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Protein expression mapping of normal human breast epithelium

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Luminal, myoepithelial, normal breast, proteomics

Introduction

Breast cancer prognosis and treatment could theoretically be improved by definition of the tumour-specific changes that take place in both gene expression and, by inference, in the protein expression profile, herein termed the proteome. Proteomics describes the unique protein expression profile of a sample by using refined two-dimensional gel analysis to produce a protein expression map (PEM) that can include information on post-translational modification and subcellular localisation. Use of normal breast epithelial cells as a baseline for these studies may be hindered by use of established cell lines that may be unrepresentative of normal breast epithelium, or conversely, by the heterogeneity of cell phenotypes contained in normal breast tissue.

Aims

To apply proteomic analysis to populations of normal human luminal and myoepithelial breast cells obtained from 10 reduction mammoplasty cases, in order to obtain baseline PEMs for the breast.

Comments

The use of proteomics to define cell populations has enormous potential. By describing the protein expression maps of two subpopulations of normal breast epithelial cells, this study provides the basis for assessing the changes that occur during breast tumorigenesis. The advantages of proteomics over gene expression (mRNA) profiling are twofold: gene product analysis may give a more accurate picture of cellular phenotype, and protein modifications such as phosphorylation state can potentially be measured by this method. The difficulties of identifying differentially expressed proteins in two-dimensional gel analysis compared to cDNA microarray techniques may be tempered by the qualitatively superior information generated.

Methods

Normal human luminal and myoepithelial breast cells were separately purified from a set of 10 reduction mammoplasties using a double antibody magnetic affinity cell sorting and Dynabead immunomagnetic technique. Proteins characteristic of each cellular phenotype were identified by mass spectrometry and database searches following separation using two-dimensional gel proteome analysis.

Results

A total of 43,302 proteins were detected across the 10 matched myoepithelial and luminal epithelial samples. A master PEM for each cell phenotype was generated which consisted of a total of 1738 unique proteins. Proteographic analysis revealed that 170 proteins were elevated twofold or more between the two breast cell types, and the identity of 51 of these was confirmed by tandem mass spectrometry. Muscle-specific enzyme isoforms and contractile intermediate filaments (including tropomyosin and smooth muscle (SM22) α protein) were detected in the myoepithelial cells, and a large number of cytokeratin subclasses and isoforms characteristic of luminal cells were detected in this cell type. The identity of a further 134 nondifferentially regulated proteins was also determined in the two breast cell types.

Discussion

The study describes the most extensive studies to date of protein expression in purified luminal and myoepithelial populations of breast epithelial cells. The use of purified populations of breast epithelial cells represents an advance on previous analyses of breast epithelial cell expression profiles which have used inappropriate breast cell lines or mixed epithelial cell populations. The determination of protein as opposed to mRNA expression may be revealing where there is no direct relationship between mRNA levels and corresponding protein levels.

References

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