the developing chick sternum are incubated with antibodies that block the binding of integrins to the extracellular matrix, they shrivel up and die. Indeed, when focal adhesions linking an epithelial cell to its extracellular matrix are broken, the caspase-dependent apoptosis pathway is activated, and the cell dies. Such “death-on-detachment” is a special type of apoptosis called anoikis, and it appears to be a major weapon against cancer (Frisch and Francis 1994; Chiarugi and Giannoni 2008).

Although the mechanisms by which bound integrins inhibit apoptosis remain controversial, the extracellular matrix is obviously an important source of signals that can be transduced into the nucleus to produce specific gene expression. Some of the genes induced by matrix attachment are being identified. When plated onto tissue culture plastic, mouse mammary gland cells will divide (Figure 1). Indeed, genes for cell division (*c-myc*, *CyclinD1*) are expressed, whereas genes for differentiated products of the mammary gland (casein, lactoferrin, whey acidic protein) are not expressed. If the same cells are plated onto plastic coated with a basal lamina, the cells stop dividing, and the genes of differentiated mammary gland cells are expressed. That happens only after the integrins of the mammary gland cells bind to the laminin of the basal lamina. Then the gene for lactoferrin is expressed, as is the gene for p21, a cell division inhibitor. The *c-myc* and *CyclinD1* genes become silent. Eventually, all the genes for the developmental products of the mammary gland are expressed, and the cell division genes remain turned off. By this time, the mammary gland cells have enveloped themselves in a basal lamina, forming a secretory epithelium reminiscent of the mammary gland tissue. The binding of integrins to laminin is essential for transcription of the *Casein* gene, and the integrins act in concert with prolactin (see Figure 4.21) to activate that gene's expression (Roskelley et al. 1994; Muschler et al. 1999).



After M. Bissell et al. 2003. In *Origination of Organismal Form*, G. B. Müller and S. A. Newman (Eds.). MIT Press: Cambridge

Figure 1 Basal lamina-directed gene expression in mammary gland tissue. (A) Mouse mammary gland tissue divides when placed on tissue culture plastic (no basal lamina). The genes encoding cell division proteins are on, and the genes capable of synthesizing the differentiated products of the mammary gland—lactoferrin, casein, and whey acidic protein (WAP)—are off. (B) When these cells are placed on a basal lamina, the genes for cell division proteins are turned off, while the genes encoding inhibitors of cell division (such as p21) and the gene for lactoferrin are turned on. (C,D) The mammary gland cells wrap the basal lamina around them, forming a secretory epithelium. The genes for casein and WAP are sequentially activated. (After Bissell et al. 2003.)

All the material on this website is protected by copyright. It may not be reproduced in any form without permission from the copyright holder.

© 2023 Oxford University Press |