The Health Specific Sense of Coherence Assessment Signature Profiles:
The Core of Morph2Health™

I. INTRODUCTION AND PURPOSE OF RESEARCH

In this document I will describe a state-of-the-art microarray technology that can be used to establish a mechanism specific, DNA taxonomy of breast tissue biopsies. With such data, *the efficacy of* our multi-dimensional assessment and planning tool, *The Health Specific Sense of Coherence Assessment Signature Profiles (HS-SOCA-SP)*, in creating individualized breast cancer treatment and prevention plans can be tested.

We will collect this data to test and verify our hypotheses that (1) the etiology of breast cancer is multi-dimensional – spiritual, mental, emotional, molecular, and cellular, and (2) *that breast cancer can be individually treated and subsequently prevented* by collecting and evaluating data from all 5 dimensions, rather than gathering data only from the cellular and molecular levels.

With this data, individualized protocols can be structured in partnership with each woman. Our research is designed to answer the following questions: These questions are:

1. **Who is the breast cancer candidate as a whole person**, and what are the interactions of her/his 5 signatures?
    a. spiritual level – Relational Signature
    b. mental level – Mental Signature
    c. emotional level – Emotional Signature
    d. nutritional (molecular) level – Molecular Signature
    e. physical (cellular) level } DNA Taxonomy Signature
2. **What is her/his sense of coherence?**
    a. is her/his life meaningful with high life quality
    b. is her/his life comprehensible – does it make sense – with good emotional health
    c. is her/his life manageable – does s/he have adequate resources
3. **What is her/his mammographic status?**
    a. Benign
    b. Equivocal
    c. Pathological
4. **What is her/his breast tissue DNA taxonomy?**
    a. Benign
    b. Equivocal
    c. Pathological

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Using clusters of gene families, researchers recently identified (1) several patterns of gene expression that could be used to create a molecular taxonomy for breast cancer tumor types. For instance, ER-positive tumors had distinct features compared with ER-negative tumors. They proposed several tumor categories that shared several gene expression patterns.

Patterns of Tumor Gene Expression

1. ER-positive/luminal type, which shared the features of normal luminal epithelial cells in the breast, including expression of the keratins 8 and 18, as well as ER;

2. Basal-like, which expressed cytokeratins 5/6 or 17, resembling the basal epithelial cells of the breast, and tended to lack ER expression;

3. HER-2-positive tumors, which also lacked ER expression;

4. "Normal" tumors that had a molecular expression pattern most closely resembling that of normal breast tissue, including expression of epithelial and adipose genes.

Such classifications are a foreshadowing of the type of new taxonomy that DNA microchip analyses may provide in the future. Of course, as the number of tested genes and the ability to characterize complex patterns continues to escalate, there will be hundreds, if not thousands, of possible classification schemes.

As demonstrated with these breast tumors, traditional pathologic landmarks such as histologic features, as well as ER and HER-2 expression, serve as key mileposts for the new gene profiles. HS-SOCA-SP, serving as a structural scaffold for Morph2Health™, organizes and correlates pathological cell-extracellular matrix interactions - autonomic, neuro-endocrine, pharmacologic, and immunologic – that directly impact histological features (i.e., cytogenetic) found in the breast.

Morph2Health™ organizes these pathological interactions, and analyzes these data in the context of the biopsy derived DNA taxonomy, and the associated molecular and biological functional pathways reflected in the DNA taxonomy.

II. Signature DNA Cell Function Profiles Analyzed Using Morph2Health™

A. Signal Transduction Pathways
B. Cell Cycle Clock Pathways
C. Check-Point Genes
D. Apoptosis Pathways
E. Cell Differentiation Mechanisms
F. Cell Integrity/Contact Inhibition
G. Angiogensis/Metastases Pathways
H. DNA Repair Genes

Signal Transduction Pathways

1. ***Estradiol receptor (ER):*** cytoplasmic proteins that bind estradiol, migrate to the nucleus, and regulate DNA transcription.

2. ***Progeterone receptor (PR):*** specific proteins found in or on cells of progesterone target tissues that specifically combine with progesterone, and the cytosolic progesterone-receptor complex then associates with the nucleic acids to initiate protein synthesis; there are two kinds of progesterone receptors, A and B. Both are induced by estrogen and have short half-lives.

3. ***Epidermal growth factor receptor (EGFR):*** a cell surface receptor involved in regulation of cell growth and differentiation; it is specific for EPIDERMAL GROWTH FACTOR and EGF related peptides, causing activation of its intrinsic tyrosine kinase activity
4. ***HER-2/neu gene:*** the human c-erbB-2 gene, located at 17q21.2, is similar to the EGFR

5. ***Heregulin (HRG):*** growth factor involving erbB-3 and erbB–4 signal transduction, makes growth estrogen independent

Cell Cycle Clock Pathways

6. ***Cyclin D1:*** protein encoded by the bcl-1 gene which plays a critical role in regulating the cell cycle

7. ***Ki-67 (MIB1):*** nuclear antigen found in cycling cells

Apoptosis Pathways

8. ***p16 protein:*** product of the p16 tumor suppressor gene, that acts as cyclin-dependent kinase inhibitor of CDK4.

9. ***bcl-2 gene:*** the human c-bcl-2 gene is located at 18q24, known also as the B-cell leukemia/lymphoma-2 genes, responsible for blocking apoptosis in normal cells,

10. ***p53 gene:*** tumor suppressor genes located on the short arm of human chromosome 17 and coding for the phosphoprotein p53 that promotes apoptosis

Differentiation Mechanisms

11. ***E-cadherin:*** responsible for cell to cell adhesion and contact inhibition

Cell Integrity/Contact Inhibition

12. ***vimentin:*** an intermediate filament protein found in most differentiating cells

Angiogensis/Metastases pathways

13. ***Vascular Endothelial Growth Factor (VEGF):*** these growth factors are soluble mitogens secreted by a variety of organs. The factors are a mixture of two single chain polypeptides which have affinity to heparin. Their molecular weight are organ and species dependent. They have mitogenic and chemotactic effects and can stimulate endothelial cells to grow and synthesize DNA.

Finally, even though there may be hundreds of types of breast cancer, there are, so far, only a handful of distinct treatments. With the advent of our HS-SOCA-SP, therapies that can be tailoring to specific tumors are no longer a distant goal for oncology research. With HS-SOCA-SP, such therapies are a reality, now.

Reference

1.Perou CM, Sorile T, Eisen MB, et al. Molecular portraits of human breast tumours. Nature.
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