MAMMARY EPITHELIAL ANTIGENS AS A BREAKTHROUGH IN BREAST CANCER RESEARCH: NOW WHERE TO?

ROBERTO L. CERIANI, M.D., Ph.D.

John Muir Cancer and Aging Research Institute, 2055 North Broadway, Walnut Creek, California, 94596, U.S.A.

INTRODUCTION

The present paper will cover research related to breast epithelial antigens, which have been chosen to be defined as those antigens specific or at least characteristic to breast epithelia, for which antibodies had been generated as a result of the use of breast cells and their products for immunization. However, excluded from this paper will be studies dealing with non-breast-characteristic components such as receptors for hormones and other factors, cytokeratins, and oncogenes. An effort has been made to identify leading research efforts in a field that has increased prodigiously in size and scope in the last ten years, provide some current and pertinent experimental examples and identify areas requiring further research involvement.

The uniqueness of the breast as an organ is demonstrated by its identity as a cutaneous appendage, by its late appearance in the phylogeny, and by the release of its secretory products to the exterior of the organism to nurture yet another being. Thus, the rather recent appearance of this appendage in the class Mammalia, could be the reason for the uniqueness of its products when compared to those of other secretory organs of the body. Phosphorylated proteins such as the caseins, regulatory ones like α-lactalbumin, and the products of the latter's intervention, (the disaccharide lactose) were very early identified as specific products of the breast. These products were of interest to biologists and comparative anatomists, and were used in tissue and organ phenotyping by embryologists, to study the lactational
process by physiologists, and by pathologists for histopathological diagnosis. Pathologists employed these markers to process tissue samples altered by disease, thus these differentiated products had to be also expressed in such samples. With this expectation in mind, we created the first anti-casein polyclonal antibodies that were used in embryological and cell biology studies (1). Unfortunately, it was soon recognized that specific products such as casein or α-lactalbumin (2) followed the same pattern of refractoriness to hormonal stimulation as other specific products have shown for other organs after neoplastic transformation (3). Thus, in most breast tumors these hormonally regulated lactational products, were present at very low levels or absent. To make the need for markers even more pressing, with the advent of cell isolation techniques, most of the embryological, physiological and biochemical studies of breast tissue were carried out in vitro, either on organ or cell cultures. In these cultures composed of cell mixtures where breast epithelial cells were only a fraction of the population, here again, the ability of hormones to stimulate the breast epithelial cells was either diminished or abolished and both casein and α-lactalbumin, were not expressed at high enough levels (4) to serve as markers for cell identification.

Thus, it became evident that in the search for antigens that will identify breast epithelial cells in culture or in transformed tissues, tissue specific antigens with constitutive synthesis were to be the ones of choice. In other organs such as the testicle, the thyroid, or the brain, organ specific antigens had been already described with polyclonal antibodies (5). These antibodies had been rendered specific by many sequential absorptions with cross-reacting tissues. Multiple absorptions, of course, diminish the titer of the antisera and contaminate it with cellular material of the absorbing cell. As a result of this, most of the antisera available, although able to identify the immunizing tissue, had however, a diminished capacity for use in histopathology or in quantitative techniques such as immunoassays. The main problem in the preparation of specific