Incorporating Omics Into the Nursing Process: Assessment, Planning, and Implementation

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Exemplar: Metabolomics, Chronic Stress and Birth Outcomes

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Disclosure and Acknowledgement

This presentation was funded through grants from the National Institute of Health

- Biobehavioral Determinants of the Microbiome, Chronic Stress, and Preterm Birth in Black Women (R01NR014800/ 3R01NR014800)
- Maternal Stress and the Gut-Brain Axis in African American Infants (R01MD009747)
- The Impact of Intrauterine and Early Childhood Environments on Neurocognitive and Metabolic Development in African American Youth: Focus on the Gut-Brain Axis (UG30D023318)
- Center for Children’s Health, the Environment, the Microbiome, and Metabolomics (P50ES026071)
Metabolomics

- **An emerging technology**
  - Liquid chromatography + High-resolution mass spectrometry (LC-MS)
  - Capable of detecting >20,000 ions (via mass, chemical size, polarity, retention time and ion intensity)
  - Then uses specialized computer software and computational algorithms for data processing and metabolic modeling.
  - Identifies small molecules that indicate physiological and biochemical activities
Revolutionary analytical capabilities

- Identifies metabolites and metabolic pathways that differentiate between individuals who do and don’t develop disease.

- Developing a score to rank metabolite features.

- Using flexible linear modeling techniques, compares groups and differentiates metabolites between groups with/without disease.
**Workflow of LC-MS metabolomics experiments**

- The biological question dictates what samples to use.
- Samples undergo chromatographic separation.
- And then are analyzed in a mass spectrometer.
- Puts out quantitative information and peaks – can identify the metabolite.
- Statistical analyses identify the metabolic pathways and networks that led to that molecule.
The steps to translation:

• Identify altered community phenotypes (e.g., diseases, risk factors, prognoses)
• Then, find out what metabolites are involved
• Then test the metabolites in animal studies and see if they do actually lead to the phenotype
• If so, then test to block in humans with the disease
An Example: Acetaminophen Overdose

Acetaminophen overdose is the leading cause of liver failure in the U.S.

Nearly half of overdoses are unintentional.

Check the medication's label and do not exceed 4,000 mg of acetaminophen daily, or less if you drink alcohol.

DID YOU KNOW?

Acetaminophen can be:
- Unintentionally ingested by young children
- Taken in an intentional overdose by adolescents and adults
- Inappropriately dosed in all ages

Acetaminophen poisoning
Prof Dr Saduf Ali
Manila Hospital

Type of overdose

<table>
<thead>
<tr>
<th>Acute</th>
<th>Chronic</th>
</tr>
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<tbody>
<tr>
<td>A toxic dose ingested in &lt; 8 hours</td>
<td>A toxic dose ingested in &gt; 8 hours</td>
</tr>
</tbody>
</table>

*Rumack nomogram is useful!*

*Rumack nomogram not used.*

Toxic dose = 150 mg/Kg


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Metabolomics - The science of the small molecules

Compound Classes:
- sugars
- amino acids
- steroids
- fatty acids
- lipids
- phospholipids
- organic acids

Molecules under investigation

3D model of a molecule with surface plot
Metabolomics optimizes the other-Omics

- Genomics
- Epigenomics
- Microbiomics
- Proteomics
Non-invasive

- Plasma
- Serum
- Urine
- Bronchoalveolar lavage
Clinical Examples

• Real time monitoring of patients:
  – Lung transplant patients with detectible bile acids metabolites
    - increased risk of negative outcomes\(^1\)
  – Identification of predictor metabolites of preeclampsia vs
    controls: > alanine, hydroxyhexanoylcarnitine, phenylalanine, &
    glutamate in preeclamptics\(^2\)
  – Citric acid pathway metabolites deranged in myocardial
    ischemia\(^3,4\)

\(^1\)Neujahr et al, 2014;
\(^2\)Odibo, 2011;
\(^3\)Gerszten & Wang, 2008;
\(^4\)Sabatine et al., 2005
If we could identify the metabolites or metabolic pathways associated with chronic stress during pregnancy AND are likewise associated with preterm birth...

• We could watch for those metabolites and pathways early on

• We could *potentially* intervene to block those pathways occurring

• We could target those pathways when they are present
Metabolic Pathways* Associated with Chronic Stress (P<0.05)

Metabolite features from untargeted LC-MS metabolomics were ranked by their Pearson correlation with DexIC_{50} levels (N=274). The ranked features were input to mummichog for pathway and network analysis. Pathways with p<0.05 and more than 3 significant metabolites are shown here.

(*Adjusted for age, BMI, parity)
Metabolic Pathways Associated with Preterm Birth (preliminary data) (P<0.05)

Metabolite features from untargeted LC-MS metabolomics between women delivering spontaneous preterm (n=41) and full term (n=169) were compared using Mann Whitney U test. The ranked list of features were input to mummichog for pathway and network analysis (Li et al, 2013). Pathways with p < 0.05 and >3 significant metabolites are shown here.
The future of symptom science?

Precision Prevention, Prediction, Identification & Treatment

Omics
Thank you!

Questions?
1. Acetaminophen is converted to NAPQI by CYP 2E1. NAPQI is hepatotoxic.
2. Alcohol upregulates CYP 2E1 and increases toxic NAPQI production.
3. TB medications also upregulate CYP 2E1 and increase toxic NAPQI production.
4. Malnutrition depletes glucuronide, sulfate and glutathione stores. Impaired ability to form non-toxic metabolites.