Genomic Knowledge Matrix for Nursing Scientists

PREAMBLE

Background

In 2013, the Genomic Nursing Science Blueprint was published. This document was the outcome of a multi-Institute collaboration between the National Human Genome Research Institute (NHGRI), National Cancer Institute (NCI), and National Institute of Nursing Research (NINR) to establish the state of the science and research priorities in genomics for nursing. The overall purpose was to establish a blueprint for genomic nursing science that could be used to focus research efforts to fill identified evidence gaps [1]. To support and accelerate the attainment of these recommendations, NHGRI, NCI, and NINR convened an Advisory Panel of nursing experts in key areas of genomics, education, practice and nursing research to consider opportunities to facilitate genomic nursing research, identify researcher resources and gaps, explore exemplar models to be used as a framework that supports research, and envision a platform for promotion of genomic nursing research and collaboration.

One of the primary gaps identified by the Advisory Panel was the limited knowledge, skills and training of nurse scientists to conduct genomic research. To address this, the Advisory Panel recommended establishing core educational elements for genomic nurse scientists. Drawing from members of the Advisory Panel, a Genomic Nursing Science Education Workgroup was established (Appendix A). The following document is the result of this Workgroup, namely, to inform existing nursing scientists and academic faculty training nurse scientists seeking to expand their research into genomics, and to develop strategies to promote genomic nursing science. These efforts are all aimed at achieving the Genomic Nursing Science Blueprint [1] research recommendations more quickly, efficiently, effectively, and collaboratively.

GENOMIC KNOWLEDGE MATRIX

Development Methods

There were 4 phases undertaken to create the Genomic Knowledge Matrix.

Phase 1: The **Genomic Nursing Science Education Workgroup** completed a review of the evidence and elected to focus this document on the genomic sciences of molecular biology, systems physiology, cell biology, and microbiology. Additionally, the critical components of performing genomic sciences including the technologies unique to genomics, and the supporting analytic approaches and bioinformatics were identified. Key knowledge elements were then developed for each component of the matrix.

Phase 2: **Advisory Panel Reviews** were conducted by other workgroups established from the recommendations made by the initial Advisory Panel and revisions were made to the Genomic Knowledge Matrix based on that input.

Phase 3: **Targeted Public Comment** solicited input from nursing researchers who wished to respond to the Panel's report outlining their assessment and recommendations for the Genomic Knowledge Matrix. Announcements were distributed to organizations with expertise in genomics and nursing education including AACN, NLN, and CANS. The comments were reviewed and integrated by the workgroups as deemed relevant.

Phase 4: **Endorsement** of the Genomic Knowledge Matrix was solicited from Universities and key nursing organizations. Endorsement indicated that they agreed with the content and would support and promote use of the document content in their own environment.

The Genomic Knowledge Matrix is expected to change over time as the science continues to develop. The Matrix is locked until an application for modification is received by the Workgroup which will review the content and approve or disapprove modifications.

Framework

All nursing practice fundamentally is conceptualized within a scope that includes assessment, diagnosis and treatment of client symptoms. Understanding the science that underpins the client clinical presentation is augmented by practical experience and acquired level of education. Nurses progress from novice with a focus on clinical presentation to genomic scientist in search of the molecular "omic" basis of clinical symptoms or disease mechanisms in efforts to translate bench findings to practice and improve client outcomes. The genomic nurse scientist starts from a clinical paradigm (e.g., problem or outcome) and shifts the focus of inquiry then to the laboratory to investigate the molecular contributors of the area of inquiry. These bench findings create a body of knowledge that can be translated back to practice.

This knowledge matrix builds on the existing competencies in genetics and genomics for nurses [2, 3]. In contrast to competencies that are prescriptive and define measureable outcomes [3], this document is intended as a guide that identifies key knowledge elements necessary for new and existing nursing scientists as well as faculty to increase capacity to integrate genomics into research.

The Genomic Nursing Science Education Workgroup recognizes that omic nursing science varies widely based on the individual investigator, the nature of the research, and the role a scientist plays on the research team. As such, the Genomic Knowledge Matrix occurs on a knowledge continuum developed from Blooms Taxonomy and Webb's Depth of Knowledge [4, 5]. The four knowledge levels include Basic, Intermediate, Proficient, and Applied. Table 1 below summarizes the knowledge continuum.

Table 1:

GENOMIC KNOWLEDGE CONTINUUM				
KNOWLEDGE LEVEL	**Basic** *Remembering and understanding/ Recall and reproduction*	**Intermediate** *Applying/Skills and concepts*	**Proficient** *Analyzing/ Strategic thinking*	**Applied** *Evaluating and Creating/ Extended thinking*
KNOWLEDGE	At this level the individual has mastery of basic concepts and is able to outline the primary points and/or perform simple procedures if appropriate.	At this level the individual is well versed in the topic and able to explain the 'how' and/or 'why' and apply that information in to a different case scenario or context. At this level they are able to perform routine bench procedures or commonly used statistical analyses (i.e. regression, multifactorial analysis)	At this level the individual is highly conversant with the topic and able to develop, implement and execute a research protocol involving an omics approach	At this level the individual is completely immersed in the content area and is able to apply complex reasoning, development and application to research projects utilizing one or more omics approaches.
ROLE ON THE PROJECT	Member of the research team	Co-investigator or multi Principal Investigator – clinical lead on grants where the omics approach is conducted in another collaborators lab	Principal Investigator with co-investigators with strength in bench science – at this level the individual is conversant with the bench procedures	Principal Investigator – leads and manages their own lab and conducts (or directs the conduct of) all necessary scientific bench methodology and procedures

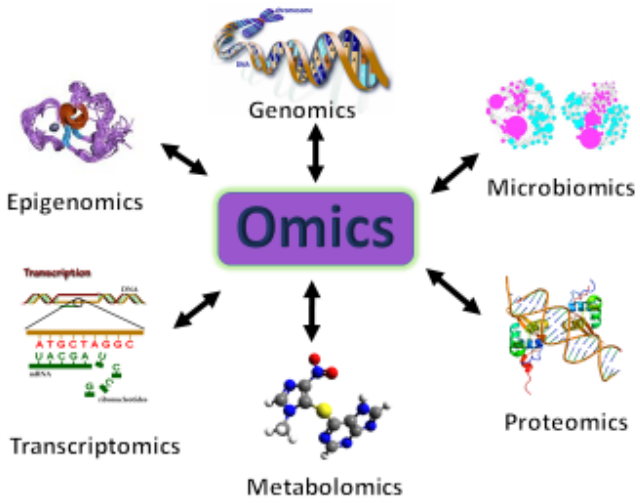
DEFINITIONS:

Genomics: Study of all of the genes in the human genome together, including their interaction with each other, the environment, and the influence of other psychosocial and cultural factors [2].

Omics: Encompasses genomics, transcriptomics, proteomics, epigenomics, microbiomics, and metabolomics [6].

Multi-Omics: Overlap and interaction between all omic sciences (i.e. microbiome, metabolomics, proteomics, epigenomics). See Figure #1.

Figure #1: Multi-Omics



MOLECULAR BIOLOGY

Definition: Knowledge and applied understanding of the formation and function of macromolecules

Key knowledge elements:

1. Genomics
    a. Genome structure/gene structure
    b. Genome variation (e.g. molecular evolution, mutations)
    c. Gene expression and epigenetics

2. Transcriptomics
    a. Transcription and transcription regulation (e.g. polyA sites and miRNA)
    b. RNA variants, mutations, base modification
    c. Trans-activation-response and open reading frame

3. Proteomics
    a. Translation
    b. Structure and function of peptides and implication of genetic variation
    c. Post-translational modifications
    d. Protein-protein interaction
    e. Polysome-associated mRNAs

4. mtDNA
    a. structure/function
    b. variants

5. Metabolomics
    a. Metabolic byproducts
        i. lipidomics
    b. Signaling molecules and hormones

Systems Physiology

Definition: Systems physiology is integrated with systems biology to provide a functionally in depth insights into the system as a whole by combining experimental, computational, and theoretical studies to advance understanding of humans and other living creatures.

Key knowledge elements:

1. Cardiovascular
2. Renal
3. Lymphatic
4. Endocrine
5. Musculoskeletal
6. Reproductive
7. Pulmonary

8. Immunology
9. Neurology
10. Nervous
11. Digestive
12. Integumentary

Cell Biology

Definition: Knowledge of cell formation, structure, components and function

Key knowledge elements:

1. Tissue organization
2. Cell structure
3. Organelles
4. Metabolism and transport
    a. Protein, lipid and carbohydrate metabolism (i.e. Kreb cycle, mitochondria)
5. Cell communication
    a. Cell excitability (ion channels, action potentials)
    b. Endocrine, paracrine, autocrine signaling
6. Growth, maintenance, repair (conception, development, aging)
    a. Mitosis and meiosis (Chromosome structure and function)
    b. Stem cells and differentiation
7. Immune cell function

Microbiology

Definition: Knowledge and understanding of structure, function and interaction between microbes living in an on the human body (collectively known as the microbiome). Microbiology is the study of microscopic organisms such as bacteria, virus, archaea, fungi, and protozoa [7].

Key knowledge elements:

1. The Human Microbiome (Microbiology in the post-genomic era)
2. Forms of microorganisms
    a. Bacteria
    b. Archaea
    c. Eukaryota (including animals, fungi, plants)
    d. Virus are not organisms in the same sense but are considerable biological importance.
3. Bacterial Taxonomy (rank-based classification, of bacteria.)
    a. Kingdom
    b. phylum
    c. class
    d. order
    e. family
    f. genus
    g. species

4. Composition, diversity, complexity - at different locations in and on the human
    a. Skin
    b. nasal passages
    c. oral cavity
    d. Gastro-intestinal tract
    e. Urogenital tract
    f. Body fluids (i.e. blood, breast milk, amniotic fluid)
5. Function
    a. Factors that influence (i.e. antibiotics)
    b. Immune system (Adaptive, Innate, Antigen-antibody)
    c. Novel diagnostics
    d. Drug targets
6. Microbes and disease (pathogen and commensal/indigenous microbes)
    a. Routes of transmission
7. Identification methods
    a. Phenotypic analyses
    b. Genetic analyses
        i. DNA-DNA hybridization
        ii. DNA profiling
        iii. Sequence
8. Phylogenetic analyses (HMP developed)
    a. 16S-based phylogeny
    b. Whole-genome sequence based analysis
9. Interaction/ inter-relationships

ANALYTIC APPROACHES AND BIOINFORMATICS (TRANSLATIONAL BIOINFORMATICS)

Definition:
Translational Bioinformatics is defined by the AMIA as "*the development of storage, analytic, and interpretive methods to optimize the transformation of increasingly voluminous biomedical data, and genomic data, into proactive, predictive, preventive, and participatory health"*[8].

Key knowledge elements:

1. Big Data Analytics Potential
    a. Delivery of higher quality of care, i.e., Evidence-based medicine
    b. Lower costs
    c. Save lives

2. Types of Health-related Data
    a. Clinical
    b. Behavioral
    c. Administrative/Operational
    d. Financial

3. Why Genomics and Big Data?

a. Increased amounts of genomic and other types of data
b. Improved analytic tools
c. Increasingly rapid development of Big Data technology
d. Need to personalize health care

4. Sequencing Methods
   a. Sequencing platform, interpretation, and reporting standards
   b. Goal to identify genetic variants that have known impacts on health and disease
   c. Multiple variant results in a single gene, in multiple genes in a single disease and multiple diseases at the same time (e.g. gene panels)
   d. Multiple findings are possible including incidental findings
   e. Sequencing results can have variable clinical relevance to patients' and provider's decision making and patients' outcomes.

5. Genomic Data Processing: Pathway Analysis & The Reconstruction of Networks
   a. Functional effects of genes differentially expressed are analyzed
   b. Reconstruction of networks from signals measured using high-throughput techniques- analyzed to reconstruct underlying regulatory physiological networks
      i. Pathway analysis toolkits-Onto-Express
         Go Miner, ClueGo, GSEA, Pathway-Express
   c. Reconstruction of metabolic networks toolkit
      i. Recon 2
   d. Reconstruction of gene regulatory networks methods
      i. Boolean methods
      ii. ODE models

6. Genomics Study Designs
   a. Twin-based epidemiological studies
      i. Used to estimate disease heritability
   b. Linkage studies-
      i. Used to find disease-associated loci
   c. Genome-Wide Association Studies (GWAS)
      i. Used for identification of a large number of disease-associated genomic loci
      ii. Group-Based Association Tests
         (1) GWAS analysis evaluates each SNP individually with univariate statistic.
         (2) GWAS meta-analysis methods also used.
         (3) Genomic functional annotation is required for prioritizing variants and interpreting results in association studies (statistical tools available)
   d. Next-Generation Sequencing (NGS)
      i. Used to identify not only single nucleotide variants (SNVs) but also SVs
      ii. Targeted Sequencing and Whole-Genome Sequencing study design

7. Limitations to Genomics Study Design
   a. Difficulty in interpreting GWAS results,
   b. Missing heritability or large gap between proportion of variance

8. Limitations to Data-Oriented Science
    a. Sampling Bias
        i. individuals being analyzed are not representative of the broader population
    b. Completeness
        i. risk that the most important items have not been measured and/or analyzed
    c. Repeatability
        i. reproducibility is critical but difficult without controls
    d. Constraints
        i. much is not known about the data

9. Innovation First Steps-Build Prospective Analytical Models: Team member requirements
    a. Subject matter expertise
    b. Advanced analytical expertise
    c. Data expertise
    d. Project management experience with software development practices

References

1. Genomic Nursing State of the Science Advisory Panel, C., K.A., Jenkins, J., Bakos, A.D., Cashion, A.K., Donaldson, N., Feero, W.G., Feetham, S., Grady, P.A., Hinshaw, A.S., Knebel, A.R., Robinson, N., Ropka, M.E., Seibert, D., Stevens, K.R., Tully, L.A., Webb, J.A., *A Blueprint for Genomic Nursing Science.* Journal of Nursing Scholarship, 2013. **45**(1): p. 96-104.
2. Consensus Panel on Genetic/Genomic Nursing Competencies, *Essentials of Genetic and Genomic Nursing: Competencies, Curricula Guidelines, and Outcome Indicators, 2nd Edition*. 2nd ed. 2009, Silver Spring, MD: American Nurses Association.
3. Greco, K.E., Tinley, S., Seibert, D. *Essential genetic and genomic competencies for nurses with graduate degrees*. 2012 [cited 2012 5/22/2012]; Available from: http://www.nursingworld.org/MainMenuCategories/EthicsStandards/Genetics-1/Essential-Genetic-and-Genomic-Competencies-for-Nurses-With-Graduate-Degrees.pdf.
4. Anderson, L.W., Krathwohl, D. R., Bloom, B. S. , *A taxonomy for learning, teaching, and assessing: A revision of Bloom's taxonomy of educational objectives*. 2001, Boston, MA: Allyn and Bacon.
5. Webb, N., *Research Monograph Number 6: Criteria for alignment of expectations and assessments on mathematics and science education*. 1997, CCSSO: Washington, DC.
6. Conley, Y.P., et al., *Educating future nursing scientists: Recommendations for integrating omics content in PhD programs.* Nurs Outlook, 2015. **63**(4): p. 417-27.
7. Nature. *Microbiology*. 2016 [cited 2016 3/24/2016]; Available from: http://www.nature.com/subjects/microbiology.
8. Tenenbaum, J.D., *Translational Bioinformatics: Past, Present, and Future.* Genomics Proteomics Bioinformatics, 2016. **14**(1): p. 31-41.